Pharmacognosy Reviews
Vol 1, Issue 2, Jul-Dec, 2007

PHCOG REV.
An official Publication of Phcog.Net

Phcog Rev.: Review Article
Potential Wound Healers from Plant Origin

Prasanna V. Habbu*, Hanumanthachar Joshi and B. S. Patil

Division of Pharmacognosy and Phytomedicine,
Department of postgraduate studies and Research
SET's College of Pharmacy,
S.R. Nagar, Dharwad-02, Karnataka, India.
*Author for correspondence*Prasherbs@yahoo.com, Phone: 944822494*
**** Corresponding Author***

ABSTRACT

Herbal medicine (medicinal plants, polyherbal formulations) is still the mainstay of about 75-80% of world population, mainly in the developing countries for primary health care. Wound is a loss of cellular and anatomic or functional continuity of living tissues. Wound healing proceeds in three interrelated dynamic phases, irrespective of the wound type and degree of tissue damage. This sequence of physiological events occurs by a process of connective tissue repair. In view of this a detailed review of literature was carried out on natural prohealers, phytoconstituents, polyherbal formulations and various nutraceuticals responsible for wound healing activity, with special emphasis on different stages of wound healing, which could be of enormous help in managing and treating various types of wounds.

KEY WORDS: formulations, nutrients, phytochemicals, pro-healers, wound healing,

INTRODUCTION

Wounds are visible results of individual cell death or damage. It is a disruption of tissue integrity that is typically associated with a loss of substance. Deeper injuries to the muscle-tissue, the skeletal system or the inner organs are defined as complicated wounds. In addition pressure ulcers, a type of skin ulcers are also considered as wounds. Further every wound initiates the restoration of tissue integrity through formation of new structure that more or less matches the original function. Therefore wound is a loss of cellular and anatomic or functional continuity of living tissues (1). Different synthetic drugs are avaible to enhance the wound healing in modern medicine. In spite of tremendous advances in the chemical drug industry, the availability of substances capable of stimulating the process of wound repair is still limited (2). Topical antibiotics such as Neosporin, Bacitracin and combination of these two with Polymixin B, Metranidazole and Mupirocin are used to treat the skin infections and promote wound healing. Moreover the management of chronic wounds is another major problem due to the high cost of therapy and side effects (3, 4). More than 80% of the world population still depends upon traditional medicines for various skin diseases (5). Herbal medicines are crucial in wound healing since they initiate disinfection, debridement and providing a moist environment to encourage the establishment of the suitable environment for natural healing process (6). In view of this a detailed review of literature was carried out in this article on natural prohealers, phytoconstituents, polyherbal formulations and various nutraceuticals responsible for wound healing activity, with special emphasis on different stages of wound healing, which could be helpful in therapeutic practice.

Stages of wound healing

Wound healing, a complex sequence of events, is initiated by the stimulus of injury to the tissues. This sequence of physiological events occurs by a process of connective tissue repair. Every wound healing proceeds in three interrelated dynamic phases, irrespective of the wound type and degree of tissue damage. Clinically these phases are distinguished as Inflammatory or exudative phase Proliferative phase and Differentiation or regeneration phases. In every day practice, the three phases are also denoted with the abbreviated terms, cleansing phase, granulation phase and epithelisation phase. The course of wound healing is characterized by anabolic activities which are instigated in the connective tissue immediately after wounding, and which dominate the beginning of wound repair. Conditions for wound healing are more favorable when less tissue is damaged. The best prognosis for successful wound healing is found with smooth, closely abutting incision wounds without substantial tissue loss or presence of foreign bodies. In those situations when tissue defects have to be refilled, the surfaces do not lie closely adjacent to each other, new tissue called granulation tissue must be grown (7, 8, 9, 10).

I) ***The inflammatory phase/ Exudative phase***

Tissue wounding disrupts capillaries, destroys and damages cells. Blood and plasma pass in to the extravascular phase. The primary goal of repair mechanisms is the prevention of local hemorrhage. Platelets adhere to the collagenous fibers of connective tissue and aggregate with the release of vasoactive substances. Simultaneously coagulation system is activated. The process of coagulation involves numerous factors (factor I to XIII). Fibrin formation at the end of coagulation process is initiated by the catalytic activity of thrombin cleaves fibrinogen in to polypeptides. The fibrin aggregates and forms long fibers. The resulting fibrin network will later serve as scaffold for migrating fibroblasts. After one or two hours an edema is formed in response to vasoactive substances like histamine, serotonin and cytokines and also

partly due to local acidosis in the wound area. Local acidosis with O_2 depletion and increased CO_2 pressure enhances catabolism, and local accumulation of liquid in the wound area cause dilution of toxic debris. With the exudation of blood plasma, number of cells like inflammatory cells, T-lymphocytes, Leucocytes especially neutrophil granulocytes monocytes reach the wound area and are involved in wound cleansing. The amoeboid neutrophil granulocytes in particular play a central role in wound cleansing and resistance to infection. Following neutrophils macrophages play a key role in wound healing. These secrete biologically active substances, the so called growth factors and influence on subsequent phases of proliferation and tissue differentiation. Macrophage mediate conversion of macromolecules in to reasonable amino acids and glycosides, attract further macrophages, stimulate fibroblast proliferation, initiate neovascular growth and excrete lactate and derivatives of H_2O_2 in to the wound site.

II) ***The proliferative phase***

The second phase of wound healing is dominated by cell proliferation, which is aimed at generation of new replacement tissue to fill the defect. Granulation tissue was described as a temporary primitive tissue input that after having fulfilled its function is converted to regression and gradually gradually converted in to scar tissue. Formation of granulation tissue is a complex event involving Leucocytes, histocytes, and plasma cells and in particular fibroblasts that promote tissue growth through production of collagen. Fibroblasts use the fibrinous net formed during coagulation for collagen insertion. Fibroblasts arrive at the site of injury after blood clots have been resolved and necrotic tissue has been removed. The extent of granulation tissue formation is directly related the intensity of coagulation and immediate inflammation. The major function of fibroblasts is the synthesis of collagen that already begins at the 2nd day after injury and in primary haling reaches its peak activity between days 5-7. Collagen is one of the basic body proteins. Collagen synthesis occurs in several steps 1) Fibroblasts synthesize polypeptide chains from Glycin, Hydroxyproline and Hydroxylysine, 2) Three polypeptide chains are packed tightly together to form triple helix molecule procollagen, 3) Procollagen is then excreted in to extra cellular space through cellular microtubules, to form collagen fibrils and filaments of considerable tensile strength to adapt to the needs of wound area. In addition to collagen synthesis fibroblasts also produce acidic hexosamine containing mucopolysacchrides that serve as major matrix constituents and contribute to the integrity of granulation tissue. Development of granulation tissue therefore involves separation of ischemic, nonvital parts of the tissue that are then gradually eliminated through lytic processes. Vitamin C and O_2 play an important role in collagen synthesis.

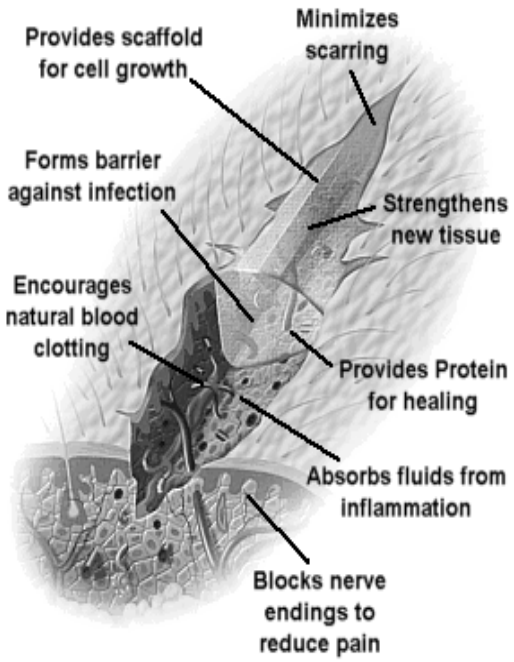
III) ***Differentiation Phase***

Maturation of collagen fibers is initiated between 6-10 days after wounding. The wound contracts under the influence of myofibroblasts, granulation tissue becomes increasingly depleted of fluid and blood vessels, begins to strengthen, and undergoes remodeling to form scar tissue. Wound healing is then completed by epithelisation, a process beginning mainly at the edges of the wound that involves the formation of new epidermal cells by mitosis and cell migration along pathways created by liquefied fibrin.

Wound contraction is remarkable physiological event (Fig.1) that leads to spontaneous closure of open lesions, i.e. it is inward movement of the intact edges of the injured tissue and decrease in the dimension of the area to its smallest possible extent. Wound contraction is mediated by fibroblasts of the granulation tissue. Fibroblasts can convert into a cell type that shares many structural and functional features with smooth muscle cells, including the formation of contractile smooth muscle protein actomyosin.

Cuticularisation is the final stage of wound healing, and processes of epithelisation are very closely related to the development and proceedings during wound granulation. The granulation tissue produces the chemostatic signals for migration of epithelial cells from the edges of the wound. Effective cell migration requires mature granulation tissue and a slippery gliding surface are prerequisites for final epidermisation. Epidermal cells that are metabolically active and capable of promoting wound healing reactions contain an unlimited potential for mitosis. Tissue specific inhibitors, called epidermal chalcones, usually control their proliferative activity. A dermal injury causes a local decrease in chalcone level due to the loss of several chalcone producing cells in the wound site. This promotes a correspondingly high mitotic activity in the basal cell layer of the epidermis and initiates the necessary cell proliferation to resurface the denuded area. The final product of healing process is a scar or replacement with healthy tissue.

Fig.1. Etiology of Wound Healing



PHCOG REV.
An official Publication of Phcog.Net

Table. No. 1. Potential medicinal plants having wound healing activity

S. No.	Botanical source	Plant part	Models / mechanism studied	Reference
1	*Buddleja globosa* (Loganiaceae)	Leaves	Improved growth of fibroblasts *in-vitro*	10
2	*Stryphanodendron polyphyllum, Stryphanodendron obovatum* (Leguminosae)	Stem	Improved epithelial proliferation in cutaneous wounds	11
3	*Terminalia arjuna* (Combertaceae)	Bark	Excision and Incision wounds	12
4	*Datura alba* (Solanaceae)	Leaves	Proepithelisation and improved burn wounds	13
5	*Portu laca oleraceae* (Portulacaceae)	Leaves	Prohealing activity by decreasing wound area and increasing tensile strength	14
6	*Desmodium tirquetrum* (Leguminosae)	Leaves	Enhanced epithelisation, increased tensile srtrength and hydroxyproline content	15
7	*Dodonaea viscosa* (Sapindaceae)	Leaves	Facilitated wound contraction and epithelisation process	16
8	*Indigofera enneaphylla* (Papilionaceae)	Aerial parts	Incision and excision wound	17
9	*Hyptis suaveolens* (Labiatae)	Leaves	Incision , excision and dead space wound	18
10	*Tinospora cordifolia* (Menispermaceae)	Stem and Leaves	Incision, excision and dead space wound	19
11	*Saussurea lappa* (Asteraceae)	Root	Incision, excision and dead space wound	20
12	*Eucalyptus globulus* (Myrtaceae)	Leaves	Increased wound contraction and tensile strength	21
13	*Argemone mexicana* (Papaveraceae)	Leaves and latex	Excision and Incision wounds	22
14	*Lawsonia alba* (Lythraceae)	Leaves	Excision and Incision wounds	23
15	*Gentiana luteae* (Genitianaceae)	Whole plant	Incision, excision and dead space wound	24
16	*Anogeissus latifolia* (Combretaceae)	Bark	Decreased epithelisation period , increase in tensile strength and hydroxyproline content	25
17	*Ocimum sanctum* (Lamiaceae)	Leaves	Incision , excision and dead space wound	26
18	*Biophytum petersianum* (Oxalidaceae)	Aerial parts	Complement fixing activity	27
19	*Pentas lanceolata* (Rubiaceae)	Flowers	Increased granulation tissue weight, tensile strength, hydroxyproline and glucosaminoglycan content	28
20	*Hylocereus undatus* (Cactaceae)	Leaves,rind,fruit pulp and flowers	Incision,excision wound and nature of granulation tissue	29
22	*Calotropis gigantea* (Ascletiadaceae)	Latex	Reduced the coagulation time of citrated plasma and promoted blood coagulation	30
23	*Hippophae rhamnoides* (Elaeagnaceae)	Leaves	Cutaneous excision punch wound model	31
24	*Pterocarpus santalinus* (Papilionaceae)	Wood	Punch and burn wound model in normal and diabetic rat	32
25	*Eleusine coracana And Paspalum scrobiculatum* ((poaceae)	Flour paste	Increased protein and collagen content and decreased lipid peroxides	33

26	*Gentiana luteae* (Genitianaceae)	Whole plant	Incision, excision and dead space wound	24
27	*Anogeissus latifolia* (Combretaceae)	Bark	Decreased epithelisation period , increase in tensile strength and hydroxyproline content	25
28	*Ocimum sanctum* (Lamiaceae)	Leaves	Incision , excision and dead space wound	26
29	*Biophytum petersianum* (Oxalidaceae)	Aerial parts	Complement fixing activity	27
30	*Pentas lanceolata* (Rubiaceae)	Flowers	Increased granulation tissue weight, tensile strength, hydroxyproline and glucosaminoglycan content	28
31	*Hylocereus undatus* (Cactaceae)	Leaves,rind,fruit pulp and flowers	Incision,excision wound and nature of granulation tissue	29
32	*Calotropis gigantea* (Ascletiadaceae)	Latex	Reduced the coagulation time of citrated plasma and promoted blood coagulation	30
33	*Hippophae rhamnoides* (Elaeagnaceae)	Leaves	Cutaneous excision punch wound model	31
34	*Pterocarpus santalinus* (Papilionaceae)	Wood	Punch and burn wound model in normal and diabetic rat	32
35	*Eleusine coracana And Paspalum scrobiculatum* ((poaceae)	Flour paste	Increased protein and collagen content and decreased lipid peroxides	33
36	*Butea monosperma* (Papilionaceae)	Bark	Increased cellular proliferation and collagen synthesis at the wound site increased DNA, total protein and total collagen content of granulation tissues.	34
37	*Celosia argentea* (Amaranthaceae)	Whole plant	Burn wound model	35
38	*Ocimum gratissimum* (Lamiaceae)	Leaves (wound dressing)	Wound dimension and wound morphometry were studied	36
39	*Carica papaya* (Caricaceae)	Fruit pulp	Infected burns Reduced the severity of local inflammation in burn wound	37, 38
40	*Punica gratum* (Punicaceae)	Peels	Excision wound model	39
41	*Curcuma longa* (Zingiberaceae)	Rhizome	Effect of curcumin on wound healing activity exposed to whole body Gamma radiation	40
42	*Ageratum conyzoides* (Astereceae)	Leaves	Wound dressing– increased wound contraction	41
43	*Aloe vera* (Liliaceae)	Gel of leaves	Burn wounds, Re-epithelization, Decreased the wound diameter, improved tensile strength, Increased the collagen content of the granulation tissue and degree of cross linking	42-58
44	*Thymus vulgaris* (thymus oil) (Lamiaceae)	Essential oil	Burn wound	59
45	*Cinnamomum zeylanicum* (Lauraceae)	Bark	Incision, excision wound and dead space wound	60
46	*Aristolochia bracteolate* (Aristolochiaceae)	Leaves	Incision, excision wound and dead space wound	61
47	*Hamelia patens* (Rubiaceae)	Whole plant	Double incision wound	62
48	*Musa paradisica* (Musaceae)	Leaf dressing	Partial thickness burn wound	63

49	*Apple and beet*	Fruit pectins	Burn wounds (II-IIIA)	64
50	*Lithospermum erythrorhison* (fam)	Root	Healing impaired diabetic mice	65
51	*Alkanna tinctoria* (Boraginaceae)	Root	Excellent wound healing	66, 67
		Root	Partial thickness and hot olive oil burn wound	
52	*Copiafera langsdorffi* (Leguminosae)	Bark	Tensile strength in healing incised wounds	68
53	*Vernonia scorpioides* (Asteraceae)	Leaves	Improved regeneration and organization of the new tissue	69
54	*Vitis vinifera* (Vitaceae)	Seeds (Reservatrol)	Potentially up regulated oxidant and VEGF expression in human keratinocytes, Topical application accelerated wound contraction in dermal wound	70, 71
55	*Terminalia chebula* (Combertaceae)	Leaves	Improved rate of contraction and decreased period of epithelisation	72
56	*Panax ginseng* (Araliaceae)	Root	GinsenosideRb2 stimulated epidermal cell proliferation	73
57	*Scrophularia nodosa* (Scrphulariaceae)	Seed pods	Stimulated the growth of human dermal fibroblasts in vitro	74
58	*Echinaceae pallida* (Asteraceae)	Root	Excision wound	75
59	*Heliotropium indicum* (Boraginaceae)	Whole plant	Excision and incision wound	76
60	*Chromolaena odorata* (Eupolin), (Asteraceae)	Leaves	Enhanced growth of fibroblasts, endothelial cells, proliferation of fibroblasts, endothelial cells and keratinocytes, stimulation of keratinocyte migration in an *in-vitro* wound assay	77-81
61	*Piperomia galoides*	Whole plant	Incision wound	82
62	*Cimicifuga racemosa* (Ranunculaceae)	Rhizomes	Inhibition of collagenolytic activity	83
63	*Thespesia populnea* (Malvaceae)	Fruit	Excision and incision wound	84
64	*Opuntia ficus-indica* (Cactaceae)	Stem	Prohealing activity	85
65	*Hypericum patulum* (Hyperaceae)	Leaves	Excision and incision wound	86
66	*Hypericum hookarianum* (Hyperaceae)	Leaves and stem	Excision and incision wound	87
67	*Hydenocarpus pentandra* (Flacourtiaceae)	Seed	Incision and dead space wound	88
68	*Leucaus lavandulaefolia* (labiatae)	Whole plant	Excision and incision wound	89
69	*Solanum tuberosum* (Solanaceae)	Tuber	Excision wound	90
70	*Choerospondias axillaries* (Anacardiaceae)	Bark	Second degree burn wound	91
71	*Tridax procumbens* (Astraceae)	Leaf juice	Excision and incision wound	92
		Leaves	Dead space wound	93
			Burn wound	

		Leaves		94
72	*Calendula officinalis* (Compositae)	Flower	Stimulated regeneration and epithelisation of tissue at the wound site	95
73	*Allamnanda cathartica* (Apocyanaceae) and *Laurus nobilis* (Lauraceae)	Leaves	Excision Incision wound	96
74	*Sphaeranthus indicus* (Astraceae)	Arial parts	Enhanced the rate of wound contraction and period of epthelisation	97
75	*Plagiochasma appendiculatum* (Aytoniaceae)	Whole plant	Increased wound contraction and tensile strength	98
76	*Chamaemelum nobile* (Asteraceae)	Flower	Decrease in area and drying tendency	99
77	*Pterocarpus marsupium* (Papilionaceae)	Stem bark	Excision, Incision and dead space wound model	100
78	*Oxalis corniculata* (Oxalidaceae)	Whole plant	Excision , incision and dead space wound model	101
79	*Argyreia speciosa* (Convolvulaceae)	Root	Incision, Excision and dead space wound.	102
80	*Centella asiatica* (Apiaceae)	Leaves	Increased the percentage of collagen in human skin fibroblasts, Increased cellular proliferation and collegen synthesis at wound site in open wounds	103-109
81	*Calotropis procera* (Asclepiadaceae)	Latex	Increased collagen, DNA, protein synthesis and epithelisation	110

Table No.2. Herbal formulations with wound healing activity

S.No.	Name of the formulation	Wound model/mechanism	Reference
01	Darvhi Ghrita (Herbal formulation)	Incision and excision wound model	111
02	Mulathiadi Ghrita (Ghee based herbal formulation)	Incision and excision wound model	112
03	Himax ointment and Lotion (Herbal formulation)	Incision and excision wound model	113
04	Septilin formulation (Proprietary preparation)	Incision and excision wound model	114
05	Hepatogard formulation (Phytopharmaceutical product)	Incision wound model	115
06	Aekol preparation (artificial seabuck thorn oil)	Incision and excision wound model	116
07	Chandanadi Yamaka (Panchagavya based formulation)	Incision and excision wound model, histological study reveals good keratinisation, epithelisation and angiogenesis	117

Table No. 3. Phytoconstituents possessing wound healing activity

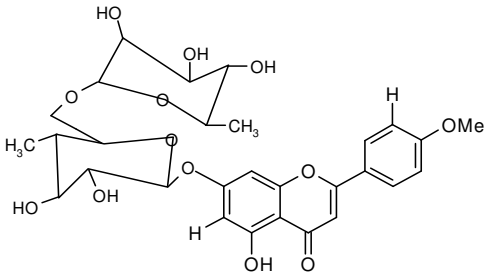
Name of the plant	*Plant part*	Phytoconstituents	Reference
Buddleja globosa	Leaves	Verbascoside, Echinacoside, Linnamarin, Luteolin and 6-hydroxy luteolin	10
Lawsonia alba	Leaves	Lawsone	23
Anogeissus latifolia	Bark	(+)-Leucocyanidin, Ellagic acid, Flavellagic acid	26
Biophytum petersianum	Aerial parts	Rhamnogalacturonan, Xylogalacturonan	28
Calotropis gigentea	Latex	Cysteine proteases	31
Centella asiatica	Leaves	Asiaticoside, Asiatic acid, madecassic acid	35
Punica gratum	Dried peels	Phenolic compounds: gallic acid and Catechins	47
Curcuma longa	Rhizomes	Curcumin	48
Aloe vera	gel/juice	Glycoprotein fraction (G1G1M1 D12)	64
Alkanna tinctoria	Roots	Alkannin esters of beta, beta-dimethyl acrylic acid, beta, acetoxy-isovaleric acid, isovaleric acid and angelic acid	74
Copiafera langsdorffi	Bark	Oleoresin	76
Vitis vinifera	Seeds	Reservatrol (Proanthocyanidin)	79
Panax ginseng	Roots	Ginsenoside Rb2	81
Scrophularia nodosa	Dried seed pods	Acylated irridoid glycosides: Scpolioside A, Schrophuloside A	82
Chromolaena odorata	Leaves	Phenolic acids; Protocatechuic acid, P-hydroxy benzoic acid, P-coumaric acid, ferulic acid vannilic acid, Lipophilic flavanoid aglycones	89
Piperomia galiodes	Whole plant	Alpha-bisabolol and alpha terpeniol	90
Cumicifuga racemosa	Rhizomes	Fukinolic acid and Cimicifugic acids A B C.	91
Plantago major	Leaves	Flavonoids, Caffeic acid derivatives, Long chained saturated primary alcohols, Pectic polysaccharides.	118

Table No. 4 . Nutritional Supplements useful in wound healing

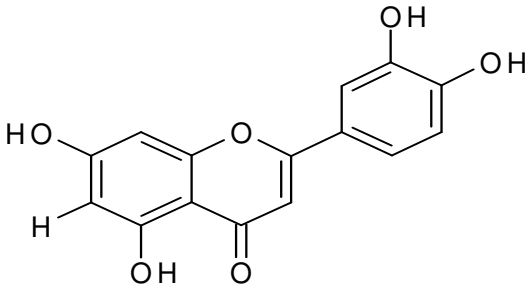
S.No	Nutritional supplement	Activity	Reference
01	Bromelain (Enzyme derived from pine apple stem)	Accelerates healing of soft tissue, reduces swelling, bruising, healing time and pain	119
02	Thaimine (Vitamin B_1	Accelerates wound healing	120
03	Pantothenic acid (Vitamin B_5)	Accelerates wound healing	121
04	Vitamin C	Required to make collagen and speed healing of wounds	122
05	Zinc	Reduced the healing time of surgical wound	123
06	Ornithine alpha glutarate	Improves wound healing in burn wounds	124
07	Vitamin A	Improves wound healing in surgical wounds	125
08	Vitamin E	Decreases the formation of unwanted adhesions following a surgical wound	126
09	Copper	Plays important role in cross linking connective tissue and is required to promote wound healing.	127
10	Glucosamine	Improved tissue healing	128
11	Arginine	Increases protein synthesis and improves wound healing	129
12	Carnosine	Promotes wound healing	130

PHCOG REV.
An official Publication of Phcog.Net

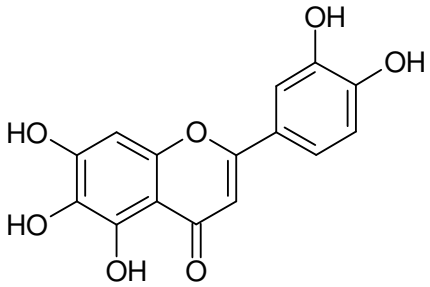
Structures Of Phytoconstituents Possessing Wound Healing Activity



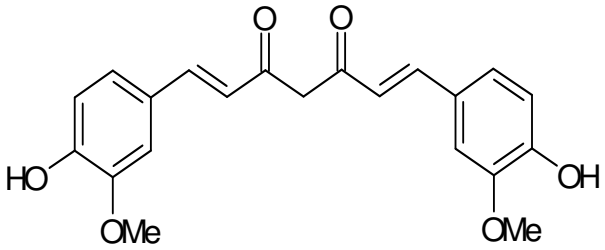
Linarin(acacetin-7-O-rutinoside)



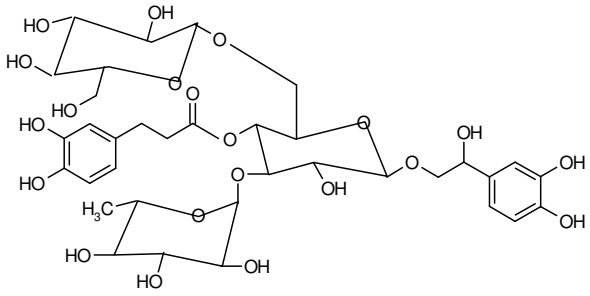
Luteolin



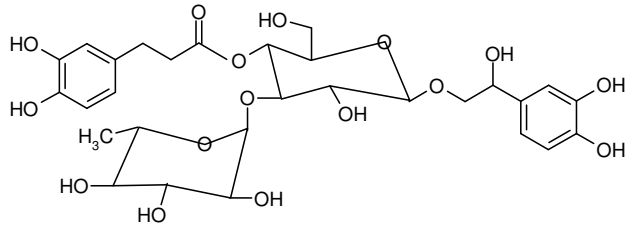
6-hydroxyluteolin



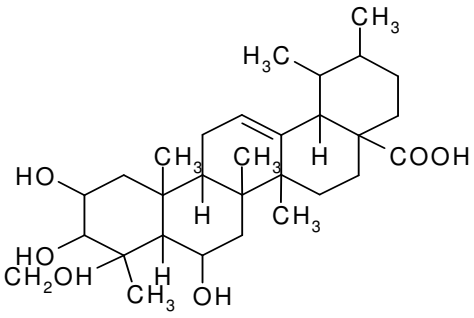
Curcumin



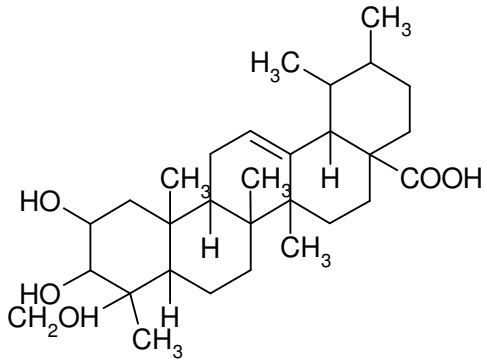
Echinacoside



Verbascoside

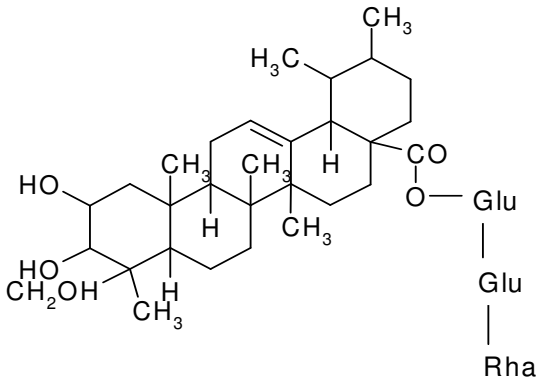


Madecassic acid

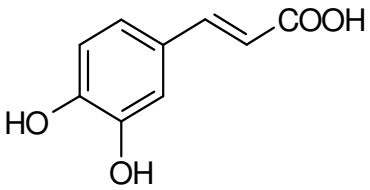


Asiatic acid

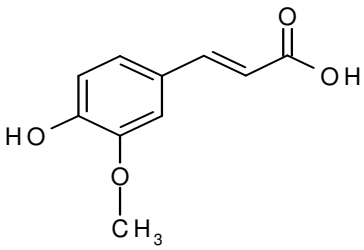
PHCOG REV.
An official Publication of Phcog.Net



Asuaticoside



Caffeic acid



Ferulic acid

Management and treatment of wound using various medicinal plants and their derivatives has been n clinical practice since time immemorial. A good number of medicinal plants especially those mentioned in traditional systems of medicine have been well exploited and their usefulness has been now established. Hence it was worthwhile to garner knowledge on these medicinal plants and derivatives used for treating wounds with special reference to their mechanism of action and or wounds models in which they have exerted profound pro healing activities. For the past few decades there has been an awakening in the developing and developed countries for the revival and full utilization of traditional systems of medicine in many human ailments including natural pro-healers. Medicinal plants and herbal medicines known in different traditional systems of medicine are vast treasure house for research and development. This systematic review of medicinal plants and derivatives possessing wound-healing activities can be of enormous use for researchers and medical practitioners working in the areas of management of wounds.

The efficacy of these drugs has been well established by scientific investigations utilizing proper scientific methods through modern parameters (Table.1 & 3). By conducting research on herbal medicines in a systematic way by chemical fractionation, isolation and biological evaluation it is possible to find new remedies for various ailments. Ayurveda has some remedies for treating various types of wounds and other wound associated complications. The major herb is selected to design a formulation according to the symptoms of the disease and the other herbs are involved in prevention of the major symptoms as well as the clinical complications that may be associated with the use of the chief herb (Table.2). Nutraceuticals are found to support the wound healing by stimulating or modulating the immune system. Several studies have proved the efficacy of macro and micronutrients in the management of surgical wounds (Table.4). These nutrients may be the key to fine-tuning the eternal formulas for specific clinical scenarios.

The utilization of such a potential is necessary for the economic well being of the society with proper policy decision and motivated scientific personnel. The drug potential of medicinal plants can be tapped for health, wealth and happiness of mankind. Where God has allowed a disease to flourish, he should have arranged for the drug to be found in the neighborhood. We have only to discover it from NATURE.

REFERENCES

1. M.S. Charde, S.V. Fulzele, P.M. Satturwar, S.B. Joshi, A.V. Ksature, A.K. Dorle. Study on wound healing activity of Mulathiadi ghrita. *J. Pharma. Res.* **4(1):** 8-12 (2005).
2. A.L. Udupa, D.R. Kulkarni, S.L. Udupa. Effect of *Tridax procumbens* extracts on wound healing. *Int J. Pharmacol.* **33:** 37-40 (1995).
3. B.H. Porras-Reyes, W.H. Lewis, J. Roman, L. Simchowitz, T.A. Mustoe. Enhancement of wound healing by the alkaloid tapsine defining mechanism of action. *Soci. Experi. Boil. Med.* **203:** 18-25 (1993).
4. D.D. Suh, I. P. Schwartz, D.A. Canning, H.M. Snyder, S.A. Zderic, A.J. Krisch. Comparison dermal and epithelial approaches to laser tissue soldering for skin flap closure. *Laser. surg. Med.* **22:** 268-74 (1998).
5. K. Shamuga priya, A. Gnanamani, N. Radhakrishnan., Mary babu. Healing potential of *Datura alba* on burn wounds in albino rats. *J. Ethnopharmacol.* **83:** 193-99 (2002).
6. S.K. Purna, M. Babu. Collagen based dressings- a review. *Burns.* **26:** 54-62 (2000).

7. S.H. Baie, K.A. Sheikh. The wound healing properties of *Channa striatus*-cetrimide cream tensile strength measurement. *J. Ethnopharmacol.* **71:** 93-100 (2000a).
8. S.H. Baie, K.A. Sheikh. The wound healing properties of *Channa striatus*-cetrimide cream Wound contraction and glycosaminoglycan measurement. *J. Ethnopharmacol*. **73:** 15-30 (2000b).
9. R. Ross. Inflammation, cell proliferating and connective tissue formation in wound repair, In: T.K. Hunt: *wound healing and wound infection.* Appleton-centurry-Crofts, New York.
10. A.Y. Mensah, J. Sampson, P.J. Houghton, P. J. Hylands, J. Westbrook, M. Dunn M.A., Hughes, G.W. Cherry. Effects of *Buddleja globosa* leaf and its constituents relevant to wound healing. *J. Ethnopharmacol.* **77:** 219-26 (2001).
11. C. L. Gisley, C.C.S. Andreia, V.N. Celso, P.D. Benedito, H. Luzmerina, P.D.Joao Carlos. Influence of extracts of *Stryphnodendron polyphyllum* Mart., and *Styphnodendron obovatum* Benth,. on the cicatrisation of cutaneous wounds in rats. *J. Ethnopharmacol.* **99:** 265-72 (2005).
12. M.M. Rane, S.A. Mengi. Comparative effect of oral administration and topical application of alcoholic extract of *Terminalia arjuna* bark on incision and excision wounds in rats. *Fitoterpia.* **74:** 553-58 (2003).
13. K. Shanmugapriya, A. Gnanamani, N. Radhakrishnan, M. Babu. Healing potential of *Datura alba* on burn wounds in albino rats. *J. Ethnopharmacol.* **83:** 193-99 (2002).
14. A. N. Rashed, F.U. Afifi, A.M. Disi. Simple evaluation of the wound healing activity of a crude exract of *portulaca oleraceae* L. (growing in Jordan), in Mus musculus JV-1. *J. Ethnopharmacol.* **88 (2-3):** 131-36 (2003).
15. A. Shirwaikar, S. Jahagirdar and A. L Udupa. Wound healing activity of *Desmodium triquetrum* leaves. *Ind. J. Pharm. Sci.* **65(5):** 461-64 (2003).
16. S.D. Joshi, M.B. Aravind, K. Ashok, V.P. Veerapur, C.S. Shastry. Wound healing activity of *Dodonaea viscosa* leaves. *Indian Drugs.* **40(9):** 549 (2003).
17. S. Hemalatha, N. Subramanian, V. Ravichandran and K. Chinnaswamy. Wound healing activity of *Indigofera enneaphylla. Ind. J. Pharm. Sci.* 331-33 (2001).
18. A. Shirwaikar, R. Shenoy, A.L. Udupa, S.L. Udupa, S. Shetty. Wound healing property of ethanolic extract of leaves of *Hyptis Suaveolens* with supportive role of antioxidant enzymes. *Ind. J. Expt. Biol.* **41:** 238-41(2003).
19. T. Shanbhag, S. Shenoy, M.C. Rao. Wound healing profile of *Tinospora cordifolia. Indian Drugs.* **42(2):** 217-21 (2005).
20. M.S. Ganachari, S. Kumar, and A. Patel. Wound healing activity of *Saussurea lappa* roots. *Indian Drugs.* **42(5):** 295-98 (2005).
21. V.I. Hukkeri, R.V. Karadi, K.S. Akki, R.V. Savadi, B. Jaiprakash, I. J. Kuppast, M.B. Patil. Wound healing property of *Eucalyptus globules* L. leaf extract. *Indian Drugs.* **39(9):** 481-83 (2002).
22. T. Ghosh., G. K. Das, A. Bose, B. R. Panda. Wound healing properties of *Argemone mexicana. Ind J. Nat. Prod.* **20(4):** 3-6 (2004).
23. S.D. Mandawagde, K.S. Patil. Wound healing potential of some active principles of *Lawsonia alba* Lam. Leaves. *Ind. J. Pharm. Sci.* **65(4):** 390-94 (2003).
24. A. Mathew, A.D. Taranalli, S.S. Torgal. Evaluation of anti-inflammatory and wound healing activity of *Gentiana lutea* rhizome extracts in animals. *Pharma. Biol.* 42: 8-12 (2004).
25. R. Govindarajan, M. Vijayakumar, C. Venkateshwararao, A. Shirwaikar, S. Mehrotra and P. Pushpangadan. Healing potential of *Anogeissus latifolia* for dermal wounds in rats. *Acta. Pharm.* **54(4):** 331-38 *(*2004).
26. S.L. Udupa, S. Shetty, A.L. Udupa, S.N. Somayaji. Effect of *Ocimum sanctum* Linn. on normal and dexamethasone suppressed wound healing. *Ind. J. Exp. Biol.* **44(1):** 49-54 (2006).
27. K.T. Inngjerdingen, A. Coulibaly, D. Diallo, T.E. Michaelsen, B. S. Paulsen. A complement fixing polysaccharide from *Biophytum petersianum* Klotzsch, a medicinal plant from Mali, West Africa. *Biomacromolecules.* **7(1):** 48-53 (2006).
28. B.S. Nayak, B. Vinutha, B. Geeta, B. Sudha. Experimental evaluation of *Pentas lanceolata* flowers for wound healing activity in rats. *Fitoterapia.* **76(7-8):** 671-75 (2005).
29. G.R.M. Perez, S.R. Vargas, H.Y.D. Ortiz. Wound healing properties of *Hylocereus undatus* on diabetic rats. *Phytother Res.* **19(8):** 665-68 (2005).
30. R. Rajesh, C.D. Raghavendra Gowda, A. Nataraju, B.L. Dhananjaya, K. Kempraju B.S. Vishwnath. Procoagulant activity of *Calotropis gigantea. Toxicon.* **46(1):** 84-92 (2005).
31. A. Gupta, R. Kumar, K. Pal, P.K. Banerjee, R.C. Sawhney. A preclinical study of the effects of seabuckthorn *(Hippophae rhamnoides* L.) leaf extract on cutaneous wound healing in albino rats. *Int. J. Low. Extrem. Wounds.* **4(2):** 88-92 (2005).
32. T.K. Biswas, L.N. Maity, B. Mukherjee. Wound healing potential of *Pterocarpus santalinus* linn. a pharmacological evaluation. *Int. J. Low. Extrem. Wounds.* **3(3):** 143-50 (2004).
33. P.S. Hegde, B. Anitha, T.S. Chandra. In vivo effect of whole grain flour of finger millet *(Eleusine coracana)* and kodo millet *(Paspalum scorbiculatum)* on rat dermal wound healing. *Ind. J. Exp. Biol.* **43(3):** 254-58 (2005).
34. M. Sumitra, P. Manikandan, L. Suguna. Efficacy of *Butea monosperma* on dermal wound healing in rats. *Int. J .Biochem. Cell Biol.* **37(3):** 566-73 (2005).
35. K.S. Priya, G. Armugam, B. Rathinam, A. Wells, M. Babu. *Celosia argentea* Linn. Leaf extract improves wound healing in a rat burn wound model. *Wound Repair Regen.* **12(6):** 618-25 (2004).
36. F.C. Osuagwa, O.W. Oladejo, I.O. Imosemi, B.A. Adewoyin, A. Aiku, O.E, Ekpo, O.O. Oluwadara, P.C. Ozegbe, E.E. Akang. Wound healing activities of methanolic extracts of *Ocimum gratissimum* leaf in wistar rats- a preliminary study, *Afr. J. Med. Med. Sci.* **33(1):** 23-26 (2004).
37. I.F. Starley, P. Mohammed, G. Schneider, S.W. Bickler. The treatment of pediatric burns using topical papaya. *Burns.* **25(7):** 636-39 (1999).
38. E.V. Mikhal'chik, A.V. Ivanova, M.V. Anurov, S.M. Titkova, L.Y. Pen'kov, Z.F. Kharaeva, L.G. Korkina. Wound healing effect of papaya-based preparation in experimental thermal trauma. *Bull. Exp. Biol. Med.* **137(6):** 560-62 (2004).
39. K.N. Murthy, V.K. Reddy, J.M. Veigas, U.D. Murthy. Study on wound healing activity of *Punica gratum* peel. *J. Med. Food.* **7(2):** 256-59 (2004).
40. G.C. Jagetia, G.K. Rajanikant. Role of curcumin, a naturally occurring phenolic compound of turmeric in accelerating the repair of excision wound, in mice whole body exposed to various doses of gamma radiation. *J. Surg. Res.* 120(1): 127-38 (2004).
41. O.W. Oladejo, I.O. Imosemi, F.C. Osuagw, O.O. Oyedele, O.O. Oluwadara, O.E. Ekpo, A. Aiku, O. Adewoyin, E.E. Akang. A comparative study of the wound healing properties of honey and *Ageratum conyzoides. Afr. J. Med. Med Sci.* **32(2):** 193-96 (2003).
42. M. Rodrriguez-Bigas, N.I. Cruz, A. Suarez. Comparative evaluation of *Aloe vera* in the management of burn wounds in guinea pigs. *Plast. Reconstr. Surg.* **81(3):** 386-89 (1988).
43. R.H. Davis, M.G. Leitner, J. M. Russo, M. E. Byrne. Wound healing. Oral and topical activity of *Aloe vera. J. Am. Padiatr. Med. Assoc.* **79(11):** 559-62 (1989).
44. J.E. Fulton. The stimulation of post dermabrasion wound healing with stabilized *Aloe vera* gel-polyethylene oxide dressing. *J. Dermatol. Surg. Oncol.* **16(5):** 460-67 (1990).
45. R.H. Davis, J.J. Donata, G.M. Hartman, R.C. Hass. Antiinflammatory and wound healing activity of a growth substance in *Aloe vera. J. Am Padiatr. Med. Assoc.* **84(2):** 77-81 (1994).
46. R.H. Davis, W.L. Parker, R.T. Samson, D.P. Murdoch. Isolation of a stimulatory system in an Aloe extract. *J. Am. Padiatr. Med. Assoc.* **81(9):** 473-78 (1991).
47. R.H. Davis, J.J. DiDonato, R.W. Johnson, C.B. Stewart. *Aloe vera*, hydrocortisone, and sterol influence on wound tensile strength and antiinflammation. *J. Am. Padiatr. Med. Assoc.* **84(12):** 614-21 (1994).
48. V. Visuthikosol, B. Chowchuen, Y. Sukwanarat, S. Sriurairatana, V. Boonpucknavig. Effect of *Aloe vera* gel to healing of burn wound a clinical and histologic study. *J. Med. Assoc. Thai.* **78(8):** 403-09 (1995).
49. J. P. Heggers, A. Kucukcelebi, D. Listengarten, J. Stabanau, F. Ko, L.D. Broemeling, M.C. Robson, W.D. Winters. Beneficial effect of *aloe* on wound healing in an excision wound model. *J. Altern. Complement. Med.* **2(2):** 271-77 (1996).
50. J.P. Heggers, H. Elzaim, R. Garfield, R. Goodheart, D. Listengarten, J. Zhao, L.G. Philips. Effect of *Aloe vera*, nitroglycerine, and L-NAME on wound healing in the rat excisional model**.** *J. Altern. Complement. Med.* **3(2):** 149-53. (1997).
51. P. Chitra, G. B. Sajitlal, G. Chandrakasan. Influence of *Aloe vera* on the glycosaminoglycans in the matrix of healing dermal wounds in rats, *J. Ethnopharmacol.* **59(3):** 179-86 (1998).
52. P. Chitra, G. B. Sajitlal, G. Chandrakasan. Influence of *Aloe vera* on the healing of dermal wounds in diabetic rats. *J. Ethnopharmacol.* **59(3):** 195-201 (1998).
53. P. Chitra, G. B. Sajitlal, G. Chandrakasan. Influence of *Aloe vera* on collagen characteristics in healing dermal wounds in rats. *Mol. Cell. Biochem.* **181(1-2):** 71-76. (1998).
54. P. Chitra, G. B. Sajitlal, G. Chandrakasan. Influence of *Aloe vera* on collagen turnover in healing of dermal wounds in rats. *Indian J. Exp. Biol.* **36(9):** 896-901. (1998).
55. J. Somboonwong, S. Thanamittramanee, A. Jariyapongskull, S. Patumraj. Therapeutic effects of *Aloe vera* on cutaneous microcirculation and wound healing in second degree burn model in rats. *J. Med. Assoc. Thai.* **83(4):** 417-25 (2000).
56. S.W. Choi, B W. Son, Y. S. Son, Y. I. Park, S.K. Lee, M.H. Chung. The wound healing effect of a glycoprotein fraction isolated from *Aloe vera. Br. J. Dermatol.* **145(4):** 535-45 (2001).
57. M.J. Mulle,r M.A. Hollyoak, Z. Moaveni, T. L. Brown, D.N. Herndon, J. P. Heggers. Retardation of wound healing by silver sulfadiazine is reversed by *Aloe vera* and nystatin. *Burns.* 29(8), 834-36 (2003).
58. K.M. Abdullah, A. Abdullah, M. L. Johnson, J. J. Bilski, K. Petry, D.A. Redmer, L. P. Reynolds, A.T. Grazul-Bilska. Effects of *Aloe vera* on gap junctional intercellular communication and proliferation of human diabetic and nondiabetic skin fibroblasts. *J. Altern. Complement. Med.* **9(5):** 711-18 (2003).
59. N. Dursun, N**.** Liman, I. Ozyazgan, I. Gunes, R. Saraymen. Role of Thymus oil in burn wound healing. *J. Burn Care Rehabil.* **24(6):** 395-99 (2003).
60. J.V. Kamath, A.C. Rana, A.R. Chowdhury. Prohealing effect of *Cinnamomum zeylanicum* bark. *Phytother. Res.* **17(8):** 970-72 (2003).

61. A. Shirwaikar A.P. Somahekar, A.L. Udupa, S.L. Udupa, S. Somashekar. Wound healing studies of *Aristolochia bracteolate* Lam, with supportive action of antioxidant enzymes. *Phytomedicine.* **10(6-7):** 558-62 (2003).
62. A. Gomez-Beloz, J.C. Rucunski, M.J. Balick, C. Tipton. Double incision wound healing bioassay using *Hamelia patens* from El Salvador. *J. Ethnopharmacol.* **88(2-3):** 169-73 (2003).
63. M.A. Gore, D. Akolekar. Evaluation of Banana leaf dressing for partial thickness burn wounds, *Burns.* **29(5):** 487-92 (2003).
64. E.B. Lazareva, T.G. Spiridonova, E.N. Chernega, L.G. Plesskaia, I.V. Grunenkova, S.V., Smirnov, D.D. Menshikov. Topical pectins for the treatment of burn wounds, *Antibiot. Khimioter.* **47(9):** 9-13 (2002).
65. N. Fujita, I. Sakaguchi, H. Kobayashi, N. Ikeda, Y. Kato, M. Minamino, M. Ishii. An extract of the root of *Lithospermum erythrorhison* accelerates wound healing in diabetic mice. *Biol. Pharm. Bull.* 26(3): 329-35 (2003).
66. V.P. Papageorgiou. Wound healing properties of napthoquinone pigments from *Alkanna tinctoria. Experientia.* **34(11):** 1499-1501 (1978).
67. Z. Ogurtan, F. Hatipoglu, C. Ceylan, The effect of *Alkana tinctoria* Tausch on burn wound healing in rabbits. *Dtsch. Tierarztl. Wochenschr.* **109(11):** 481-85 (2002).
68. L.A. Paiva, de Alencar, K. M. Cunha, F.A. Santos, N.V. Gramosa, E.R. Silveria, V.S. Rao. Investigation on the wound healing activity of oleo-resin from *Copaifera langsdorffi* in rats. *Phytother Res.* 16(8): 737-39 (2002).
69. S.N. Leite, G. Palhano, S. Almedia, M.W. Biavatti. Wound healing activity and systemic effects of *Vernonia scorpoides* extract in guinea pig. *Fitoterapia.* **73(6):** 496-500 (2002).
70. S. Khanna, S. Roy, D. Bagchi, M. Bagchi, C.K. Sen. Upregulation of Oxidant induced VEGF expression in cultured keratinocytes by a grape seed proanthocyanidin extract, *Free. radic. Biol. Med.* 31(1): 38-42 (2001).
71. S. Khanna, M. Venojarvi, S. Roy, N. Sharma, P. Trikha, D. Bagechi, M. Bagchi, C.K. Sen. Dermal wound healing properties of redox-active grape seed proanthocyanidins. *Free. Radic. Biol Med.* 15, **33(8):** 1089-96 (2002).
72. L. Suguna, S. Singh, P. Sivkumar, P. Sampath, G. Chandrakasan. Influence of *Terminalia chebula* on dermal wound healing in rats. *Phytother Res.* **16(3):** 227-31 (2002).
73. S. Choi, Epidermis prolferative effect of the *Panax ginseng* ginsenoside Rb_2. *Arch Pharm Res.* **25(1):** 71-76 (2002).
74. P.C. Stevenson, M.S. Simmonds, J. Sampson, P.J. Houghton, P. Grice. Wound healing activity of irridoid glycosides from *Scrophularia nodosa. Phytother. Res.* **16(1):** 33-35 (2002).
75. E. Speroni, P. Govoni, S. Guizzardi, C. Renzulli, M.C. Guerra, Antiinflammatory and cicatrizing activity of *Echinacae pallida* Nutt. Root extract. *J. Ethnopharmacol.* **79(2):** 265-72 (2002).
76. J.S. Reddy, P.R. Rao, M.S. Reddy. Wound healing effects of *Heliotropium indicum, Plumbago zelanicum and Acalypha indica* in rats. *J. Ethnopharmacol.* **79(2):** 249-251 (2002).
77. T.T. Phan, M.A. Hughes, G.W. Cherry, T.T. Le, H. M. Phan. An aqueous extract of the leaves of *Chromolaena odorata* (Eupolin) inhibits hydrated collagen lattice contraction by normal human dermal fibroblasts. *J. Altern. Complement Med.* **2(3):** 335-43 (1996).
78. T.T. Phan, M.A. Hughes, G.W. Cherry. Enhanced proliferation of fibroblasts and endothelial cells treated with an extract of the leaves of *Chromolaena odorata* (Eupolin), an herbal remedy for treating wounds. *Plast. Reconstr. Surg.* **101(3):** 756-65 (1998).
79. P.T. Thang, S. Ptrick, L.S. Teik, C.S. Yung. Antioxidant effects of the extracts of the leaves of *Chromolaena odorata* on dermal fibroblasts and epidermal keratinocytes against hydrogen peroxide and hypoxanthine-xanthine oxidase induced damage. *Burns.* **27(4):** 319-27 (2001).
80. T.T. Phan, M.A. Hughes, G.W. Cherry. Effcts of an aqueous extract from the leaves of *Chromolaena odorata* (Eupolin) on the proliferation of human keratinocytes and on their migration in an in vitro model of reepithelization. *Wound Repair Regen.* **9(4):** 305-13 (2001).
81. T.T. Phan, L. Wang, P. See, R. J. Grayer, S.Y. Chan, S.T. Lee. Phenolic compounds of *Chromolaena odorata* protect cultured skin cells from oxidative damage, implication for cutaneous wound healing. *Biol Pharm Bull.* **24(12):** 1373-79 (2001).
82. L.F. Villegas, A. Marcalo, J. Martin, I. D. Fernandez, H. Maldonado, A.J. Vaisberg, G.B. Hammond. (+)-epi-Alpha-bisabolol is the wound healing principle of *Piperomia galiodes:* investigation of the *in vivo* wound-healing activity of related terpenoides. *J. Nat. Prod.* **64(10):** 1357-59 (2001).
83. A. Kusano, Y. Seyama, M. Nagai, M. Shibano, G. Ksano. Effects of fukinolic acid and cimicifugic acid from Cimicifuga species on collagenolytic activity. *Biol. Pharm. Bull.* **24(10):** 1198-01 (2001).
84. A.N. Nagappa, B. Cheriyan, Wound healing activity of the aqueous extract of *Thespesia populnea* fruit. *Fitoterapia.* **72(5):** 503-06 (2001).
85. E.H. Park, M.J. Chun. Wound healing activity of *Opuntia ficus-indica*, *Fitoterapia.* **72(2):** 165-67 (2001).
86. P.K. Mukherjee, R. Verpoorte, B. Suresh. Evaluation of *in-vivo* wound healing activity of *Hypericum patulum* (family: hypericaceae) leaf extract on different wound model in rats. *J. Ethnopharmacol.* **70(3):** 315-21 (2000).
87. P.K. Mukherjee, B. Suresh. The evaluation of wound healing of *Hypericum hookerianum* leaf and stem extracts. *J. Altern. Complement. Med.* **6(1):** 61-69 (2000).
88. S. T. Oommen, M. Rao, C. V. Raju. Effect of oil of Hydnocarpus on wound healing. *Int. J. Lepr. Other Mycobact. Dis.* **67(2):** 154-158 (1999).
89. K. Saha, P.K. Mukherkee, J. Das, M. Pal, B.P. Saha. Wound healing activity of *Leucas lavandulaefolia* Rees. *J. Ethnopharmacol.* **56(2):** 139-44 (1997).
90. T. Suzuki, H. Tada, E. Sato, Y. Sagae. Application of sweet potato fibre to skin wound in rat. *Biol. Pharm. Bull.* **19(7):** 977-83 (1996).
91. D.D. Nguyen, N.H. Nguyen, T.T. Nguyen, T.S. Phan, V.D. Nguyen, M. Grabe, R. Johansson, G. Lindgren, N.E. Stjernstrom, T.A. Soderberg. The use of water extract from the bark of *Choerospondias axillaries* in the treatment of second degree burns. *Scand J. Plast. Reconstr. Surg. Hand Surg.* **30(2):** 139-44 (1996).
92. P.V. Diwan, L.D. Tillo, D.R. Kulkarni. Steroid depressed wound healing and *Tridax procumbens. Ind. J. Physiol. Pharmacol.* **27(1):** 32-36 (1983).
93. G. Babu, Sanjeeva and K.L. Bairy. Effect of *Tridax procumbens* on burn wound healing. *Indian Drugs.* **40(8):** 488-91 (2003).
94. S.L. Udupa, A. L. Udupa, D.R. Kulkarni. Influence of *Tridax procumbens* on lysyl oxidase activity and wound healing. *Planta Med.* **57(4):** 325-27 (1991).
95. E. Klouchek-popova, A. Popova, N. Pavlova, S. Krusteva. Influence of the physiologiclal regeneration and epithelisation using fractions isolated from *Calendula officinalis. Acta. Physiol. Pharmacol. Bulg.* 8(4): 63-67 (1982).
96. N. Shivanand, N. Poorna, S. Steve. B. Vidyasagar, A. Andrew. Evaluation of wound healing activity of *Allamanda cathartica*. L. and *Laurus nobilis.* L. *BMC. Compl Altern. Medicine.* **6:** 12-16 (2006).
97. S. Furzana, S. Reberan, A. Mahammad, A. Syediqbal, Z. Navaid. Healing potential of Cream containing extract of *Sphaeranthus indicus* on dermal wound in guinea pigs. *J. Ethnopharmaco.l* **107 (2):** 161-63 (2006).
98. S. Meenakshi, G. Raghavan, Virendranath., S. R. Ajaykumar, M. Shanta. Antimicrobial, wound healing and antioxidant activity of *Plagiochasma appendiculatum. J. EthnoPharmacol.* **107(1):** 67-72 (2006).
99. H.J. Glowania, C. Raulin, M. Swoboda. Effect of Chamomile on wound healing-a clinical double-blind study. *Ind. J. Med. Res.* **75:** 460-64 (1982).
100. K.L. Mankani, V. Krishna, B. K. Manjunath, S.M. Vidya, J. Singh, Y.N. Manohar, M.K. Kumar, N.S. Pavan. Evaluation of Wound healing activity of *Pterocarpus marsupium* stem bark. *Indian Drugs.* **42 (7):** 432-36 (2005).
101. A.D. Taranalli, S.V. Tipare, Shivkumar, S.S. Torgal. Wound healing activity of *Oxalis corniculata* whole plant extract in rats. *Ind. J. Ph. Sci.* 444-46. (2004).
102. R. Kartik, S.K. Ojha, C.V. Rao, S. Mehotra, P. Puspangadan. Ethnopharmacological evaluation of *Argyreia speciosa* (Roxb) sweet for wound healing, and anti-inflammatory activity, National seminar on New millennium strategies for Quality, safety and GMP's of herbal drugs/products, NBRI, Lucknow, Nov. 11-13, pp 142. (2003).
103. R. Tenni, G. Zanaboni De, M. P. Agostini, A. Rossi, C. Bendotti, G. Cetta. Effect of triterpenoid fraction of *Centella asiatica* on macromolecules of the connective matrix in human skin fibroblast cultures. *Ital. J. Biochem.* **37(2):** 69-77 (1988).
104. L. Suguna, P. Shivakumar, G. Chandrakasan. Effects of *Centella asiatica* extract on dermal wound healing in rats. *Ind. J. Exp. Biol.* 34, 1208-11 (1996).
105. Sunilkumar, S. Parameshwaraiah, H.G. Shivakumar. Evaluation of topical formulations of aqueous extract of *Centella asiatica* on open wounds in rats. *Ind. J. Exp. Biol.* **36(6):** 569-72 (1998).
106. A. Shukla, A.M. Rasik, B.N. Dhawan, Asiaticoside induced elevation of antioxidant levels in healing wounds. *Phytother Res.* **13(1):** 50-54 (1999).
107. F.X. Maquart, F. Chastang, A. Simeon, P. Birembaut, P. Gillery, Y. Wegrowski. Triterpenes from *Centella asiatica* stimulate extrcellular matrix accumulation in rat wounds. *Eur. J. Dermatol.* **9(4):** 289-96 (1999).
108. C.D. Coldren, P. Hashim, J. M. Ali, J.M. Oh. A.J. Sinskey, C. Rha. Gene expression changes in the human fibroblasts induced by *Centella asiatica* triterpenoids. *Planta Med.* **69(8):** 725-32 (2003).
109. S.S. Hong, J.H. Kim H.Li, C.K. Shim. Advanced formulation and pharmacological activity of hydrogel of the titrated extract of *Centella asiatica. Arch. Pharm. Res.* 28(4): 502-08 (2005).
110. A.M. Rasik, R, Raghubir, A. Gupta, A, Shukla, M.P. Dubey, S, Srivastav, H.K. Jain, D.K. Kulshrestha. Healing potential of *Calotropis procera* on dermal wounds in guinea pigs. *J. Ethnopharmacol.* 68(1-3): 261-66 (1999)
111. M.S. Charde, S.V. Fluzele, P.M. Saturwar, A.K. Dore. Study of the topical wound healing activity of Darvi Ghrita. *Indian drugs* **40(2):** 115-18 (2003).
112. M.S. Charde, S.V. Fluzele, P.M. Saturwar, S.B. Joshi, A.V. Kasture, A.K. Dore. Study on wound healing activity of Mulathyadi Ghrita. *Phytother. Res.* **4 (1):** 8. (2005).
113. P. K. Mukherjee, K. Mukherjee, M. Rajesh kumar, B.P. Sana. Evaluation of wound healing activity of herbal formulations. *Phytother. Res.* **17(3):** 265-68 (2003).
114. A.L. Udupa, S.G. Rao, D.R. Kulkarni. Wound healing profile of Septilin, *Ind. J. Phy. Pharmacol.* **33(1):** 39-42 (1989).

115. S.S. Nadig, S.G. Rao. Effect of Hepatogard- an indigenous formulation on dexamethasone induced antihealing effects in male albino rats. *Ind. J. Physiol. Pharmacol.* **43(2):** 230-34 (1999).
116. S.V. Fulzelle, P.M. satturwar, S.B. Joshi, A.K. Dorle. Wound healing activity of Chandanadi Yamaka in rats. *Ind. J. Pharm. Sci.* 301-04 (2003).
117. E.V. Kostrikova. Experimental study of wound healing effect of the preparation "Aekol" (Artificial sea buck thorn oil). *Ortop Travmatol protez.* **(1):** 32-36 (1989).
118. A.B. Samuelson. The traditional uses, chemical constituents and biological activities of *Plantago major* L. A review. *J. Ethanopharmacol.* 71: 01-21 (2000).
119. G.Tassman, J. Zafran, G. Zayon. A double blind crossovere study of a plantproteolytic enzyme in oral surgery. *J. Dent. Med.* **20:** 51-54 (1965).
120. O.M. Alvarez, R.L. Gilbreath. Effect of dietary thiamine on intermolecular collagen cross linking during wound repair: a mechanical and biochemical assessment. *J. Trauma.* **22:** 20-24 (1982).
121. M. Aprahamian, A. dentinger, C. Stock-damage. Effects of supplemental pantothenic acid on wond healing: experimental study in rabbit. *A. J. Clin. Nutr.* **41:** 578-89 (1985).
122. W.M. Ringsdorf, E. Cheraskin. Vimin C and human wound healing. *Oral. Surg. Oral. Med. Oral Pathol.* **53:** 231-36 (1982).
123. W.J. Pories, J.H. Henzel, C.G. Rob, S.H. Strain. Acceleration of healing with zinc sulfate. *Ann. Surg.* **165:** 432-36 (1967).
124. J.P. Debandt, C. Coudray-Lucas, N. Lioret, A randomized controlled trial of the influence of the mode of enteral ornithine alpha-ketogluterate administration in burn patients. *J. Nutr.* **128:** 563-69 (1998).
125. T.K. Hunt. Vitamin A and wound healing. *J. A. Acad. Dermatol.* **15:** 817-21 (1986).
126. E. Bartolomucci. Action of Vitamin E on healing of experimental wounds on paranchymatous organs. *JAMA* **113:** 1079 (1939).
127. R.B. Rucker, T. Kosonen, M.S. Clegg et al. Copper lysyl oxidase and extracellular matrix protein cross linking. *A. J. Clin. Nutr.* **67(5):** 996-1002 (1998).
128. L.M. Morrison, K. Murata. Absorption, distribution, metabolism and excretion of acid mucopolysaccharides administered to animals and patients. In: L.M. Morrison, Schjeide, K. Meyer. Coronary heart disease and the mucopolysaccharides (glycosaminoglycans). Springfield: charles C. Thomas. pp 109-27 (1974).
129. A. Barbul, G. Rettura S.M. Levenson et al. Wound healing and thymotropic effects of arginine: a pituitary mechanism of action. *A. J. Clin. Nutr.* **37:** 786-94 (1983).
130. P.R. Roberts, K.W. Black, J.T. Santamauro, G.P. Zaloga. Dietary peptides improve the wound healing following surgery. *Nutrition.* **14:** 226-29 (1998).