A comprehensive review of plant-based natural compounds for wound healing.

Monika Dagar[1], Surabhi Bajpai[1]*, and Rakesh Mishra[2]

[1]Department of Bioscience and Biotechnology, Banasthali Vidyapith, Banasthali-304022, Rajasthan, India

[2]Institute for Stem Cell Biology and Regenerative Medicine (inStem), NCBS Campus, Bengaluru-560065

Abstract

Restoration of the structure and function of damaged tissues, which is an intricate process, is governed by the discharge of multiple cytokines and growth factors at the site of injury. Various plants or substances derive from plants that have high antioxidant concentrations as well as anti-inflammatory, immunomodulatory, and antibacterial activities may be very beneficial for the healing of wounds. This review paper aims to enhance our understanding of plant-derived compounds suitable for serving as bioactive elements in bandages or other products designed for wound care.

Keywords: Wound healing, Antioxidant, Anti-inflammatory, Plant-Based Compounds.

Introduction

Wounds can be developed by both accidental and surgical trauma, as well as a variety of medical conditions. These wounds often lead to discomfort, inflammation and impaired functionality, collectively impacting a patient's quality of life and financial burdens [1]. Many contemporary wound-care methods, including advanced wound dressings, growth factor therapy, stem cell therapy, and gene therapy, exhibit limited efficacy. Additionally, frequent antibiotic use for open wound treatment often results in the development of multi-drug resistance. Plant-based medication is becoming increasingly popular since they are regarded to be safe since they have no side effects, less expensive and more suited for wound treatment.

The repair of damaged cellular structures during wound healing involves four interrelated phases: Hemostasis, Inflammation, Proliferation, and Remodeling [2].

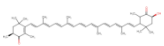
Wound healing involves multiple stages, and any interruption during this sequence can result in improper wound healing. Key factors in this intricate mechanism include inflammatory cells, growth factors, proteases, such as matrix metalloproteinase (MMPs), and cellular and extracellular components.

Extracted compounds from medicinal plants have shown wound-healing properties, and several of these have been used in the development of groundbreaking pharmaceutical drugs. Traditional medicinal plants have a unique perspective on wound treatment and care. The medicinal usefulness of plant-derived chemicals that have physiological effects on the human body. These compounds are categorized as alkaloids, essential oils, flavonoids, tannins, terpenoids, saponins, and phenolics [3]. The study presents a comprehensive assessment of plant-sourced natural compounds for wound healing, encompassing their chemical origins and the biological processes involved in their therapeutic effects on wound healing.

Natural compounds that help in wound healing

Wound healing is a complex and highly regulated mechanism that restores the structure and functionality of injured tissues. This intricate procedure involves the release of multiple growth factors and cytokines at the wound site and is tightly controlled. The main objective of this review is to focus on the significance of plant-derived compounds in the context of wound healing and to explain the mechanisms that make them effective. These natural products have been widely employed in the management of wounds, consistently producing outstanding outcomes (Table 1).

Table 1. *Plant-Based compounds for wound healing.*

Sr. No.	Compound	Origin	Mechanism in wound healing	Structure	References
1	Astaxanthin	*Haematococcus pluvialis*	Protects the cell membrane from RONS and oxidative stress. Astaxanthin most likely accelerates wound contraction during the proliferative and maturation phases by enhancing the function of myofibroblasts, which differ from tissue fibroblasts and play an essential part in the process.		[1]

***Correspondence to:** Surabhi Bajpai, Department of Bioscience and Biotechnology, Banasthali Vidyapith, Banasthali-304022, Rajasthan, India. E-mail: surabhibiochem@gmail.com

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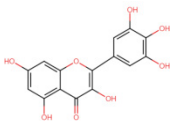
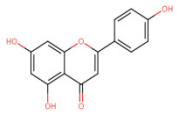
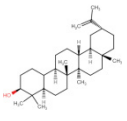
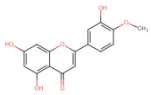
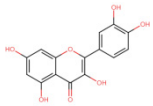
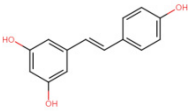
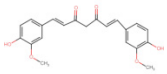
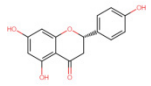
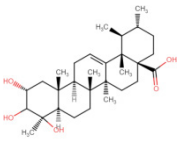
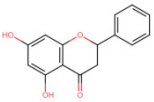
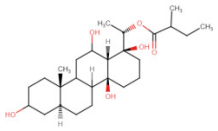
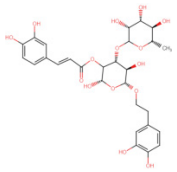
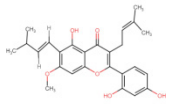
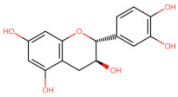
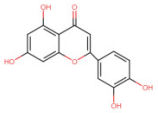
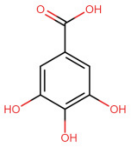
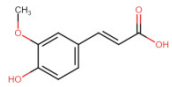
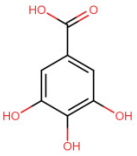
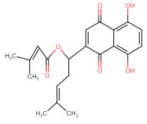
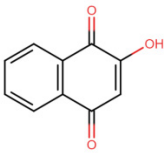
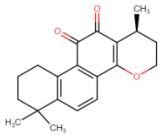
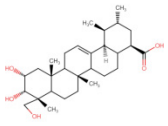
2	Myricetin	*Myricaceae, Polygonaceae, Primulaceae, Pinaceae, and Anacardiaceae*	Myricetin improves healing by hastening the transition from inflammatory to anti-inflammatory reactions.		[4][5]
3	Apigenin	*Matricaria chamomilla*	Apigenin has been shown to reduce inflammatory cytokine levels within keratinocytes through the inhibition of several critical pathways, including activator protein 1 (AP-1), mitogen-activated protein kinase (MAPk), and nuclear factor kappa B (NF-kB). Additionally, it promotes autophagy by deactivating Akt and Protein kinase C (PKC) while concurrently blocking mTOR. Moreover, Apigenin offers protection against oxidative stress-induced cell death.		[6][7]
4	Lupeol	*Alnus rubra, Acacia visco, or Abronia villosa*	The primary factor responsible for cutaneous wound healing during the 7-day treatment regimen was the promotion of angiogenesis, which resulted in an increase in the expression of Ki-67, vascular endothelial growth factor, epidermal growth factor, and transforming growth factor beta-1.		[8]
5	Hesperetin	*Brassica oleracea var. sabauda, Dalbergia parviflora*	Hesperidin was discovered to decrease the levels of various cytokines, including TNF, IL-6, and IL-8, in both rat skin and human keratinocyte cultures.		[9]
6	Quercetin	*Foeniculum vulgare*	Quercetin accelerated the healing process in mice by stimulating the proliferation and migration of fibroblasts, reducing inflammation, and enhancing the production of growth factors. This is achieved by activating the Wnt/β-catenin signaling pathway and TERT, which is a telomerase reverse transcriptase.		[10]
7	Resveratrol	*white hellebore (Veratrum grandiflorum O. Loes)*	It suppresses inflammatory responses and demonstrates anti-inflammatory potential by directly impacting nuclear factor κB (NFκB), the expression of proinflammatory cytokines like interleukin 6 (IL6), and genes associated with eicosanoid synthesis.		[11][12][13]
8	Curcumin	*Rhizomatous herbaceous perennial plant*	This substance displays anti-inflammatory effects by obstructing the inflammatory reaction in endothelial cells stimulated by TNF, thereby hindering the activity of NF-κB. Furthermore, it can effectively suppress platelet-derived growth factor (PDGF) effectively.		[14][15]
9	Naringenin	*Smyrna-type Ficus carica*	The purpose of this procedure is to regulate the AKT1, RELA, and Mitogen-activated protein kinase (MAPK) 1/3 signaling pathways with the intention of minimizing the generation of reactive oxygen species (ROS) and the expression of inflammatory cytokines.		[16][17]
10	Asiatic acid	*Centella asiatica*	The compound enhances the healing process by increasing collagen production, promoting cell growth, enhancing fibroblast division, and contributing to the regrowth of skin tissue during both the early and late stages of wound healing.		[18][19]
11	Pinocembrin	*Pinus heartwood Eucalyptus*	This compound diminishes the functionality of the RAGE receptor and regulates its downstream targets, including the NF-κB and MAPK pathways, resulting in anti-inflammatory effects on macrophages.		[20]

12	Steroial glycoside	*Oleaceae Liliaceae Scrophulariaceae*	The application of steroidal glycoside wound therapy stimulated the expression of genes related to inflammation, such as IL2, IL4, IL10, CD40LG, IFNG, and CXCL11, as well as genes involved in tissue remodeling, including CTSG, F13A1, FGA, MMP, and PLG.		[21][22]
13	Verbascoside	*Arrabidaea pulchra, buddleja brasiliensis, verbasom phlomoides, penstemon barbatus*	Levels of TNF, INF, IL-6, MCP-1, and IL-12p70 were significantly decreased.		[23]
14	Artocarpin	*A.altilis plant*	This substance stimulates the proliferation and migration of human skin cells by activating the ERK and P38 signaling pathways and promotes the proliferation and formation of blood vessel cells through the Akt and P38 pathways.		[24][25]
15	Catechin	*Camellia sinesis*	The substance in question has been observed to reduce the production of pro-inflammatory cytokines such as IL-1 and TNF, while increasing the production of the anti-inflammatory cytokine IL-10.		[26][27]
16	Luteolin	*Reseda luteola*	Lutein promoted wound healing in diabetic mice by decreasing inflammation and oxidative stress, which was achieved by inactivating NF-κB and upregulating Nrf2.		[28][29]
17	Gallic acid	*Arctostaphylos uva-ursi, Quercus spp.*	Gallic acid promotes wound healing by activating focal adhesion kinases (FAK), c-Jun N-terminal kinases (JNK), and extracellular signal-regulated kinases (ERK).		[30][31][32]
18	Ferulic acid	*commelinid plants, Cynara cardunculus*	Ferulic acid ointment mitigates lipid peroxidation and enhances the levels of catalase, superoxide dismutase, and glutathione during the healing process, thereby hastening wound healing.		[33][34]
19	Tannins	*Caesalpinia spinosa, Rhus coriaria*	Tannins may potentially promote wound healing by neutralizing free radicals and reactive oxygen species (ROS), leading to faster contraction and the growth of capillary vessels and fibroblasts.		[35][36]
20	Arnebin-1	*Arnebia nobilis*	Arnebin-1 accelerates wound healing by promoting cell proliferation, blood vessel formation, and collagen production. Specifically, it leads to an increase in the levels of fibronectin (FN), transforming growth factor-beta 1 (TGF-1), and collagen in the wounds.		[37][38][39]
21	Lawsone	*Lithospermum Erythrorhizon*	Aryl Hydrocarbon Receptors (AhRs) play a crucial role in regulating tissue regeneration, pathogenesis, inflammation, and homeostasis. AhR is essential for maintaining skin integrity and for supporting the immune system.		[40][41]

22	Cryptotanshinone (CPT)	*salvia Miltiorrhiza Bunge*	The substance impedes the proliferation of Huh 7 cells, stimulates apoptosis, and enhances autophagy while dampening the P13/AKt/mTOR signaling pathway.		[42][43][44]
23	Asiaticoside	*Cantella asiatica grass*	This substance promotes the production of type 1 collagen in human dermal fibroblasts through the Smad signaling pathway, without the involvement of TGF beta receptor 1 kinase. In addition, it increases the levels of antioxidants.		[45] [46]

Conclusion

Many plant-derived chemicals with strong wound healing capabilities are exploited in the development of topical formulations and wound dressings. However, there are little publications on the dosage levels, toxicology and adverse effects of these substances. Because of their ease of access and low cost, effective wound healing therapies based on natural ingredients are extremely advantageous to patients. This paper advocated a comprehensive investigation of plant-based natural compounds for wound healing. Readers were given data tables that detailed the origin, mechanism, and structure.

Consent for publication

No applicable.

Declaration of competing interest

Author Monika (M), Rakesh Mishra (RK) and Surabhi Bajpai (SB), declare no conflict of interest.

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