Plants that heal wounds. A review

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Summary

Plants have traditionally been used as a source of medicine in India by indigenous people of different ethnic groups inhabiting various terrains for the control of various ailments afflicting human and their domestic animals. Recently, focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional systems. More than 13,000 plants have been studied during last 5 years. Our review aims to compile data generated through the research activity using modern scientific approaches and innovative scientific tools in last few years. This article represent wound healing activity of various plants found and used traditionally. We have made an attempt to give an insight into different plants of potential wound healing properties which could be beneficial in therapeutic practice.

Key words: wound healing, phytoconstituents, pharmacological actions

INTRODUCTION

The development of traditional medicinal systems incorporating plants as means of therapy can be traced back to the Middle Paleolithic age some 60,000 years ago as found from fossil studies [1]. Recently, developed countries have

turned totraditional medicinal systems that involve the use of herbal drugs and remedies [2] and according to the World Health Organization (WHO), almost 65% of the world's population has incorporated the value of plants as a methodology of medicinal agents into their primary modality of health care [3]. It is often noted that 25% of all drugs prescribed today come from plants [4, 5]. This estimate suggests that plant-derived drugs make up a significant segment of natural product—based pharmaceuticals. Over the past 20 years, our knowledge of the wound healing process has increased dramatically. Along with this knowledge the development of new, exciting technologies that accelerate normal wound healing and counter the pathophysiologic processes that lead to chronic wound formation has come. From growth factors to bioengineered skin substitutes, the future of wound healing holds great promise.

HEALING OF WOUNDS

Wound is defined as a loss or breaking of cellular and anatomic or functional continuity of living tissues [6]. Healing of wound is a biological process that is initiated by trauma and often terminated by scar formation [7]. The process of wound healing occurs in different phases such as coagulation, epithelization, granulation, collegenation and tissue remodeling [8].

Collagen, the major component which strengthens and supports extracellular tissue, contains substantial amounts of hydroxyproline, which has been used as a biochemical marker for tissue collagen [9]. Wound contraction occurs as a myofibroblasts contract. Platelets release growth factors and other cytokines [10].

MECHANISM OF WOUND HEALING

Wound healing is the physiological response to the tissue injury that results in the replacement of destroyed tissue by living tissue and thus restoration of tissue integrity. The mechanism of wound repair occurs by four basic processes such as inflammation, wound contraction, epithelialization and granulation tissue formation.

Inflammation starts immediately after the disruption of tissue integrity. The platelets became adherent with clotting factors and form haemostatic plug to stop bleeding from the vessels. The prostaglandins (PGE₁ and PGE₂) are released in the inflammation area and seem to be the final mediators of acute inflammation. They also can play a haemostatic role for white cells and fibroblasts. The active motile white cells migrate into the wound and start engulfing cellular debris. At the initial stages wound contraction begin slowly but became rapid on the day 3 or 4. The myofibroblasts present in the margin of the wound appear to constitute the machinery for the wound contraction. These are responsible for overlaying debris. The epithelialization of the wound occurs mainly by proliferation and migration of

the marginal basal cells lying close to the wound margin. The hematoma within the wound may be replaced by granulation tissue which consists of new capillaries and fibroblasts. The fibroblasts are responsible for the production of the mucopolysacharide ground substance. The lymphatics develop new nerve fibers and also acts in the formation of scar tissue in which collagen turn over increases [11].

PHYTOCONSTITUENTS

Various plants of wound healing property and also contain flavonoids as active constituents have been found. Tannins promote the wound healing through several cellular mechanisms, chelating of the free radicals and reactive species of oxygen, promoting contraction of the wound and increasing the formation of capillary vessels and fibroblasts [12, 13]. The process of wound healing is promoted by several natural products [14], plant products composed of active principles like triterpenes, alkaloids, flavonoids [15] and biomolecules [16].

MEDICINAL PLANTS

Plants or chemical entities derived from plants used in the treatment and management of wounds need to be identified and formulated. For this case, a number of herbal products are being investigated at present. Various herbal products have been used in the management and treatment of wounds for years.

Alternanthera sessilis (L.) R.Br. ex DC. (Amaranthaceae)

The plant consists of chemical constituents like α - and β -spinasterols, lupeal isolated from roots. Apart from the above, plant also contains β - sitosterol (fig. 1), stigmasterol (fig. 2) etc. The leaves are used in eye diseases, in cuts and wounds, antidote to snake bite and scorpion sting, in skin diseases [17].

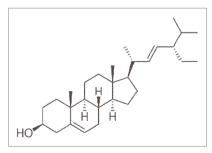


Figure 1 Stigmasterol

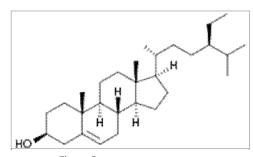


Figure 2 β- sitosterol

kerba polo**ni**ca

Arnebia densiflora (Nordm.) Ledeb. (Boraginaceae)

The roots of some genera of the Boraginaceae family are rich in naphthoquinones. Shikonin (fig. 3) (*R*-configuration) and alkannin (*S*-configuration) found in those families are enantiomers and their derivatives are potent pharmaceutical substances with a wide spectrum of biological properties, namely wound healing etc. [18].

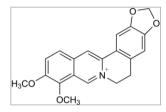


Figure 3 Shikonin

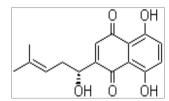


Figure 4 Berberine

Berberis lyceum Royle (Berberidaceae)

The root of *Berberis lyceum* contains flavonoids, alkaloids including berberine (fig. 4), tannins, saponins and triterpenoids. Triterpenoids and saponins are thought to promote the wound healing process due to their antioxidant and antimicrobial activities. Their astringent and antimicrobial properties also contribute to wound contraction and increase the rate of epithelialization [19].

Carallia brachiata Merrill (Rhizophoracea)

The bark is mentioned to be useful in the treatment of itching, cuts and wounds, oral ulcers, inflammation of throat and stomatitis. From the bark, new proanthocyanidins (fig. 5) were reported to possess free radical scavenging activity. A new megastigmane diglycoside (3-hydroxy-5, 6-epoxy- β -ionol-3-O- β -apiofuranosyl (1 \rightarrow 6)- β -glucopyranoside), two megastigmanes, condensed tannins, flavonoids and glyceroglycolipids were isolated from the leaves. The presence of alkaloid hygroline in the leaves was also reported [20].

Centella asiatica (L.) Urban (Mackinlayaceae)

The titrated extract of *C. asiatica* contains 3 principal ingredients – Asiaticoside (fig. 6), asiatic acid, and madecassic acid – all known to be clinically effective in

the treatment of systemic scleroderma, abnormal scar formation and keloids. This extract significantly shortens the wound-healing time, acting more specifically on the immediate process of healing [21, 22]. Asiaticoside, isolated from *C. asiatica*, is the main active constituent and exhibits significant wound-healing activity in normal and delayed-healing models [23].

Figure 5 Proanthocyanidins

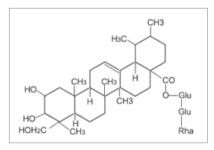


Figure 6
Asiaticoside

Curcuma longa L. (Zingiberaceae)

The part used are rhizomes containing curcumin (fig. 7) (diferuloyl methane), turmeric oil or turmerol and 1, 7-bis, 6- hepta-diene-3, 5-dione. *Curcuma longa* also contains protein, fats, vitamins (A, B, C etc.) all of which have an important role in would healing and regeneration. Turmeric has been used for treating the wounds in the rats [24].

Figure 7 Curcumin

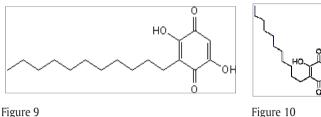
Figure 8 Epifriedelinol

Elephantopus scaber L. (Asteraceae)

The whole plant is macerated and applied on the wound surface to promote wound healing. Phytochemically the plant has been reported to contain sesquiterpene lactones deoxyelephantopin, isodeoxyelephantopin and scabertopin. It also contains epifriedelinol (fig. 8], lupeol and stigmasterol [25].

Embelia ribes Burm. (Myrsinaceae)

Leaf pastes of this species are used to cure cut wounds and leprosy. Fruits contain a quinone derivative embelin (fig. 9) (3-undecyl 2,5-dihydroxy, 1,4-benzo-quinone), an alkaloid christembine and a volatile oil vilangin(fig. 10); its chemical constituent is 2,5-dihydroxy-4-undecyl-3, 6-benzoquinone [26].



HO OH

Figure 9 Embelin

Figure 10 Vilangin

Hibiscus rosa sinensis L. (Malvaceae)

It is used as an herb in Ayurvedic or alternative medicine in India to treat colds, wound healing, and damaged and/or inflamed tissue as well as to rejuvenate the skin. The phytochemical analysis of the flower extract both by qualitative and thin layer chromatography showed the absence of active constituents such as polyphenols, triterpenoids (fig. 11), tannins, saponins, flavonoids, alkaloids, and carboxylic acids [27].

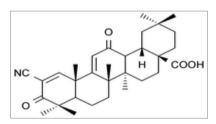


Figure 11 Triterpenoids

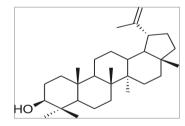


Figure 12 Lupeol

Jasminum auriculatum Vahl. (Oleaceae)

The alcohol free defatted extract of *J. auriculatum* leaves has been reported to contain lupeol (fig. 12) and jasminol [28]. Juice of leaves of *J. auriculatum* has been shown to be beneficial in wound healing. When applied in the form of jelly, locally

on linear uniform excised wound in rats, the juice is found to promote wound healing [29, 30].

Lycopodium serratum (Lycopodiaceae)

The plant is reported to contain alkaloids like serrtezomines A-C, lycoposerramine-A, Lycoposerramine F-O, quinolizine (fig. 13) or pyridine and alpha-pyridone (fig. 14) type alkaloids which are the potent inhibitors of acetylcholineesterase and triterpenoids. The tribal groups of Western Ghats of Chikamagalur region use this plant for treating wounds. The whole plant is ground in hot water and the thick paste is thus obtained and applied externally to sores, cuts, wounds and burns [31].

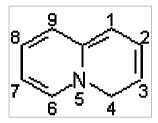


Figure 13 Quinolizine

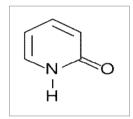


Figure 14 Alpha-pyridone

SAFETY AND EFFICACY OF PLANT MATERIAL

No system of medicine is entirely safe. Some of the risks are inherent in the medication prescribed; however, the experience of the practitioner also plays an important role.

The evidence of efficacy is derived from randomized, controlled trials, a methodology that has not been used in Ayurvedic or other traditional systems of medicine. I argue that other clinical parameters such as patient satisfaction, improvement of well-being, improved or faster healing, as well as the number of wounds that attain healing are a part of the objective that is efficacy.

MECHANISM OF ACTION OF WOUND HEALING PLANTS

Plants with mechanism of action are given in table 1.

Plants with mechanism of action

Table 1.

No.	Plant name	Part used	Mechanism of action	Ref.
	Ageratum conyzoides Linn. (Asteraceae)	roots	by antioxidant and antimicrobial activities	32
	Aloe vera (Liliacea)	gel	by enhancing keratinocyte multiplication and migration, expression of proliferation related factors, and epidermis formation.	33
	Alternanthera sessilis (Linn.) R. Br. ex DC (Amaranthaceae)	leaves	by increasing collagen content and degree of collagen cross-linkage within the wound they may also promote cell division, growth of bone, cartilage and other connective tissues	17
	Arnebia densiflora (Nordm.) Ledeb. (Boraginaceae)	roots	an increase in the synthesis of collagen, fibronectin, and transforming growth factor-β1, which enhance healing of wounds	18
	Aspilia africana C. D. Adams (Compositae)	leaves	by arresting wound bleeding, inhibiting the growth of microbial wound contaminants	34
	Berberis lyceum Royle (Berberidaceae)	roots	by astringent and antimicrobial properties	19
	Catharanthus roseus L. (Apocyanaceae)	flowers	by increasing wound contraction and tensile strength, augmented hydroxyproline content	35
	Calendula officinalis L. (Asteraceae)	flowers	by stimulating the proliferation and, to a higher extent, the migration of fibroblasts.	36
	Carapa guianensis L. (Meliaceae)	leaves	by increasing rate of wound contraction, skin breaking strength and hydroxyproline content	37
	Elephantopus scaber Linn. (Asteraceae)	leaf	by increasing cellular proliferation, formation of granulation tissue,synthesis of collagen and by increase in the rate of wound contraction	25
	Euphorbia nerifollia Linn. (Euphorbiaceae)	latex	due to its epithelial proliferative action	38
	Hevea brasiliensis Müll. Arg. (Euphorbiaceae)	latex	by increasing vascular permeability and angiogenesis	39
	Hibiscus rosa sinensis L. (Malvaceae)	flowers	by enhancing wound contraction, shortened epithelialization period, increased tensile strength	27

0.	Plant name	Part used	Mechanism of action	Ref.
	Hippophae rhamnoides L. (Elaeagnaceae)	seed oil	possesses antioxidant properties as evidenced by significant increase in reduced glutathione (GSH) level and reduced production of reactive oxygen species (ROS) in wound granulation tissue	40
	Hypericum perforatum L. (Cluciaceae = Guttiferae)	aerial parts	may be a result of the fibroblast migration and stimulation of collagen synthesis	41
	Leucas hirta (Roth) Spreng., (Labiateae)	leaves	by increasing rate of wound contraction, reduction in the epithelization. Increase in collagen deposition. Breaking strength and hydroxyprolline in granulation tissue	42
	Mimosa tenuiflora (Willd.) Poirett (Mimosaceae)	bark	by stimulating mitochondrial activity and proliferation of dermal fibroblasts.	43
	Morinda citrifolia Linn. (Rubiaceae)	leaves	by astringent and antimicrobial property, which seems to be responsible for wound contraction and increased rate of epithelialization	44
	Pterocarpus santalinus Linn. (Fabaceae)	stem	by stimulating a growth factor or factors signal cascade system	45
	Radix paeoniae (Paeonaceae)	root	by decreasing the surface area of the wound and increasing the tensile strength	46
	Radix Rehmanniae (RR) (Scrophulariaceae)	herb	by better developed scars and epithelialization as well as good formation of capillaries with enhanced VEGF expression.	47
	Rheum officinale Baill (Polygonaceae)	roots	by accelerating healing of cutaneous wounds which is related to TGF-β1/Smad signaling pathway and improves reorganization of the regenerating tissue.	48
	Terminalia bellirica Roxb. (Combretaceae)	fruits	by cellular mechanism; chelating of the free radicals and reactive species of oxygen. Promoting contraction of the wound and increasing the formation of capillary vessels and fibroblasts	49
	Vanda roxburghii R. Br. (Orchidaceae)	leaves	by increasing the migration of epithelial cells	50

PLANTS THAT HEAL WOUND

Plants which have been used in management and treatment of wounds over the years are given in table 2.

Table 2.

Plants that heal wound

No.	Plant name	Extract used	Model studied	Ref.
	Acalypha indica Linn. (Euphorbiaceae)	whole plant ethanolic extract	excision and incision	51
	Aegle marmelos Corr. (Rutaceae)	methanolic extract of plant	excision and incision	52
	Allamanda cathartica Linn. (Apocyanaceae)	aqueous extract	excision and incision	53
	Alternanthera sessilis (Linn.) R.Br.ex DC (Amaranthaceae)	chloroform extract of leaves	incision and excision	17
	Alternanthera brasiliana Kuntz (Amaranthacea)	methanolic extract of leaves	excision and incision	54
	Anogeissus latifolia (Roxb. ex DC) Wall, ex Guill & Pern (Combretaceae)	ethanolic extract of bark	excision and incision	55
	Aristolochia bracteolate Lam. (Aristolochiaceae)	ethanol extract	excision, incision and dead space	56
	Areca catechu L. (Arecaceae)	betel nut extract	excision, incision and dead space	57
	Argemone mexicana Linn. (Papaveraceae)	ethanolic extract	excision, incision and dead space wounds	58
	Arnebia densiflora (Nordm.) Ledeb. (Boraginaceae)	the extract of the roots in olive oil	incision and excision	18
	Azadirachta indica (Meliaceae)	pure neem oil and neem ointment	incised and gap wounds in bovine calves	59
	Berberis lyceum Royle (Berberidaceae)	aqueous and methanolic extract of root	excision, incision and dead space	19
	Bryophyllum pinnatum (Lam.) (Crassulaceae)	leaf, alcoholic and water extracts	excision, incision and dead space	60
	Butea monosperma (Lam.) Kuntze (Papilionaceae)	alcoholic bark extract	excision	61
	Calotropis gigantea L. (Asclepiadaceae)	latex	excision and incision	62
	Canthium parviflorum Lam. (Rubiaceae)	aqueous and ethanolic extract	excision	63
	Carallia brachiata Merrill (Rhizophoracea)	petroleum, ethyl acetate and methanol extract of bark	excision and incision	20
	Cassia fistula Linn. (Leguminosae)	alcoholic leaf extract	excision	64

No.	Plant name	Extract used	Model studied	Ref
	Cecropia peltata L. (Cecropiaceae)	aqueous and ethanolic extract of leafs	excision	65
	Celosia argentea Linn. (Amaranthaceae)	alcoholic extract	burn wound	66
	Centella asiatica L. (Umbelliferae)	ethanolic extract	incision, excision, and dead space	21, 22
	Cinnamomum zeylanicum Blume (Lauracea)	ethanol extract of bark	excision, incision and dead space	67
	Cocos nucifera Linn. (Arecaceae)	oil	burn	68
	Coronopus didynamous (Brassicaceae)	ethanol and aqueous extracts of whole plant	incision	69
	Cyperus rotundus Linn. (Cyperaceae)	extract of tuber	excision, incision and dead space	70
	Datura alba (Bernh.) Rumph. ex Nees (Solanaccae)	alcoholic leaf extract	burn rat wound	71
	Dendrophthoe falcata (L.f) Ettingsh (Loranthaceae)	ethanolic extract of aerial parts	excision and incision	72
	Desmodium triquetrum (Leguminosae)	ethanolic leaf extract	excision, incision and dead space	73
	Elephantopus scaber Linn. (Asteraceae)	aqueous ethanol	excision, incision and dead space	25
	Embelia ribes Burm (Myrsinaceae)	ethanol extract of the leaves	excision, incision and dead space	26
	Eucalyptus globulus (Myrtaceae)	ethanolic extract of leaf	excision, incision and dead space	74
	Euphorbia nerifollia Linn. (Euphorbiaceae)	aqueous extract of latex	excision	38
	Flaveria trinerva (Asteraceae)	methanol extract	excision and incision	75
	Gmelina arborea Roxb. (Verbenaceae)	alcoholic extract of leaf	excision, incision and dead space	76
	Heliotropium indicum (Boraginaceae)	whole plant ethanolic extract	excision and incision	51
	Hemigraphis colorata (Blume) H.G. Hallier (Acanthaceae)	crude leaf paste	excision	77
	Hibiscus rosa sinensis L. (Malvaceae)	ethanol extract of flower	excision, incision and dead space models	27
	Hippophae rhamnoides L. (Elaeagnaceae)	aqueous extract of leaf	excision	78

No.	Plant name	Extract used	Model studied	Ref.
	Hippophae rhamnoides L. (Elaeagnaceae)	seed oil	burn wounds	40
	Hypericum hookeriaпит (Hypericaceae)	methanolic extracts of leaf	incision and excision	79
	Hypericum mysorense Wight and Arn. (Hypericaceae)	methanol extract of leaf	excision and incision	80
	Hypericum patulatum Thumb (Hypericaceae)	methanolic extract of leaf	excision and incision	81
	Hyptis suaveolens (L.) (Lamiaceae)	ethanolic extract of leaf	excision, incision and dead space	82
	Indigofera enneaphylla Linn. (Fabaceae)	alcoholic extract of aerial parts	excision and incision	83
	Ixora coccinea Linn. (Rubiaceae)	alcoholic extract of flowers	dead space	84
	Lantana camara Linn. (Verbenaceae)	leaf juice and hydroalcoholic extract	excision	85
	Laurus nobilis Linn. (Lauraceae)	aqueous extracts	excision and incision	53
	Lawsonia alba Lam. (Lythraceae)	difference extracts of leaf	excision and incision	86
	Leucas hirta (Roth) Spreng., (Labiateae)	aqueous and methanolic leaf extracts	excision, incision and dead space	42
	Leucas lavandulaefolia Rees. (Labiatae)	methanol extract	excision and incision	87
	Lycopodium serratum (Lycopodiaceae)	70% ethanolic extract	excision	31
	Moringa oleifera Lam. (Moringaceae)	ethyl acetate extract of dried leaf	excision, incision and dead space	88, 89
	Nelumbo nucifera (Nymphaceae)	methanol extract of rhizomes	excision, incision and dead space	90
	Ocimum sanctum Linn. (Labiaceae)	ethanolic extract of leaves	excision, incision and dead space	91
	Oxalis corniculata (Oxalidaceae)	alcohol and petroleum ether extracts of whole plant	excision, incision and dead space	92
	Pentas lanceolata (Rubiaceae)	ethanolic extract of flowers	excision	93
	Phyllanthus emblica Linn. (Euphorbiaceae)	plant extract	excision	94

No.	Plant name	Extract used	Model studied	Ref.
	Plagiochasma appendiculatum Lehm. et Lind. (Aytoniaceae)	alcohol and ethanolic extract	excision and incision	95
	Polyscias scutellaria (Burm. f.) Fosberg. (Araliaceae)	leaf saponin extract	excision, incision and dead space	96
	Punica granatum L. (Punicaceae)	methanolic extract of peels	excision	97
	Quercus infectoria Oliver (Fagaceae)	crude aqueous extract of galls	excision, incision and dead space	98
	Rafflesia hasseltii (Rafflesiaeae)	methanol extract of flower	induced wounds	99
	Sphaeranthus indicus Linn. (Asteraceae)	ethanolic extract of aerial parts	excision	100
	Tephrosia purpurea (Linn.) Pers. (Leguminosae)	ethanolic extract	excision, incision and dead space	101
	Terminalia arjuna (Roxb.) W&A. (Combreteaceae)	50% ethanolic extract of bark and tannins	excision and incision	102
	Terminalia bellirica Roxb. (Combretaceae)	ethanol extract of fruits	excision and incision wounds	49
	Terminalia chebula Retz. (Combretaceae)	alcoholic extract of leaf	incision and in vitro	103
	Thespesia populnea Soland ex Correa (Malvaceae)	aqueous extract of fruit	incision and excision	104
	Toddalia asiatica (Linn.) Lam. (Rutaceae)	ethanol, petroleum ether, chloroform, acetone extracts	excision and incision	105
	Tragia involucrate L. (Euphorbiaceae)	methanol extract	excision	106
	Tridax procumbens Linn. (Compositeae)	whole plant, aqueous extract,	dead space	107, 108
	Trigonella foenum-graecum Linn. (Fabaceae)	aqueous extract of seed	excision, incision and dead space	109
	Vanda roxburghii R. Br. (Orchidaceae)	extract of whole plant	excision	50
	Vernonia arborea HK (Asteraceae)	aqueous and methanol leaf extracts	excision, incision and dead space	110
	Vanda roxburghii R. Br. (Orchidaceae)	crude aqueous extract of plant	excision, incision and dead space	111
	Wedelia calendulacea (L.) Less. (Asteraceae)	aqueous extract	incision and excision	112

DISCUSSION

The search for "natural remedies" for a common disorder such as wounds has drawn attention to herbals. From ancient times, herbals have been routinely used to treat wounds and in many cultures their use in traditional medicine has persisted to present times. While it is possible that some time-tested herbal remedies are indeed effective, it seems to be often the case that the patient knows more about this form of medicine than the physician. In spite of the various challenges encountered in the medicinal plant-based drug discovery, natural products isolated from plants will still remain an essential component in the search of new medicines. Proper utilization of these resources and tools in bioprospecting will certainly help in discovering novel lead molecules from plants by employing modern drug discovery techniques and the coordinated efforts of various disciplines.

CONCLUSION

Wound healing is a fundamental response to tissue injury that results in restoration of tissue integrity. This is mainly achieved by the synthesis of the connective tissue matrix. Collagen is a major protein of the extracellular matrix and is the major component that ultimately contributes to wound strength. Utilization of plants for medicinal purposes in India has been documented long back in ancient literature because they are essential to human survival. The consumption, management and valuation of wild plants are central aspects of traditional knowledge in many human populations. Thus, plants gathering the diffusion and conservation of knowledge within the community are traditional practices that have contribution to the subsistence of many cultures. Plants and their extracts have immense potential for the management and treatment of wounds. Therefore, it is important to study and examine all options available with which wound management may be improved. However, there is a need for scientific validation, standardization and safety evaluation of plants of the traditional medicine before these could be recommended for healing of the wounds. This review is an approach towards the herbal plants having wound healing potentials involving the observation, description, and experimental investigation of indigenous drugs and their biological activities. It is based on botany, chemistry, biochemistry, pharmacology, and many other disciplines that contribute to the discovery of natural products of biological activity.

REFERENCES

- 1. Solecki R, Shanidar IV. A Neanderthal flower burial in northern Iraq. Science 1975; 190 (4217):880-1.
- 2. Lanfranco G. Popular use of Medicinal plants in the Maltese Islands. Insula 1992; 1: 34-5.

- 3. Farnsworth NR, Akerele O, Bingel AS, Soejarto DD, Guo Z. Medicinal plants in therapy. Bull WHO 1985; 63(6): 965-81.
- 4. Farnsworth NR, Morris RW. Higher plants-the sleeping giant of drug development. Am J Pharm Sci Support Public Health 1976; 148(2): 46-52.
- 5. Raskin I, Ripoll C. Can an apple a day keep the doctor away? Curr Pharm Des 2004; 10(27): 3419-29.
- 6. Ayello EA. What does the wound say? Why determining etiology is essential for appropriate wound care. Adv in Skin Wound Care 2005; 18: 98-109.
- 7. Rubin E, Fabrex JL. Repair, regeneration and fibrosis. In: Pathology, 2nd ed. Philadelphia 1996:7-15.
- 8. Fulzele SV, Satturwar PM, Joshi SB, Dorle AK. Wound healing activity of *Hingvadya ghrita* in rats. Indian Drugs 2002; 39:606-9.
- Kumar R, Katoch SS, Sharma SB. Adrenoceptor agonist treatment reverses denervation atrophy with augmentation of collagen proliferation in denervated mice gastrocnemius muscle. Indian J Exp Biol 2006; 44: 371-6.
- 10. Lawrence WT, Diegelmann RF. Growth factors in wound healing. Clin Dermatol 1994; 12:157-69.
- 11. Swamy HMK, Krishna V, Shankarmurthy K, Rahiman BA, et al. Wound healing activity of embelin isolated from the ethanol extract of leaves of *Embelia Ribes* Burm. J Ethanopharmacol 2007; 109:533.
- 12. Fernandez O, Capdevila JZ, Dalla G, Melchor G. Efficiacy of *Rhizophora mangle* aqueous barks extract in the healing of open surgical wounds, Fitoterpia 2002; 73:564-8.
- 13. Deters A, Dauer A, Schnetz E, Fartasch M, et al. High molecular compounds (Polysaccharides and Proanthocyanidins) from *Hamamelis virginiana* bark influence on human skin keratinocyte proliferation and differentiation and influence on irritated skin. Phytochem 2001; 58:949-58.
- 14. Suguna L, Chandrakasan G, Joseph KT. Influence of honey on biochemical and biophysical parameters of wounds in rats. J Clin Biochem and Nutr 1999; 14: 91-9.
- 15. Sharma SP, Aithal KS, Srinivasan KK, Udupa AL, et al. Anti-inflammatory and wound healing activities of the crude alcoholic extracts and flavonoids of *Vitex leucoxylon*. Fitoterapia 1990; 61: 263-5.
- 16. Chithra P, Suguna L, Chandrakasan G. Influence of arginine wound healing in rats. J Clin Biochem and Nutr 1995; 18:111-17.
- 17. Jalalpure S, Agrawal N, Patil M.B, Chimkode R, et al.. Antimicrobial and wound healing activities of leaves of *Alternanthera sessilis* Linn. Int J Green Pharmacy 2009; 141-44.
- 18. Akkol EK, Koca U, Pesin I, Yilmazer D, et al. Exploring the wound healing activity of *Arnebia Densiflora* (Nordm.) Ledeb. by *in vivo* models. J Ethanopharmacol 2009; 124: 137-141.
- 19. Asif A, Kabub G, Mehmood S, Khunum R, et al. Wound healing activity of root extract of *Berberis Lyceum* Royle in rats. Phytother Res 2007; 21: 589-91.
- 20. Krishnaveni B, Neeharika V, Venkatesh S, Padmavathy R, et al. Wound healing activity of *Carallia brachiata* bark. Ind J Pharm Sci 2009; 576-8.
- 21. Suguna L, Sivakumar P, Chandrakasan G. Effects of *Centella asiatica* extract on dermal wound healing in rats. Ind J Exper Biol 1996; 34: 1208-11.
- Shetty, BS, Udupa SL, Udupa AL, Somayaji SN. Effect of *Centella asiatica* L. (Umbelliferae) on normal and dexamethasone-suppressed wound healing in Wistar Albino rats. J Lower Extremity Wounds 2006; 5: 137-43.
- 23. Shukla A, Rasik AM, Dhavan BN. Asiaticoside-induced elevation of antioxidant levels in healing wounds. Phytother Res 1999; 13(1):50-4.
- 24. Rao SGV, Selvaraj J, Senthil R, Radhakrishnan RN, et al. Efficacy of some indigenous medicines in wound healing in rats. Ind J Animal Sci 2003; 73:652-3.
- 25. Singh SDJ, Krishna V, Mankani KL, Manjunatha BK, et al. Wound healing activity of the leaf extracts and deoxyelephantopin isolated from *Elephantopus scaber* Linn. Ind J Pharmacol 2005; 37:238-42.
- Swamy HMK, Krishna V, Shankarmurthy K, Rahiman BA, et al. Wound healing activity of embelin isolated from the ethanol extract of leaves of *Embelia ribes* Burm. J Ethanopharmacol 2007; 109:529-34.
- 27. Nayak B, Raju SS, Orette FA, Rao AVC. Effects of *Hibiscus rosa sinensis* L. (Malvaceae) on wound healing activity: a preclinical study in a Sprague dawley rat. Int J Low Extrem Wounds 2007; 6:76-81.
- 28. Deshpande SM, Upadyaya RR. Chemical studies of *Jasminum auriculatum* (VAHL) leaves. Curr Sci 1967; 36:233.
- 29. Deshpande PJ, Pathak SN. Med Surg 1966a; 6:21.

- 30. Deshpande PJ, Pathak SN. Indian J Med Res1966b; 1(1):81.
- 31. Manjunatha BK, Krishna V, Vidya SM, Mankani KL, et al. Wound healing activity of *lycopodium serratum*. Indian J Pharma Sci 2007; 69 (2): 283-7.
- 32. Jain S, Jain N, Tiwari A, Balekar N, Jain DK. Simple evaluation of wound healing activity of polyherbal formulation of roots of *Ageratum conyzoids* Linn. Asian J Research Chem 2009; 2(2):135-8.
- 33. Choi S-W, Son B-W, Son Y-S, Park Y-K, et al. The wound healing effect of a glycoprotein fraction isolated from *Aloe vera*. Brit J Dermatol 2001; 145:535-45.
- 34. Okoli CO, Akah PA, Okoli AS. Potentials of leaves of *Aspilia Africana* (Compositae) in wound care: an experimental evaluation. BMC Complement Altern Med 2007; 7:24:1-7.
- 35. Nayak BS, Pereira LMP. *Catharanthus roseus* flower extract has wound healing activity in Sprague Dawley rats. BMC Complement Alternat Med 2006; 6:41:1-6.
- 36. Fronza M, Heinzmann B, Hamburger M. Laufer S, et al. Determination of the wound healing effect of *Calendula* extracts using the starch assay with 3T3 fibroblasts. J Ethanopharmacol 2009; 126: 463-7.
- 37. Nayak BS, Kanhai J, Milne DM, Pereira LP, et al. Experimental evaluation of ethanolic extract of *Carapa guianensis* L. leaf for its wound healing activity using three wound models. Evidence Based Complementary and Alternative Medicine 2009: 13:1-7.
- 38. Rasik AM, Shukla A, Patnail GK. Wound healing activity of latex of *Euphorbia neriifolia* Linn. Ind J Pharmacol 1996; 28:107-9
- 39. Mendonca RJ, Mauricio VB, Teixeira LDB, et al. Increased vascular permeability, angiogenesis and wound healing induced by the serum of natural latex of the rubber tree *Hevea Brasiliensis*. Phytother Res 2010; 24:746-8.
- 40. Upadhyay NK, kumar R, Mandotra SK, Meena RN, et al. Saftey and healing efficacy of Sea buckthorn (*Hippophae rhamnoides* l.) seed oil on burn wounds in rats. Food Chem Toxicol 2009; 47:1146-53.
- 41. Oztruk N, korkmaz S, Ozturk Y. Wound healing activity of St. John's Wort (*Hpericum perforatum* L.) on chicken embryonic fibroblasts. I Ethanopharmacol 2007; 111:33-9.
- 42. Manjunatha BK, Vidya SM, Krishna V, Mankani KL.Wound healing activity of *Leucas hirta*. Ind J Pharm Sci 2006; 68: 380-4.
- 43. Zippel J, Deters A, Hensel A. Arabinogalactans from *Mimosa tenuiflora* (Willd.) poiret bark as active principles for wound healing properties: Specific enhancement of dermal fibroblasts activity and minor influence on HaCaT Keratinocytes. Journal of Ethanopharmacology 2009; 124:391-6.
- 44. Nayak BS, Sandiford S, Maxwell A. Evaluation of the wound healing activity of ethanolic extract of *Morinda citrifolia* L. leaf. Advance Access Publication 2009; 6:351-6.
- 45. Biswas TK, Maity LN, Mukherjee B. Wound healing potential of *Petrcarpus santalinus* Linn: A pharmacological evaluation. Int J Low Extrem Wounds 2004; 3:143-50.
- 46. Malviya N, Jain S. Wound healing activity of aqueous extract of *Radix paeoniae* root. Acta Poloniae Pharmaceutica- Drug Research 2009; 66:5:543-7.
- 47. Lau TW, Lam FFY, Lau KM, Chan YW, et al. Pharmacological investigation on thr wound healing effects of *Radix rehmanniae* in animal model of diabetic foot ulcer. J Ethanopahrmacol 2009; 123:155-62.
- 48. Tang T, Yin L, Yang J, Shan G. Emodin, an anthraquinone derivative from *Rheum officinale* Baill, enhances cutaneous wound healing in rats. European Journal of Pharmacology 2007; 567: 177-185.
- 49. Choudhary, G.P. Wound healing activity of the ethanol extract of *Terminalia Bellirica* Roxb. Fruits. Nat Prod Radiance 2008; 7(1):19-21.
- 50. Nayak BS, Suresh R, Rao AV, Pillai GK, et al. Evaluation of wound healing activity of *Vanda roxburghii* R. Br (Orchidaceae): a preclinical study in a rat model. J Lower Extremity Wounds 2005; 4:200-4.
- 51. Reddy JS, Rao PR, Reddy M.S. Wound healing effects of *Heliotropium indicum*, *Plumbago zeylanicum* and *Acalypha indica* in rats. J Ethnopharmacol 2002; 79:249-51.
- 52. Jaswanth A, Akilandeswari LV, Manimaran SRS. Wound healing activity of *Aegle marmelos*. Ind J Pharm Sci 2001; 63:41-4.
- 53. Nayak S, Nalabothu P, Sandiford S, Bhogadi V, et al. Evaluation of wound healing activity of *Allamanda cathartica*. L. and *Laurus nobilis*. L. extracts on rats. BMC Complementary Alter Med 2006; 5: 6-12.
- 54. Barua CC, Talukdar A, Begum SA, Sharma DK, et al. Wound healing activity of methanolic extract of leaves of *Alternanthera brasiliana* Kuntz using *in vivo* and *in vitro* model. Ind J Exper Biol 2009; 47:1001-5.

- 55. Govindarajan R, Vijayakumar M, Rao CV, Shirwaikar A, et al. Healing potential of *Anogeissus latifolia* for dermal wounds in rats. Acta Pharmaceutica. 2004; 54: 331-8.
- 56. Shirwaikar A, Somashekar AP, Udupa AL, Udupa SL, et al. Wound healing studies of *Aristolochia bracteolate* Lam. with supportive action of antioxidant enzymes. Phytomedicine. 2003a; 10: 558-62.
- 57. Padmaja PN, Bairy KL, Kulkarni DR. Pro-healing effect of betel nut and its polyphenols. Fitoterapia 1994; 65: 298-300.
- 58. Patil MD, Jalalpure SS, Ali A. Preliminary phytochemical investigation and wound healing activity of the leaves of *Argemone mexicana* Linn. Indian Drugs 2001; 38: 288-93.
- 59. Bhardwaj RL, Sharma DN. Evaluation of neem (*Azadirachta indica* Juss) oil as a potent wound healer. Histomorphological and histochemical study. Ind Veter Med J 1997; 21: 187-90.
- 60. Khan M, Patil PA, Shobha JC. Influence of *Bryophyllum pinnatum* (Lam.) leaf extract on wound healing in albino rats. J Natural Remedies 2004; 4: 41-6.
- Sumitra M, Manikandan P, Suguna L. Efficacy of *Butea monosperma* on dermal wound healing in rats. J Biochem Cell Biol 2005; 37: 566-73.
- 62. Nalwaya N, Pokharna G, Deb L, Jain NK. Wound healing activity of latex of *Calotropis gigantean*. Int J Pharmacy Pharm Sci 2009: 1 (1):176-81.
- 63. Mohideen S, Illavarasan R, Hemalatha S, Anitha N, et al. Wound healing and diuretic activity of *Canthium parviflorum* Lam. Natural Product Sci 2003; 4:102-4.
- 64. Senthil KM, Sripriya R, Vijaya RH, Sehgal PK. Wound healing potential of *Cassia fistula* on infected albino rat model. J Surgical Res 2006; 131:283-9.
- 65. Nayak BS. *Cecropia peltata* L. (Cecropiaceae) has wound-healing potential: A preclinical study in a Sprague dawley rat model. Int J Low Extrem Wounds 2006; 5:20-26.
- 66. Priya KS, Arumugam G, Bhuvaneswari R, Wells A, Mary B. *Celosia argentea* Linn. leaf extract improves wound healing in a rat burn wound model. Wound Repair and Regeneration 2004; 12: 618.
- 67. Kamath JV, Rana AC, Chowdhury AR. Pro-healing effect of *Cinnamomum zeylanicum* bark. Phytother Res 2003; 17:970-72.
- 68. Srivastava P, Durgaprasad S. Burn wound healing property of *Cocos nucifera*: An appraisal. Indian J Pharmacol 2008; 40 (4):144-6.
- 69. Prabhakar KR, Srinivasan KK, Rao PGM. Chemical investigations, antiinflammatory and wound healing properties of *Coronopus didynamous*. Pharm Biol 2002; 40: 490-3.
- 70. Puratchikody A, Devi CN, Nagalakshmi G,. Wound healing activity of *Cyperus rotundus* Linn. Ind J Pharm Sci 2006; 68:97-101.
- 71. Priya KS, Gnanamani A, Radhakrishnan N, Babu M. Healing potential of *Datura alba* on burn wounds in albino rats. J Ethnopharmacol 2002; 83:193-9.
- 72. Pattanayak SP, Sunita P. Wound healing, anti-microbial and antioxidant potential of *Dendrophthoe falcate* (L.f.) Ettingsh. J Ethanopharmacol 2008; 120: 241-7.
- 73. Shirwaikar A, Jahangirdas S, Udupa L. Wound healing activity of *Desmodium triquetrum* leaves. Indian Journal of Pharmaceutical Sciences. 2004; 65: 461-4.
- 74. Hukkeri VT, Karadi RV, Akki KS, Savadi RV, et al. Wound healing property of *Eucalyptus globulus* leaf extract. Indian Drugs. 2002; 39: 481-3.
- 75. Umadevi S, Mohanta GP, Kalaichelvan VK, Manavalan R. Studies on wound healing effect of *Flaveria trinervia* leaf in mice. Ind J Pharm Sci 2006; 68:106-8.
- Shirwaikar A, Ghosh S, Rao PGM. Effect of *Gmelina arborea* Roxb. leaves on wound healing in rats. J Natur Remedies 2002; 3: 45-8.
- 77. Subramoniam A, Evans DA, Rajasekharan S, Nair GS. Effect of *Hemigraphis colorata* (Blume) H.G. Hallier leaf on wound healing and inflammation in mice. Ind J Pharmacol 2001; 33: 283-5.
- 78. Gupta A, Kumar R, Pal K, Banerjee PK, et al. A preclinical study of the effects of seabuckthorn (*Hippophae rhamnoides* L.) leaf extract on cutaneous wound healing in albino rats. J Lower Extremity Wounds 2005; 4: 88-92.
- 79. Mukherjee PK, Suresh B. The evaluation of wound healing potential of *Hypericum hookerianum* leaf and stem extracts. J Alter Complementary Med 2000b; 6: 61-9.
- 80. Mukherjee PK, Suresh B. Studies on *in vivo* wound healing activity of leaf extract of *Hypericum mysorense* with different wound models in rats. Natural Product Sciences. 2000a; 6: 73-8.

- 81. Mukherjee PK, Verpoorte R, Suresh B. Evaluation of *in vivo* wound healing activity of *Hypericum patulum* (Family: Hypericaceae) leaf extract on different wound models in rats. J Ethnopharmacol 2000a; 70: 315-21.
- 82. Shirwaikar A, Shenoy R, Udupa AL, Udupa SL, et al. Wound healing property of ethanolic extract of leaves of *Hyptis suaveolens* with supportive role of antioxidant enzymes. Ind J Exper Biol 2004; 41: 238-41.
- 83. Hemalatha S, Subramanian N, Ravichandran V, Chinnaswamy K. Wound healing activity of *Indigofera enneaphylla* Linn. Ind J Pharm Sci 2001; 63: 331-3.
- 84. Nayak BS, Udupa AL, Udupa SL. Effect of *Ixora coccinea* flowers on dead space wound healing in rats. Fitoterapia 1999; 70: 233-6.
- 85. Dash GK, Suresh P, Ganapathy S. Studies on hypoglycaemic and wound healing activities of *Lantana camara* Linn. J Natural Remedies 2001; 1: 105-10.
- 86. Patil KS, Mandewgade SD. Wound healing activity of leaves of *Lawsonia alba*. J Natur Remedies 2003; 3: 129-33.
- 87. Saha K, Mukherjee PK, Das J, Pal M, Saha BP. Wound healing activity of *Leucas lavandulaefolia* Rees. J Ethnopharmacol 1997; 56: 139-44.
- 88. Udupa SL, Udupa AL, Kulkarni DR. Studies on anti-inflammatory and wound healing properties of *Moringa oleifera* and *Aegle marmelos*. Fitoterapia 1994b; 65: 119-23.
- 89. Hukkeri VI, Nagathan CV, Karadi RV, Patil BS. Antipyretic and wound healing activities of *Moringa oleifera* Lam. in rats. Ind J Pharm Sci 2006; 68: 124-6.
- 90. Mukherjee PK, Mukherjee K, Pal M, Saha BP. Wound healing potential of *Nelumbo nucifera* (Nymphaceae) rhizome extract. Phytomedicine 2000b; 7:66.
- 91. Udupa SL, Shetty S, Udupa AL, Somayaji SN. Effect of *Ocimum sanctum* Linn. on normal and dexamethasone suppressed wound healing. Ind J.Exper Biol 2006; 44: 49-54.
- 92. Taranalli AD, Tipare SV, Kumar S, Torgal SS. Wound healing activity of *Oxalis corniculata* whole plant extract in rats. Ind J Pharm Sci 2004; 66: 444-6.
- 93. Nayak BS, Vinutha B, Geetha B, Sudha B. Experimental evaluation of *Pentas lanceolata* flowers for wound healing activity in rats. Fitoterapia 2005b; 76: 671-5.
- 94. Suguna L, Sumitra M, Chandrakasan G. Influence of *Phyllanthus emblica* extract on dermal wound healing in rats. J Med Aromatic Plants 2000; 32: 2-3.
- 95. Singh M, Govindarajan R, Nath V, Rawat AK, et al. Antimicrobial, wound healing and antioxidant activity of *Plagiochasma appendiculatum* Lehm. et Lind. J Ethnopharmacol 2006; 107: 67-72.
- 96. Divakar MC, Devi SL, Kumar PS, Rao SB. Studies of wound healing property of *Polyscias scuttellaria* leaf saponins. Ind J Natural Prod 2001; 17: 37-42.
- 97. Murthy KN, Reddy VK, Veigas JM, Murthy UD. Study on wound healing activity of *Punica granatum* peel. J Med Herbs, Foods Spices 2004; 7: 256-9.
- 98. Jalalpure SS, Patil MB, Alagawadi KR. Wound healing activity of the galls of *Quercus infectoria* Oliver. J Natural Remedies 2002; 2:1.
- 99. Abdulla MA, Ahmed KA, Ali HM, Noor SM, et al. Wound healing activities of *Rafflesia hasseltii* extracts in rats. J Clin Biochem Nutr 2009; 45:304-8.
- 100. Sadaf F, Saleem R, Ahmed M, Ahmad SI, et al. Healing potential of cream containing extract of *Sphaeranthus indicus* on dermal wounds in Guinea pigs. J Ethanopharmacol 2006: 107: 161-3.
- 101. Lodhi S, Pawar RS, Jain AP, Singhai AK. Wound healing potential of *Tephrosia purpurea* (Linn.) Pers. in rats. J Ethnopharmacol 2006; 08: 204-10.
- 102. Chaudhari M, Mengi S. Evaluation of phytoconstituents of *Terminalia arjuna* for wound healing activity in rats. Phytother Res 2006; 20: 799-805.
- 103. Suguna L, Singh S, Sivakumar P, Sampath P, et al. Influence of *Terminalia chebula* on dermal wound healing in rats. Phytother Res 2002; 16: 227-31.
- 104. Nagappa AN, Cheriyan B. Wound healing activity of the aqueous extract of *Thespesia populnea* fruit. Fitoterapia 2001; 72: 503-6.
- 105. Kar DM, Mohanty A, Sethi RK, Dash GK. Antimicrobial and wound healing properties of stem bark of *Toddalia asiatica* Linn. Ind J Pharm Sci 2005; 67: 220-3.
- 106. Perumal SR, Gopalakrishnakone P, Sarumathi M, Ignacimuthu S. Wound healing potential of *Tragia involucrata* extract in rats. Fitoterapia 2006; 77: 300-2.
- 107. Diwan PV, Tillo LD, Kulkarni DR. Influence of *Tridax procumbens* on wound healing. Ind J Med Res1982; 75:460-4.

- Udupa AL, Kulkarni DR, Udupa SL. Effect of *Tridax procumbens* extracts on wound healing. Int J Pharmacognosv. 1995; 33: 37-40.
- 109. Taranalli AD, Kuppast IJ. Study of wound healing activity of seeds of *Trigonella foenum-graecum* in rats. Ind J Pharm Sci 1996; 58: 117-9.
- 110. Manjunatha BK, Vidya SM, Rashmi KV, Mankani KL, et al. Evaluation of wound-healing potency of *Vernonia arborea* Hk, Ind J Pharmacol 2005; 37: 223-6.
- 111. Sidhartha P, Sarma K, Srinivasa A, Srinivasan KK, et al. Anti-inflammatory and wound healing activities of the crude alcoholic extract and flavonoids of *Vitex leucoxylon*. Fitoterapia 1990; 61: 263-5.
- 112. Hedge DA, Khosa RL, Chansouria JPN. A Study of the effect of *Wedelia calendulacea* less on wound healing in rats. Phytotherapy Res 1994; 8:439.

HEDGE DA, KHOSA RL, CHANSOURIA JPN. A STUDY OF THE EFFECT OF WEDELIA CALENDULACEA LESS ON WOUND HEALING IN RATS. PHYTOTHER RES 1994; 8:439. ROŚLINY O DZIAŁANIU GOJĄCYM

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Streszczenie

Ludność z grup etnicznych zamieszkujących różne rejony Indii tradycyjnie używa roślin do leczenia wielu dolegliwości u ludzi i zwierząt domowych. Ostatnio na świecie odnotowuje się zwiększone zainteresowanie lekami pochodzenia roślinnego. Zebrano wiele dowodów na ogromne możliwości roślin leczniczych używanych tradycyjnie w wielu społecznościach. W ciągu ostatnich pięciu lat przestudiowano ponad 13 000 gatunków. Nasz przegląd to próba porównania danych uzyskanych w trakcie badań w ciągu ostatnich kilku lat przy użyciu nowoczesnego podejścia i innowacyjnych narzędzi badawczych. Artykuł dotyczy roślin używanych tradycyjnie na gojenie ran. Podjęto próbę przeglądu roślin o właściwościach gojących, które mogłyby być z powodzeniem stosowane w praktyce leczniczej.

Słowa kluczowe: gojenie ran, składniki roślinne, działanie lecznicze