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"Botanical Remedies: A Comprehensive Review of Plants with Wound-Healing Properties"

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Abstract:
In India, indigenous people from various ethnic groups and regions have long utilized plants as a source of medicine to treat various ailments affecting humans and their domestic animals. Recently, there has been a global surge in plant research, amassing substantial evidence demonstrating the significant potential of medicinal plants used in traditional systems. Over the past few years, more than 13,000 plants have been studied. Our review aims to compile data generated from recent research using modern scientific methods and innovative tools. This article highlights the wound healing properties of various plants traditionally used for this purpose. We have sought to provide insights into different plants with potential wound healing capabilities, which could be beneficial in therapeutic practices.
Keyword: Wound healing, Growth Factors, Pharmacological action, world health organization

Introduction:

The use of plants in traditional medicine dates back to the Middle Paleolithic era, around 60,000 years ago, as shown by fossil evidence [1]. In recent times, developed nations have increasingly adopted traditional medical systems that employ herbal remedies. According to the World Health Organization (WHO), about 65% of the global population uses plant-based treatments as part of their primary healthcare [2,3]. Moreover, approximately 25% of all modern prescription drugs are plant-derived, underscoring the importance of botanical drugs in the pharmaceutical industry [4-6].

Over the past twenty years, there has been significant progress in our understanding of the wound healing process. This has led to the development of new technologies that not only speed up normal wound healing but also address the underlying issues that cause chronic wounds. Innovations range from the use of growth factors to the development of bioengineered skin substitutes, making the future of wound healing promising [7-8].

Wound healing is a complex, dynamic process vital for restoring the integrity and function of damaged tissues [9]. Grasping the core principles of wound healing is essential for creating effective treatments and managing various types of wounds, from minor cuts to severe injuries and chronic ulcers. This review aims to offer a detailed overview of the wound healing process, including the stages involved, key cellular and molecular mechanisms, and factors influencing healing outcomes [10,11].

Overview of Wound Healing:

Wound healing takes place through a highly organized sequence of events that are traditionally divided into four overlapping phases: hemostasis, inflammation, proliferation, and remodeling [12].

Hemostasis

Hemostasis is the immediate response following tissue injury, aiming to prevent excessive blood loss. This phase involves vasoconstriction, platelet aggregation, and clot formation. Platelets play a crucial role by releasing various growth factors, such as platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF-β), which initiate the subsequent phases of healing [13,14].

Inflammation

The inflammatory phase is characterized by the infiltration of leukocytes, primarily neutrophils and macrophages, to the wound site. Neutrophils are the first responders, tasked with clearing debris and preventing infection through phagocytosis. Macrophages follow, orchestrating the

transition from inflammation to proliferation by secreting cytokines and growth factors that promote tissue repair. This phase is essential for creating a clean wound environment conducive to healing [15,16].

Proliferation

During the proliferation phase, new tissue formation occurs. Key processes include angiogenesis, fibroplasia, and re-epithelialization. Angiogenesis, the formation of new blood vessels, is critical for supplying nutrients and oxygen to the healing tissue. Fibroblasts synthesize collagen and extracellular matrix (ECM), providing structural support. Keratinocytes migrate and proliferate to restore the epidermal layer. This phase results in granulation tissue formation, which is rich in blood vessels and ECM components [9, 17].

Remodeling

The final phase, remodeling, involves the maturation and reorganization of collagen fibers within the wound. This phase can last for months to years, during which type III collagen is replaced by the stronger type I collagen. Matrix metalloproteinases (MMPs) and their inhibitors regulate the degradation and synthesis of ECM components, ensuring proper tissue architecture and strength. The scar tissue formed during this phase is less functional than the original tissue but serves to restore structural integrity [18,19].

Cellular and Molecular Mechanisms

Wound healing is regulated by a complex interplay of cells, signaling molecules, and the extracellular matrix. Key cellular players include platelets, neutrophils, macrophages, fibroblasts, endothelial cells, and keratinocytes. These cells communicate through cytokines, chemokines, and growth factors, orchestrating the healing process [16,18].

Growth Factors and Cytokines

Growth factors such as PDGF, TGF-β, vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF) play pivotal roles in wound healing. They regulate cell migration, proliferation, differentiation, and ECM production. Cytokines, including interleukins and tumor necrosis factor-alpha (TNF-α), modulate the inflammatory response and facilitate the transition to the proliferative phase [18,20].

Extracellular Matrix

The ECM provides structural support and regulates cell behavior through biochemical and mechanical signals. It undergoes dynamic changes during wound healing, with provisional matrix components like fibrin and fibronectin being replaced by collagen-rich ECM. Integrins, a family of cell surface receptors, mediate cell-ECM interactions, influencing cell adhesion, migration, and survival [21, 22].

Phytoconstituents: Various plants with wound healing properties have been identified, many of which contain flavonoids as active constituents. Tannins, for example, promote wound healing through multiple cellular mechanisms, including the chelation of free radicals and reactive oxygen species, enhancing wound contraction, and increasing the formation of capillary vessels and fibroblasts. The wound healing process is further supported by natural products and plant-based compounds, which include active principles such as triterpenes, alkaloids, flavonoids, and other biomolecules [23, 24].

Factors Influencing Wound Healing

Several factors can influence the efficiency and outcome of wound healing, including the wound type, patient's age, nutritional status, comorbidities, and presence of infection.

Systemic Factors

Age-related changes can impair wound healing, as elderly individuals often exhibit delayed cellular responses and reduced angiogenesis. Nutritional deficiencies, particularly in proteins, vitamins (such as vitamin C and A), and minerals (like zinc), can impede the healing process. Comorbid conditions such as diabetes, vascular diseases, and immunosuppressive states also negatively affect wound healing [25, 26].

Local Factors

Local wound conditions, including the extent of tissue damage, perfusion, and infection, significantly impact healing. Adequate blood supply is crucial for delivering oxygen and nutrients to the wound site. Infections prolong the inflammatory phase and can lead to chronic wounds. Effective wound care practices, such as debridement and maintaining a moist wound environment, are essential for optimal healing [27,28].

Plants that heal wounds:

The table lists plants that have been traditionally used for the management and treatment of wounds over the years.

S.N.	Plant species	Family	Part used	Extract	Reference
1	*Acacia Suma Roxb*	Fabaceae	*LEAF*	Ethanol, chloroform, Aqueous	[29]
2	*Acalypha Indica*	Euphorbiaceae	Entire plant	Aqueous	[30]
3	*Acalypha Indica L.*	Euphorbiaceae	Leaf	Ethanol	[31]
4	*Achillea Eriophora*	Asteraceae	Leaf	Methanol	[32]
5	*Adhatoda Vasica*	Acanthaceae	Leaves	Methanol	[33]
6	*Ageratum conyzoides*	Asteraceae	Leaves	Methanolic	[34]
7	*Aloe Vera*	Asphodelaceae	Gel	Ethanolic	[35]
8	*Alternanthera Brasiliana Kuntz*	Amaranthaceae	Leaves	Methanol	[36]
9	*Annona Muricata*	Annonaceae	Stem bark	Ethanol	[23]
10	*Annona Squamosa*	Annonaceae	Leaves	Ethanolic	[37]
11	*Anogeissus Leiocarpus*	Combretaceae	Leaves	Methanol	[38]
12	*Aristolochia Bracteolata*	Aristolochiaceae	Leaves	Methanol	[39]
13	*Azadirachta Indica*	*Meliaceae*	Leaves	Powder	[40]
14	*Bacopa Monniera*	Scrophulariaceae	Whole plant	Ethanol	[41]
15	*Bowdichia Virgilioides*	Fabaceae	Stem barks	Aqueous	[42]
16	*Calendula Officinalis*	Compositae	Leaves	Ethanolic	[43]
17	*Calotropis Gigantea*	Asclepiadaceae	Root bark	Ethanol	[44]
18	*Capparis Zeylanica*	Capparidaceae	leaves	Ethanol	[45]
19	*Carapa Procera*	Meliaceae	Leaf	Ethanolic	[46]
20	*Cardiospermum Helicacabum Linn*	Sapindaceae	Stem	Ethanol	[48]
21	*Carica Papaya*	Caricaceae.	Stem	Ethanolic	[49]
22	*Carica Papaya L.*	Caricaceae.	Leaf	Aqueous	[50]
23	*Catharanthus Roseus*	Apocynaceae	Flower	Ethanol	[51]
24	*Centella Asiatica*	Apiaceae	Ariel part	hydroalcoholic	[52]
25	*Centella Asiatica*	Apiaceae	Aerial part	Ethyl acetate	[53]
26	*Ceylon Cinnamon*	Laurels	whole plant	Ethanolic	[54]
27	*Cleome Viscosa Linn*	Cleomaceae	Leaves, Whole Plant	Methanol	[55]
28	*Combretum Dolichopetalum*	Combretaceae	Leaf	Methanol	[56]
29	*Crotalaria Verrucosa*	Fabacea	Leaves	Aqueous	[57]
30	*Curculigo Orchioides*	Amaryllidaceae	Leaves	Methanolic	[58]
31	*Curcuma Zedoaroides*	Zingiberaceae	Rhizomes	Ethanolic	[59]
32	*Cyperus Rotundus Linn.*	Cyperaceae	Tuber	Ethanol	[60]
33	*Desmodium Gyrans*	Fabaceae	Leaves	Ethanol	[61]
34	*Eclipta alba*	Asteraceae	Leaves	Methanolic	[62]
35	*Elephantopus Sacber L.*	Asteraceae	Leaves	Aqueous	[63]
36	*Emilia Sonchifolia (L.) De*	Asteraceae	Whole	Aqueous	[64]
37	*Gossypium Herbaceum*	Malvaceae	Leaves	Methanolic	[65]
38	*Hibiscus Rosa-Sinensis L.*	Malvaceae	leaves	ethanolic	[66]

39	*Hibiscus Rosa-Sinensis L.*	Malvaceae	Leaves	Ethanolic	[67]
40	*Holarrhena Antidysenterica Wall.*	Apocynaceae	Leaves	Ethanol	[68]
41	*Holarrhena Antidysenterica Wall*	Apocynaceae	Leaf	Ethanol	[68]
42	*Hylocereus Undatus*	Cactaceae	Leaves	Aqueous	[69]
43	*Hypericum Patulum*	Hypericaceae	Leaf	Methanol	[70]
44	*Ipomoea Batatas L.*	Convolvulaceae	Peels	Methanol	[71]
45	*Ixora Coccinea*	Rubiaceae	Root	Ethanol	[72]
46	*Jasminum Mesnyi*	Oleaceae	Root	Ethanol, ethyl acetate	[73]
47	*Jasminum Auriculatum Vahl.*	Oleaceae	Leaves	Ethanol	[74]
48	*Jasminum Grsndiflorum Linn.*	Oleaceae	Leaves	Alcoholic	[75]
49	*Jasminum Sambac (Linn)*	Oleaceae	Leaves	Ethanol	[76]
50	*Jatropha Curcas L.*	Euphorbiaceae	Stem bark	Methanol	[77]
51	*Kaempferia Rotunda Linn*	Zingiberaceae	Leaves	Methanol	[78]
52	*Lantana Camara*	Verbenaceae	roots	ethanolic	[79]
53	*Lantana Camara Linn.*	Verbenaceae	Leaf	Ethanolic	[80]
54	*Mallotus Philippinensis Muell*	Euphorbiaceae	Fruit	Ethanol	[81]
55	*Michelia Champaca*	Magnoliaceae	Flower	Ethanol	[82]
56	*Mimosa Pudica*	Fabaceae	Root	Methanol	[83]
57	*Mimosa Pudica*	Mimisace	Leaves	Alcoholic	[84]
58	*Mimosa Pudica Linn.*	*Mimisace*	Leaves	Alcoholic	[85]
59	*Momordica Charantia L.*	Cucurbitaceae	Seed	Aqueous	[86]
60	*Morinda Citrifolia*	Rubiaceae	Leaves	Aqueous	[87]
61	*Moringa Oleifera*	Moringaceae	Leaves	Aqueous	[88]
62	*Morus Alba*	Moraceae	Leaves	Aqueous	[89]
63	*Mucuna Pruriens*	Fabaceae	Seed	Methanol	[90]
64	*Nyctanthes Arbortristis L.*	Oleaceae	Leaves	Alcohol	[91]
65	*Ocimum Sanctum*	Labiatae	Leaves	Ethanolic	[43]
66	*Ocimum Sanctum Linn*	Labiaceae	Leaves	Ethanolic, aqueous	[92]
67	*Piper Betle*	Piperaceae	Leaves, stem	Ethanol	[93]
68	*Piper Hayneanum*	Piperaceae	Leaves, root, stem	Ethanol	[94]
69	*Plagiochila Beddomei Steph.*	Plagiochilaceae	Thallus	Methanol	[95]
70	*Plumbago Zeylanica L.*	Plumbaginaceae	Root	Methanol	[96]
71	*Polygonatum Odoratum*	Asparagaceae	Leaf	Ethanol	[97]
72	*Polygonatum Odoratum*	Asparagaceae	Leaf	Ethanolic	[98]
73	*Primula Denticulata*	Primulaceae	Arial part	Ethanolic	[46]
74	*Punica Granatum*	*Lythraceae*	Peel	Ethanol	[99]
75	*Radix Paeoniae*	Paeonaceae	Root	Aqueous	[100]
76	*Rosmarinus Officinalis*	Lamiaceae	Whole plant	Aqueous	[101]
77	*Ruta Graveolens L.*	Rutaceae	Leaves	Methanolic	[102]
78	*Saurauia Vulcani*	Actinidiaceae	Leaves	Aqueous	[103]
79	*Scrophularia Striata*	crophulariaceae	Arial part	Methanol	[104]
80	*Sphaeranthus Indicus*	Asteraceae	Root	Methanolic	[105]

81	*Stachytarpheta Jamaicensis Linn. Vahl*	Verbenaceae	Leaf	Ethanol	[106]
82	*Stevia Rebaudiana*	Asteraceae	Leaves	Aqueous	[107]
83	*Stevia Rebaudiana*	Asteraceae	Arial part	Ethanol	[108]
84	*Swietenia Mahogoni*	Meliaceae	Leaf	Ethanolic	[109]
85	*Tagetes Erecta*	Asteraceae	Leaves	hydroalcoholic	[52]
86	*Tamarix Aphylla*	Tamaricaceae	Leaf	Ethanolic	[110]
87	*Taraxacum Officinale*	Asteraceae	Whole plant	Ethanol	[111]
88	*Tephrosia Purpurea L.*	Fabaceae	Arial part	Ethanol	[112]
89	*Tetracarpidium Conophorum*	Euphorbiaceae	Nuts	Methanol, n-Hexane	[113]
90	*Tinospora Crispa*	Menispermaceae	Stem	Chloroform, Methanol	[114]
91	*Tonna Dolium*	Taeniidae	Whole plant	Methanol	[115]
92	*Tribulus Terrestris Linn.*	Zygophyllaceae	Fruit	Ethanolic	[116]
93	*Urena Lobata Linn.*	Malvaceae	Whole plant	Methanolic	[117]
94	*Vernonia Arborea*	Asteraceae	Bark	Aqueous, methanol	[118]
95	*Zanthoxylum*	Rutaceae	Stem bark	Aqueous	[119]

Conclusion

Wound healing is a critical process in response to tissue injury, aiming to restore the integrity of the tissue. This process is primarily facilitated by the synthesis of the connective tissue matrix. Collagen, a significant protein in the extracellular matrix, plays a key role in providing wound strength. In India, the use of plants for medicinal purposes has been documented in ancient literature, highlighting their importance to human survival. The consumption, management, and valuation of wild plants are integral parts of traditional knowledge in many human societies. The collection, sharing, and preservation of knowledge about plants are traditional practices that contribute to the survival of numerous cultures. Plants and their extracts have significant potential in wound management and treatment. Therefore, it is crucial to explore all available options to enhance wound care. However, scientific validation, standardization, and safety evaluation of traditional medicinal plants are necessary before they can be recommended for wound healing. This review focuses on herbal plants with wound healing properties, encompassing observation, description, and experimental investigation of indigenous drugs and their biological activities. It draws on various disciplines, including botany, chemistry, biochemistry, and pharmacology, to discover biologically active natural products.

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