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Review Article

CHROMOLAENA ODORATA: AS NATURE'S WOUND HEALER

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ABSTRACT

According to the world health organization, more than 80% of the world's population relies on traditional medicine for their primary health needs. The use of herbal medicines represents a long history of human interactions with the environment. The study of wound-healing plants has acquired an interdisciplinary nature with a systematic investigational approach. Several biochemical are involved in the healing process of the body, including antioxidants and cytokines. Phytochemicals or biomarkers from numerous plants suggest they have positive effects on different stages of the wound healing process via the various mechanism. Injury to the soft tissues is followed by wound healing, which consists of four stages: hemostasis, inflammation, proliferation and remodeling. *Chromolaena odorata* is a weed that is traditionally used for the treatment of various ailments in humans and animals. However, it exhibits anti-inflammatory, antipyretic, analgesic, antimicrobial, cytotoxic and numerous other relevant medicinal properties on an appreciable scale, and is known in some parts of the world as a traditional medicine used to treat various ailments. To understand its specific role as nature's gift for healing wounds and its contribution to affordable health care, this plant must be scientifically assessed based on the available literature. This review aims to summarize the role of *C. odorata* and its biomarkers in the wound healing activities of biological systems, which are crucial to its potential future use for the treatment of wounds.

Keywords: *Chromolaena odorata,* Wound healing, Antioxidant, Weed

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INTRODUCTION

Wounds are physical injuries to the skin that take various forms including lacerated wounds, bruises, burns, etc. Based on the physiology of wound healing and its various phases, wounds can be classified as open or closed wounds and acute or chronic wound. Wound healing is essential for the restoration of disrupted anatomical integrity and disturbed function of the affected area. The restoration of the affected area is the main aim of quality wound rehabilitation [1]. Healing is a complex and intricate process, initiated in response to an injury that serves to restore the function and integrity of the damaged tissues. Wound healing is a normal biological process in the human body that is achieved via four rigidly coordinated phases: Hemostasis, inflammation, proliferation and remodeling. Wound healing, therefore, involves a number of processes, including inflammation, cell proliferation and contraction of the collagen lattice. In addition, the healing process may be hampered by the presence of oxygen free radicals or microbial infection [1, 2].

Chromolaena odorata (L) King and Robinson *Asteraceae* is commonly known as Siam weed, is a diffuse and a fast-growing perennial and invasive weed native to South and Central America. It has been introduced into the tropical regions of Asia, Africa and other parts of the world. It is an aggressive competitor that occupies different types of lands where it forms dense strands that prevents the establishment of other flora. It suppresses young plantations, agricultural crops and smothers vegetation as it possesses allelopathic potentialities and growth inhibitors. In recent decades, it has become a serious pest in the humid tropics of South East Asia, Africa and the Pacific Islands [3]. It spreads rapidly in lands used for forestry, pasture and plantation crops such as rubber, coffee, coconut, cocoa and cashew [4]. The genus *Chromolaena* includes 1,200 species of small herbs, shrubs or subshrubs distributed chiefly in the Americas, a few in Europe, Asia, and tropical Africa. *C. odorata* is a poisonous plant that contains exceptionally high levels of nitrates in young plants, at 5-6 times greater than the level toxic to wildlife. It is considered a menace because it affects plantations and other ecosystems due to its invasive nature. The economic value of *C. odorata* is low [5]. Consequently, there is a relative paucity of research works on it.

Scientific classification and general information of *C. Odorata*

Fig. 1: Leaves of *chromolaena odorata*

Kingdom: Plantae

Clade: Angiosperms

Clade: Eudicots

Order: Asterales

Family: Asteraceace

Genus: Chromolaena

Species: *C. Odorata*

Organism type: Herb

Habitat: Agricultural areas, natural forest, planted forests, grasslands.

Common names: Siam weeds, Triffed weed, Bitter bush/Jack in the bush [5].

Chemical constituents of *Chromolaena odorata*

C. odorata Linn has been undertaken that have identified constituents including monoterpenes, sesquiterpenes, hydrocarbons, triterpenes/

steroids, alkaloids and flavonoids. The leaves of this plant have been found to be a rich source of flavonoids including quercetin, sinensetin, sakuranetin, padmatin, kaempferol and salvagenin [7]. The leaves of *C. odorata* also contain the highest concentration of allelochemicals isolated from a plant. A study in Vietnam revealed that the aqueous extract of the leaf contained flavonoids (salvigenin, sakuranetin, isosakuranetin, kaempferide, betulenol, 2-5-7-3 tetra-o-methyl quercetagetin, tamarixetin, two chalcones and odoratin and its alcoholic compound), essential oils (geyren, bornyl acetate and β-eubeden), saponin triterpenoids, tannins, organic acids and numerous trace substances(3). The crude ethanol extract of *C. odorata* contains phenolic acids (protocatechuic, p-hydroxybenzoic, p-coumaric, ferulic and vanillic acids) and complex mixtures of lipophilic flavonoid aglycones (flavanones, flavonols, flavones and chalcones (protocatechuic, p-hydroxybenzoic, p-coumaric, ferulic and vanillic acids) and complex mixtures of lipophilic flavonoid aglycones (flavanones, flavonols, flavones and chalcones)(1,2). Till date, studies on *C. odorata* have resulted in the isolation of 17 compounds, including 5aα, 6,9,9aβ,10-pentahydro-10β-hydroxy-7-methylanthra[1,2-d] [1,3]dioxol-5-one, 1,2-methylenedioxy-6-methylanthraqui-none, 3-hydroxy-1,2,4-trimethoxy-6-methylanthraquinone, 3-hydroxy-1,2-dimethoxy-6-methylanthra-quinone and 7-methoxy-7-epi-medioresinol, as well as 12 known compounds including odoratin, 3β-acetyloleanolic acid, ursolic acid, ombuin, 4,2'-dihydroxy-4',5',6'-trime-thoxychalcone, (-)-pinoresinol, austrocortinin, tianshic acid, cleomiscosin D, (-)-medioresinol, (-)-syringaresinol, and cleomiscosin A [7, 8].

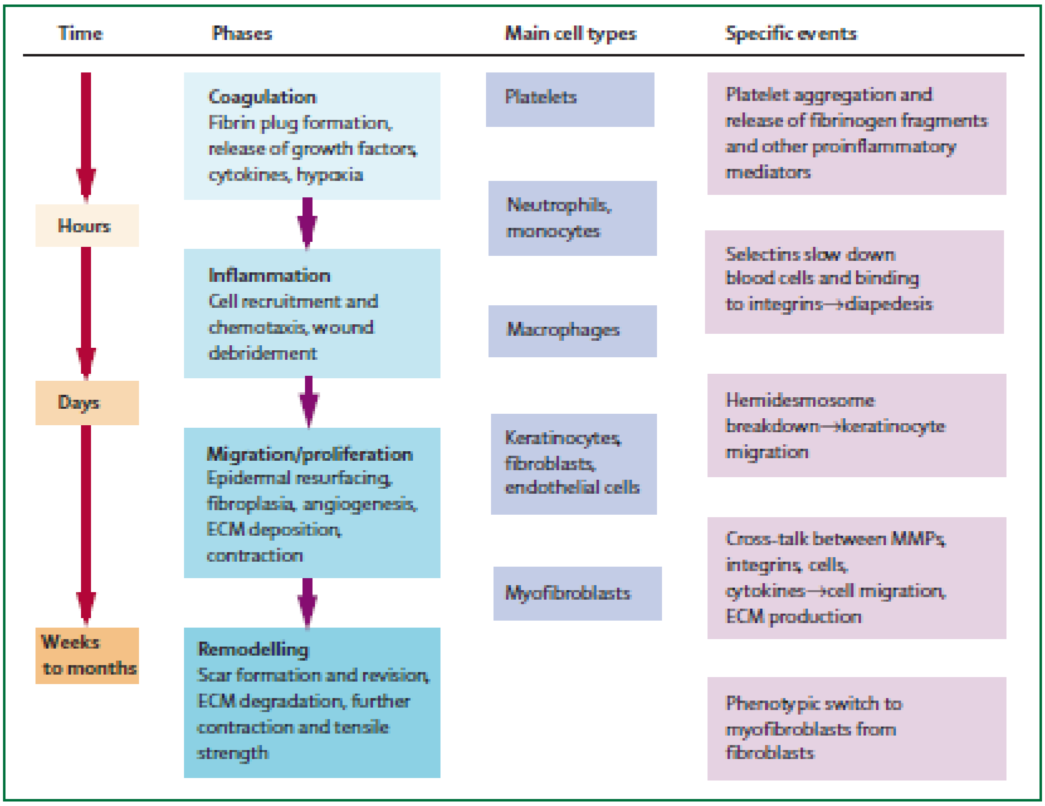

Fig. 2: Phases of wound healing, major types of cells involved in each phase, and selected speci fic events

Mechanism of wound healing

The most established effect of *C. odorata* is on wound healing. The constituents of the plant extracts modulate one or more of the overlapping wound healing stage [8]. For its traditional usage in wound healing, a paste of ground leaves is applied topically to the affected area. *In vitro* and *in vivo* studies of these extracts have demonstrated that they enhanced fibroblast, endothelial cell and keratinocyte proliferation; stimulated keratinocyte migration *in vitro*; upregulated the keratinocyte-induced production of extracellular matrix (ECM) proteins and basement membrane components; and inhibited collagen lattice contraction by fibroblasts endothelial cell and keratinocyte proliferation; stimulated keratinocyte migration *in vitro*; up regulated the keratinocyte-induced production of extracellular matrix (ECM) proteins and basement membrane components; and inhibited collagen lattice contraction by fibroblasts [8].

The process of wound healing involves four overlapping phases: Haemostasis (cessation of bleeding), inflammation, proliferation and remodeling.

Phases 1 and 2: Coagulation and inflammation the different phases of wound healing not only overlap but also have ramifications beyond their more obvious immediate purposes. Soon after the injury, a fibrin plug forms and inflammatory cells are quickly recruited to the wound. Coagulation is needed for haemostasis and wound protection. The fibrin plug consists of platelets embedded in a meshwork of mainly polymerized fibrinogen (fibrin), fibronectin, vitronectin, and thrombo-spondin; it is an immediate way to ward off bacteria and provide temporary wound coverage, but also has other roles [9]. During their incorporation within the plug, platelets aggregate and release a wide range of growth factors, including platelet-derived growth factor (PDGF) and transforming growth factor (TGF). These and other growth factors, the activation of which also depends on pH and other parameters within the injured tissue, have an early role in cell recruitment and a later one in ECM formation. As another example of multiple effects, thrombin polymerization of fibrinogen to fibrin yields fragments, such as fibrinopeptides A and B, which can recruit inflammatory cells to the wound. Then, through the endothelial expression of selectins, leucocytes are slowed down in the bloodstream enough that stronger forces generated by binding to integrins will help their movement through endothelial gaps and into the extracellular space (diapedesis). Again, these inflammatory cells recruited to the wound have several purposes [10]. Neutrophils and macrophages, whose function is impaired in diabetes, aid in wound debridement.

However, both cell types produce several key growth factors and mediators that keep fuelling the repair process: for example, connective tissue growth factor was first identified in neutrophils. Immediately after injury, the wound is hypoxic because of damage to the blood vessels. This seemingly deleterious situation has some beneficial effects and might help prepare for the next phase of healing. Hypoxia increases keratinocyte migration, early angiogenesis, proliferation and clonal expansion of fibroblasts, and the transcription and synthesis of crucial growth factors and cytokines, including PDGF, vascular endothelial growth factor, and TGF. Later, within the next 2–3 d, inflammatory and dermal cells recruited to the injury site produce a powerful armamentarium of growth factors and cytokines. Circulating monocytes take up residence at the injury site as tissue macrophages, and so do fibroblasts and endothelial cells as they form the early granulation tissue that begins the process of contraction [11].

Phases 3 and 4: Migration-proliferation and remodeling. As the inflammatory phase of wound healing is toned down (fig. 2), wound contraction begins, but stable wound closure needs to be addressed. Formation of ECM proteins, angiogenesis, contraction, and keratinocyte migration are essential components of these phases. Matrix proteins, including collagens, fibronectin, and vitronectin, provide substrates for cell movement, vehicles for changing cell behavior, and structures that return function and integrity to the tissue[12]. Angiogenesis makes possible the re-supply of oxygen and other nutrients. Contraction, aided by the formation of ECM, granulation tissue, and the emergence of myofibroblasts, is a rap id and efficient way of achieving wound closure. The balance between contraction and keratinocyte-dependent closure has much to do with the depth and location of the wound and the presence of complications due to infection and seems to be impaired in diabetic wounds. Another critical balance is the deposition, persistence, and dynamic remodelling of ECM proteins [13].

It is well established that *C. odorata* enhances the proliferation of various cell types, including dermal fibroblasts, endothelial cells and epidermal keratinocytes, which may partially explain the beneficial clinical effects on the wound healing process(7). *C. odorata* may also contribute to wound healing by stimulating the production of antioxidants at the wound site, therefore protecting tissues from oxidative damage and providing a favorable environment for tissue healing [13].

CONCLUSION

This review has aimed to justify the inclusion of this plant in the management strategy of wound healing. *C. odorata* and its constituents have proven to be helpful in enhancing wound healing activities, therefore, further research is expected to examine the purified constituents to enhance understanding of the mechanisms underlying its wound healing activity. *C. odorata* has been proven safe for application and, therefore, its activity as a wound healing agent for superficial and internal wounds, such as gastric ulcers, should be further investigated for its potential to provide affordable healthcare for wound management.

AUTHORS CONTRIBUTIONS

All the author have contributed equally

CONFLICT OF INTERESTS

Declare none

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