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Wound healing Agents from Medicinal Plants: A Review

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ABSTRACT

This paper presents a review of plants identified from various ethno botanical surveys and folklore medicinal survey with Wound healing activity. Wound is defined as the disruption of the cellular and anatomic continuity of a tissue. Wound may be produced by physical, chemical, thermal, microbial or immunological insult to the tissues. The process of wound healing consists of integrated cellular and biochemical events leading to re-establishment of structural and functional integrity with regain of strength in injured tissues.This review discuss about Wound healing potential of plants, its botanicalname, Common name, family, part used and references, which are helpful for researcher to development new Wound healing formulations for human use.

1. Introduction

Healing of wounds starts from the moment of injury and can continue for varying periods of time depending on the extent of wounding and the process can be broadly categorized into three stages; inflammatory phase, proliferate phase, and finally the remodeling phase which ultimately determines the strength and appearance of the healed tissue [1,2]. Wounds are the physical injuries that result in an opening or breaking of the skin and appropriate method for healing of wounds is essential for the restoration of disrupted anatomical continuity and disturbed functional status of the skin [3]. Wound healing is a complex series of interrelated events that are mediated through the phases by a wide range of chemically co-ordinate cellular processes as well as hormonal influences [4]. Medicinal plants have been shown to possess wound healing activity in animal studies [5,6].

2. Classification of wounds

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

2.1. Open wounds

In this case blood escapes the body and bleeding is clearly visible. It is further classified as: Incised wound, Laceration or tear wound, Abrasions or superficial wounds, Puncture wounds, Penetration wounds and gunshot wounds [7]

2.2. Closed wounds

In closed wounds blood escapes the circulatory system but remains in the body. It includes Contusion or bruises, heamatomas or blood tumor, Crush injury etc.

2.3. Acute wounds

Acute wound is a tissue injury that normally precedes through an orderly and timely reparative process that result in sustained restoration of anatomic and functional integrity. Acute wounds are usually caused by cuts or surgical incisions and complete the wound healing process within the expected time frame [8]

2.4. Chronic wounds

Chronic wounds are wounds that have failed to progress

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through the normal stages of healing and therefore enter a state of pathologic inflammation chronic wounds either require a prolonged time to heal or recur frequently. Local infection, hypoxia, trauma, foreign bodies and systemic problems such as diabetes mellitus, malnutrition, immunodeficiency or medications are the most frequent causes of chronic wounds[9,10]

3. Mechanism of wound healing

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

- The inflammatory phase
- The proliferative phase
- The remodelling phase

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

3.1. The Inflammatory phase

The inflammatory phase starts immediately after the injury that usually last between 24 and 48 hrs and may persist for up to 2 weeks in some cases The inflammatory phase launches the haemostatic mechanisms to immediately stop blood loss from the wound site. Clinically recognizable cardinal sign of inflammation, rubor, calor, tumor, dolor and function-laesa appear as the consequence. This phase is characterized by vasoconstriction and platelet aggregation to induce blood clotting and subsequently vasodilatation and phagocytosis to produce inflammation at the wound site[11].

3.2. Proliferation phase

The proliferative phase essentially involves the generation of the repair materials and majority of the skeletal muscle injuries.[12]

3.3. Remodelling phase

The remodelling phase is an essential component of tissue repair and is often overlooked. The final outcome of these combine events is that the damaged tissue will be repaired with the scar.[12]

4. Medicinal plants having wound healing activity

4. 1. Quercusinfectoria

Quercusinfectoriais a small tree (Fagaceae). It is mainly used for thetreatment of anti-inflammatory disorders and also used as dental powder, toothache treatment, gingivitis. Pharmacologically it acts as a astringent, antidiabetic, antiviral, antitremorine, local anaesthetic, antibacterial, antifungal, anti-inflammatory and larvicidal activities. It mainly contains tannin (50-70%) and small amounts of gallicacid ellagic acid.[13-15]

4.2.Aloe Vera

It is one of the oldest healing plants known to mankindAlsoacemannan (β-(1,4)-acetylated polymannose) - the majorpolysaccharide of A. vera- stimulates expressionof VEGF and other wound healing-related factors (e.g.,keratinocyte growth factor-1 and type I collagen) in gingivalfibroblasts. This can be especially beneficial in the case of oral woundhealing. Thus, crude Aloe veraextract or isolated proangiogeniccomponents may have potential pharmaceuticalapplications for the management of wounds.[16]

4.3.Hippophaerhamnoides L.

Hippophaerhamnoides L. (family Elaeagnaceae) commonlyknown as seabuckthorn (SBT) . Leaves, ripe fruits and seeds from seabuckthorn have been found to be a rich source of a large number of bioactive substances including flavonoids (isorhamnetin, quercetin, myricetin, kaempferol and their glycoside derivatives), carotenoids (α, β, δ-carotene, lycopene), vitamins (A, C, E and K), tannins, triterpenes, glycerides of palmitic, stearic and oleic acids and some essential amino acids[17].The high content of bioactive substances has been reflected in its extensiveexploitation by traditional medicine. Seabuckthorn has antioxidant [18] and anti-inflammatory activity [19] and has been reported to be useful in treating skin wounds [20]

4.4.Catharanthus roseus

Catharanthus roseus plant is a key source of monoterpenoidindol alkaloid, vincristine and vinblastine which found useful in treatment of cancer[21]. In a study of ethanolic extract of flower of this plant in a dose of 100mg/kg/day demonstrated to possess wound healing property.[22]

4.5.Lycopodium serratum

Lycopodium serratum is commonly known as club moss. Wound activity of aqueous and ethanolic leaf extract of Lycoponium was studied by exicision, incision and dead space wound model on rats.as compaired to the aqueous extract and controls the ethanolic extract showed significant decrease in the period of epithelialization and an increace in wound contractionrate,tissue breaking strength and hydroxyl proline content at the wound site.[23]

4.6.Sesamum indicum

Sesamum indicum is a member of family Pedaliaceae. sesame oil obtained from the seeds of the plant is highly nutritive as it is rich source of natural oxidant such as sesamin and sesamol.[24]The methanolic extract of root of

sesamumindicum was obtained and was incorporated in gel and ointment bases.These preparations were evaluated for in vivo wound healing on rat using exicision wound model.[25]

4.7. Radixpaeoniae

Aqueous extract of roots of radix paeoniae was screened for wound healing by exicion, incision and dead space wound models on wistar rats. Parameters studied were tissue breaking strength, epithelialization, wound contraction and granulation tissue dry weight. The test group demonstrated significant wound healing activity as compaired to nitrofurazone ointment treated control group.[26]

4.8. Morinda citrifolia Linn.

Morinda citrifoliais also known as Indian mulberry, belongs to family; Rubiaceae. It mainly contains saponins, tannins, triterpenes, alkaloids, flavonoids. It is mainly used for the bowel disorders, including arthritis, atherosclerosis, bladder infections, boils, burns, cancer, chronic fatigue syndrome, circulatory weakness, cold, congestion, constipation, diabetes, eye inflammations, fever, fractures, gastric ulcers, gingivitis, headaches, heart diseases, hypertension, immune weakness, indigestion, intestinal parasites, kidney disease, malaria, menstrual cramps, mouth sores, respiratory disorders, ringworms, sinusitis, sprains, stroke, skin inflammation and wounds [27].

4.9.Termina liabelliricaRoxb.

Termina liabellirica Roxb.belonging to the family Combretaceae, commonly known as belliricmyrobalan. Fruit is astringent, antiseptic, rejuvenative, brain tonic, expectorant and laxative. It is used in coughs, sore throat, dysentery, diarrhoea and liver disorders. It is also useful in leprosy, fever and hair care. In folk medicine it hasbeen used for the treatment of skin diseases as antiseptic and on all types of fresh wound. An ethanol extract ofTerminaliabellirica

Fruit has properties that render it capable of promoting accelerated wound healing activity compared with placebo control.[28]

4.10.Moringaoleifera Linn.

Moringaoleifera Linn. (Moringaceae) has been an ingredient of Indian diet since centuries. The leaves of the plant have also been reported for its anti-tumor, hypotensive, antioxidant, radio-protective, anti-inflammatory and diuretic properties. The aqueous extract was studied and it was found that there was significant increase in wound closure rate, skin-breaking strength, granuloma breaking strength, hydroxyproline content, granuloma dry weight and decrease in scar area was observed.[29]

5. Parameters used in assessing wound healing activity

5.1. Physical attributes

Physical attributes like wound contraction, epithelization and scar remodeling can be monitored by measuring the total wound area, open wound area, and noting the physical changes in scar e.g. size, shape and colour etc. Excision wound is ideal to study these attributes. The area measurement not only gives the rate of healing, but can distinguish between contraction and epithelization.The extent of epithelization is determined by measuring the raw wound, bound by hairless belt intervening between wound margin and then by deducting the raw wound area from total wound area. Different methods for measuring the areas are available. These may be traced on a paper, weighed and compared with that of a reference piece of same thickness and unit area or the same can be retraced on a graph paper to directly measure the area. The completion of epithelization can be assessed by noting the time for complete covering of the raw surface of the wound. "Thorotrast" a sophisticated technique with the electron opaque marker is reported for the identification of migrating epithelial cellsGranuloma study is another physical attribute of wound healing study which can be assessed by quantifying the granuloma itselfby noting its overnight dried weight[30].

5.2. Mechanical attributes

Mechanical attributes like breaking strength or tensile strength, can be monitored by measuring the force required to break a wound or tissue without regard to the dimensions. Tensile strength measurement are made in terms of load applied per unit of cross sectional area and expresses as lbs/sq.inch or kg/sq.cm or14 kg/sq.mmTensiometer or constant water flow techniquemay be applied for uniform application of force.[31]

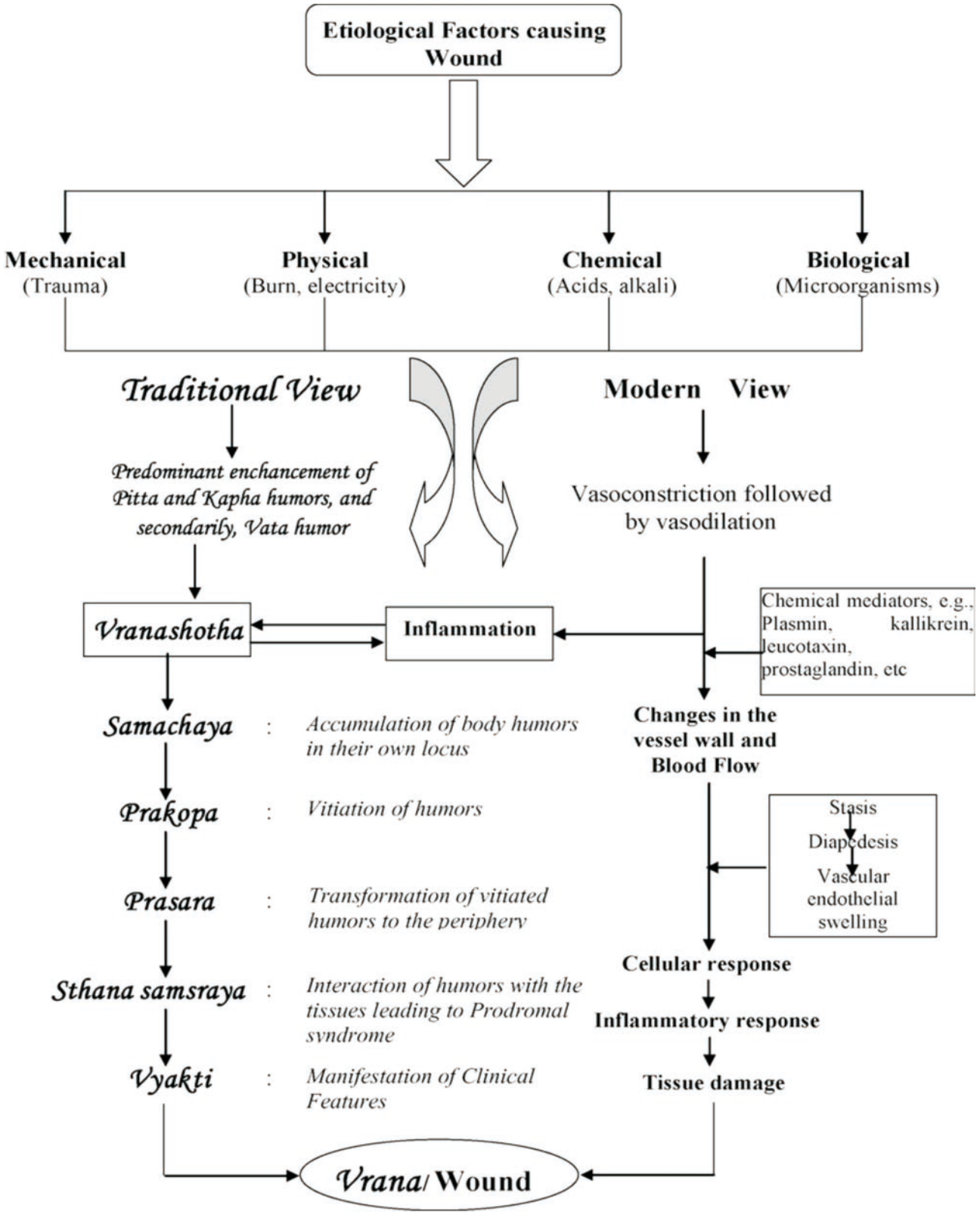
5.3. Biochemical attributes

Various chemical agents including collagen that are elaborated in the wound may be estimated. Collagen estimation in wound, is most reliable, since it contributes for wound strength. Hydroxyproline, an important amino acid in collagen, is estimated to determine the total collagen content, on index of progress in healing. Calorimetric and spectrometric or chromatographic methods are also available for its estimation[32].

5.4. Histological attributes

Monitoring the histological attribute, quantifying various cellular elements and collagen content makes this an equally useful parameter in wound healing studies. It is monitored by microscopic examination of the granulation tissue have shown that the depth of collagen invasion at the periphery of the disc is proportional to the total collagen content and fibroblast accumulation in experimental animals.[32]

5.5. Etiological factors causing wound[33]



Comparative representation of etiopathogenesis of wound in Ayurvedic and modern medicine

Medicinal plants having wound healing activity:

Sr. No.	Name of the plant	Family	Part Used	Referance
1.	Adhatodavasica Linn.	Acanthaceae	Leaves, stem	34
2.	Hippophaerhamnoides L.	Elaeagnaceae	Leaves,fruit	17,18,19,20
3.	Aloe vera	Liliaceae	Leaves	16
4.	Hibiscus rosasinesis	Malvaceae	Leaves, root	35

5.	.Lycopodiumserratum	Lycopodiaceae	Leaves	23
6.	TephrosiapurpureaLinn	Leguninosae	Leaves	36
7.	TribulusterrestrisLinn.	Zygophyllaceae	Leaves	37
8.	Gymnemasylvestre R.Br.	Asclepiadaceae.	Leaves	38
9.	Calophylluminophyllum	Clusiaceae	Leaves,Bark	39
10.	LawsoniainermisLinn.	Lythraceae,	Leaves	40
11.	Euphorbia hirtaL.	Euphorbiaceae	Leaves	43
12.	Napoleonaimperialis	Lecythidaceae	Leaves	44
13.	Mikaniamicrantha	Asteraceae	Leaves	45
14.	TerminaliabelliricaRoxb.	Combretaceae	Fruit	28
15.	MoringaoleiferaLinn.	Moringaceae	Leaves	29
16.	Morindacitrifolia	Rubiaceae	Root	27
17.	catharanthusroseus	Apocynaceae	Flower	21,22
18.	SesamumindicumLinn.	Pedaliaceae	Seed	24,25
19.	RubiacordifoliaLinn	Rubiaceae	Root	46
20.	Ulmuswallichiana Planch	Ulmaceae	Leaves	47
21	Tectonagrandis	verabinaceae	Leaves	48
22	Rubussanctus	Rosaceae	Root	49,50
23	Musa sapientum	Musaceae	Leaves	51
24	Quercusinfectoria	Fagaceae	Root	13,14,15
25	SphaeranthusindicusLinn.	Asteraceae.	Leaves	52,53
26	Acacia catechu Willd.	Mimosaceae	Bark	54
27	Acalyphaindica L.	Euphorbiaceae	Leaves	55
28	Achyranthesaspera L.	Amaranthaceae	Latex	54
29	Adhatodazeylanica M.	Acanthaceae	Leaves	56
30	AgrimoniapilosaLedeb	Rosaceae	Whole plant	57
31	Alstoniascholaris R.Br.	Apocynaceae	Latex	59
32	Anacardiumoccidentale L.	Anacardiaceae	Fruit	58
33	Areca catechu L.	Arecaceae	Fruit	57
34	Argemonemexicana L.	Papaveraceae	Latex	57
35	Aristidasetacea Retz.	Poaceae	leaves	58
36	Barleriaprionitis L.	Acanthaceae	Leaves	57
37	Begonia fallox DC.	Begoniaceae	Stem	58
38	Betulaalnoides B.H.	Betulaceae	Bark	57
39	Blepharismaderaspatensis	Acanthaceae	Leaves	58
40	Boschniakiahimalaica	Orobanchaceae	Whole plant	57
41	Brassica juncea L.	Brassicaceae	Fruit	58
42	Buxuswallichiana	Buxaceae	Bark	57
43	Calendula officinalis L.	Asteraceae	Flower	57
44	CallicarpaarboreaRoxb.	Verbenaceae	Bark	59
43	Calotropisgigantea L.	Asclepiadaceae	Sem	58
45	Calotropisprocera Br	Asclepidaceae	Leaves	57
46	Cassia alata L.	Caesalpinae	leaves	57
47	Cassia auriculata L.	Caesalpinae	Leaves,Bark	57
48	Chasaliacurviflora Wall.	Rubiaceae	Root	58
49	Chenopodium album Linn.	Chenopodiaceae	Leaves	57
48	Cirsiumsinense CBC.	Asteraceae	Root	59
50	CirsiumverutumSpreng.	Asteraceae	Root	57
51	CissampelospareiraL.	Menispermaceae	Leaves	58
52	Cleome viscosa L.	Cleomaceae	Leaves	58
53	Combretumflagrocarpum	Combretaceae	Leaves	59
54	Commelinabenghalensis	Commelinaceae	Stem	58
55	Curcuma domestica V.	Zingiberaceae	Tubers	59

56	Curcuma longa L.	Zingiberaceae	Rhizomes	57
57	CyanotisvillosaSpreng.	Commelinaceae	Stem	58
58	Daturastramonium L.	Solanaceae	Leaves	57
59	Daucascarota L.	Apiaceae	Root	57
60	Dendrophthoe falcate L.f.	Loranthaceae	Stem	58
61	Diotacanthusalbiflorus	Acanthaceae	Leaves	58
62	DodonaeaviscosaLinn.	Sapindaceae	Leaves	58
63	Eupatorium odoratum L.	Asteraceae	Leaves	58
64	Euphorbia antiquorum L.,	Euphorbiaceae	Stem	58
65	Euphorbia hirta L.	Euphorbiaceae	Latex	58
66	Euphorbia pilosa	Euphorbiaceae	Latex	57
67	Ficusbengalensis L.,	Moraceae	Leaves	58
68	Ficusreligiosa L.	Moraceae	Bark	57
69	Gelsemiumelegans	Loganiaceae	Leaves	59
70	Ixoracoccinia L.	Rubiaceae	Flowers	58
71	Jatrophagossypifolia L.	Euphorbiaceae	Resin	58
72	Jatrophacurcas L.	Euphorbiaceae	Bark	59
73	Melastomamalabathricum	Malastomataceae	Bark	59
74	Menthaviridis L.	Lamiaceae	Leaves	58
75	SolanumxanthocarpumLinn.	Solanaceae	Fruit	60
76	Morindapubescens	Rubiaceae	Leaves	58
77	Raxidpaeomiae	paeonaceae	Root	26.
78	MurrayapaniculataLinn.	Rutaceae	Leaves	58
79	Neriumindicum Mill	Apocyanaceae	Leaves	57
80	Ophiorrhizamungos L.,	Rubiaceae	Whole plant	58
81	Pinusroxburghii	Pinaceae	Bark	57
82	Ploygonatumofficinale A.	Liliaceae	Root	57
83	Pongamiapinnata Vent.	Fabaceae	Leaves	57
84	Pothosscandens L.	Araceae	Leaves	58
85	Psychotriaflavida	Rubiaceae	Root	58
86	Rubiacordifolia L.	Rubiaceae	Bark,Root	57
87	Rungiarepens L.	Acanthaceae	Whole plant	57
88	Scopariadulcis L.,	Scrophulariaceae	Leaves	57
89	SidaacutaBurm.F.	Malvaceae	Leaves	58
90	Smilax zeylanica L.,	Smilacaceae	Rhizoms	58
91	TaxuswallichianaZucc.	Taxaceae	Bark	57
92	Terminaliachebula	Combretaceae	Leaves	57
93	ThespesiapopulneaSoland	Malvaceae	Fruit	57
94	Trichosanthestricuspidata	Cucurbitaceae	Fruit	57
95	Tridaxprocumbens L.	Asteraceae	Leaves	57
96	ArnebiadensifloraLedeb	Boraginaceae	Root	62
97	LepidiumsativumLinn.	Cruciferae	Leaves	63
98	Ocimum sanctum Linn.	Labiatae	Leaves	64
99	Alternantherabrasiliana Kuntz.	Amaranthaceae	Leaves	65
100	Commiphoramukul Engl.	Burseraceae	Bark	56

Most of the natural plants in this review are those with wound healing potentials. Plants are more potent healers because they promote the repair mechanism in the natural way. The healing process can be physically monitored by assessing the rate of contraction of the wound, period of epithelization, tensile strength, histopathology, and weight of granuloma in different wound models. The healing tissue synthesizes more collagen to provide tensile strength. The demand of herbal drugs is increasing day by day in developed as well as developing countries because they are safer and well tolerated as compared to those allopathic drugs.The information is recored in plant′s scientific name, common name of plant, family, partused for the wound healing activity & References. Scientists from divergent fields are investigating new plants with an eye to their wound healing usefulness. These plants should be subjected to

animal and human studies to derermine their effectiveness.

Conflict of interest statement

We declare that we have no conflict of interest.

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