

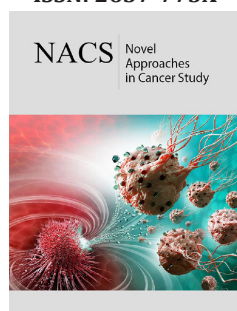
# Anti-Inflammatory Responses of Natural Products in Wounds and Cancer Infections

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## Abstract

The link between wound healing and cancer has been known for a long time. The mechanisms that control wound healing have been shown to promote malignant cell transformation and growth. Chronic inflammation has also been linked to malignant transformation in a variety of tissues. Inflammation and wound healing pathways have recently been found to boost Cancer Stem Cell (CSC) populations. These highly resistant cells can repopulate the tumour after treatment, causing local and systemic recurrences.

Although a wound appears to be a simple tissue injury, it can be very complicated depending on the individual's health and other factors. As a result, wound healing has received a lot of attention in the medical community. Through phases of hemostasis, inflammation, proliferation, and remodeling, wound healing in biology is precise and highly programmed. Antimicrobial agents, healing promoters, and the use of herbal and natural products are some of the current wound healing options. Recent scientific evidence and clinical trials conducted in wound therapy using traditional and alternative medicine show promise for the future.

**Keywords:** Phytotherapy; Alternative medicine; Traditional medicine; Wound healing; Cancer infections

## Introduction

Tumors have been described as non-healing wounds. Normal epithelial tissue is in a state of homeostasis with epithelial stem cells located within highly specialised niches that tightly control tissue regeneration. The proliferation of these stem cells and their progeny in response to proinflammatory cytokines ensures the replenishment of epithelial cell loss during tissue injury [1]. Both wounds and cancer cause an inflammatory response, and both cause the release of several key "damage" attractants, such as  $H_2O_2$ , HMGB1, and chemokines that bind CXCR2, which drive innate immune cell recruitment. For both cancer and wound healing, the inflammatory response to cancer and wound healing can be significantly influenced by the local microbiome as well as local or systemic infection [2]. Traditional medicine (also called indigenous or folk medicine) is a body of knowledge that has been passed down through generations in various societies prior to the advent of modern medicine. Herbal, Ayurveda, Siddha, Unani, Chinese, Acupuncture, and other pseudo-medical knowledge and practices are all examples of traditional medicines [3]. The global medicinal market is dominated by medicinal plant materials and herbal remedies derived from them. Throughout human history, herbal remedies and drugs have played an important role in the treatment of diseases. Despite the abundance of literature on their curative properties, there are no standard procedures for quality control of plant materials in terms of identification (phytochemical, pharmacological, and therapeutic activity). Medicinal plant standardization ensures consistency and therapeutic effectiveness. Herbal products are assessed for their identity (characterization), quality, and the quality of the extracts present, as it is necessary to assess their therapeutic efficacy, i.e., to understand their pharmacological action in order to establish authenticity [4].

## Phases of Acute Wound Healing

Hemostasis, inflammation, proliferation, and tissue remodeling or resolution are the four highly integrated and overlapping phases of wound healing. These phases and their biophysiological functions must occur in the correct order, at a specific time, and at an optimal intensity for a specific duration. Many factors can affect wound healing, interfering with one or more phases of the process and resulting in inadequate or impaired tissue repair [5]. ECM, extracellular matrix. Most chemotherapeutic drugs are designed to inhibit cellular metabolism, rapid cell division, and angiogenesis, thereby inhibiting many of the pathways required for proper wound healing. These medications reduce fibroplasia and neovascularization of wounds by inhibiting DNA, RNA, or protein synthesis [6,7]. Chemotherapeutic drugs slow cell migration into the wound, reduce early wound matrix formation, reduce collagen production, impair fibroblast proliferation, and inhibit wound contraction [7]. Furthermore, these agents impair patients' immune functions, impeding the inflammatory phase of healing and increasing the risk of wound infection. Chemotherapy causes neutropenia, anemia, and thrombocytopenia, which makes wounds vulnerable to infection, reduces oxygen delivery to the wound, and puts patients at risk of excessive bleeding at the wound site [5]. Impaired wound healing caused by chemotherapeutic drugs such as adriamycin is most common when the drugs are given prior to surgery or within 3 weeks after surgery [8]. Additionally, low post-operative albumin levels, low post-operative haemoglobin levels, advanced disease stage, and electrocautery use have all been

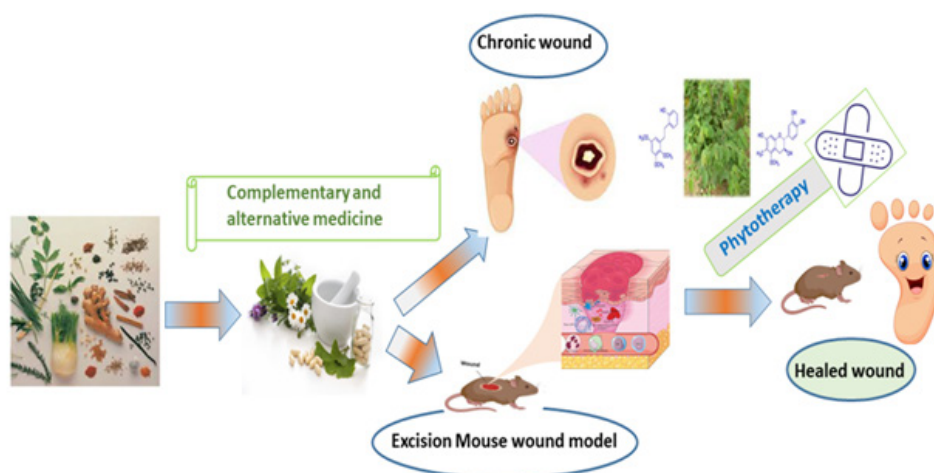
identified as risk factors for wound complications [9].

## Role of Complementary and Alternative Medicines

Alternative medicine is any healing practice "that does not fall within the realm of conventional medicine." The terms 'complementary medicine' or 'alternative medicine' is used interchangeably with traditional medicine in some countries. It is based on ancient people's or communities' traditional knowledge, which they have been using for many years. Because there was no modern or scientifically approved medicine available in prehistoric times, CAMs were the only option for treating many diseases, including wounds [10].

One of the fundamental principles of traditional medicine is the use of natural medicine and principles for healing. Although the majority are not in the mainstream due to a lack of evidence, some have successfully entered clinical utility after gaining significance in various stages of research for inflammation, cancer, and other chronic diseases. This is due to natural molecules' unique ability to interact with various biomolecules. Therefore, it's critical to understand the critical cellular components that are altered during wound healing and progression, as well as the molecules that can reverse or repair those changes. There is a lot of potential for developing a safe, long-lasting, and effective treatment module using alternative medicine derived from plants or other natural sources in this direction. This will aid in the scientific promotion of several traditional medicines for the treatment of various types of wounds [2].

## Conclusion and Future Directions



**Figure 1:** Graphical abstract-wound healing role of complementary and alternative medicine.

Wound healing is a complex biological process that consists of hemostasis, inflammation, proliferation, and remodeling. Large numbers of cell types -including neutrophils, macrophages, lymphocytes, keratinocytes, fibroblasts, and endothelial cells -are involved in this process. Multiple factors can cause impaired wound healing by affecting one or more phases of the process and are categorized into local and systemic factors. The influences of these factors are not mutually exclusive. Single or multiple factors may

play a role in any one or more individual phases, contributing to the overall outcome of the healing process. In conclusion, proteins, carbohydrates, arginine, glutamine, polyunsaturated fatty acids, vitamin A, vitamin C, vitamin E, magnesium, copper, zinc, and iron all play important roles in wound healing, and deficiencies in these nutrients have an impact on wound healing. More research is needed to fully understand how nutrition affects the healing response. In addition to this, the use of natural products and naturally derived

substances are considered safe compared to synthetic molecules and can be much cheaper than conventional therapies (Figure 1); (Table 1).

**Table 1:** Wound-healing process.

Phase	Cellular and Bio-Physiologic Events
Hemostasis	i. Vascular constriction
	ii. Platelet aggregation, degranulation, and fibrin formation (thrombus)
Inflammation	i. Neutrophil infiltration
	ii. Monocyte infiltration and differentiation to macrophage
	iii. Lymphocyte infiltration
Proliferation	i. Re-epithelialization
	ii. Angiogenesis
	iii. Collagen synthesis
	iv. ECM formation
Re-modeling	i. Collagen remodeling
	ii. Vascular maturation and regression

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