Chromolaena odorata: A neglected weed with a wide spectrum of pharmacological activities (Review)

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Abstract. The study of wound-healing plants has acquired an interdisciplinary nature with a systematic investigational approach. Several biochemicals are involved in the healing process of the body, including antioxidants and cytokines. Although several pharmaceutical preparations and formulations are available for wound care and management, it remains necessary to search for efficacious treatments, as certain current formulations cause adverse effects or lack efficacy. Phytochemicals or biomarkers from numerous plants suggest they have positive effects on different stages of the wound healing process via various mechanisms. Several herbal medicines have displayed marked activity in the management of wounds and various natural compounds have verified *in vivo* wound healing potential, and can, therefore, be considered as potential drugs of natural origin. *Chromolaena odorata* (L.) R.M. King and H. Robinson is considered a tropical weed. 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 healthcare, 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 drug design, development and application for the treatment of wounds.

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Abbreviations: ECM, extracellular matrix; HO-1, heme oxygenase-1; MMP, matrix metalloproteinase; PMNL, polymorphonuclear leukocytes; ROS, reactive oxygen species

Key words: Chromolaena odorata, wound healing, weed, signaling

Contents

1. Introduction

Wounds are physical injuries that can be classified as 'open' or 'closed', based on the underlying cause, and 'acute' or 'chronic', based on the physiology of wound healing (1-3). Wound healing is essential for the restoration of disrupted anatomical integrity and disturbed function of the affected area (4,5). 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 (6). Chronic wounds are a major concern for patients and clinicians, affecting a large number of patients and leading to a serious reduction in their quality of life (7). Recent estimates indicate that ~6 million people suffer from chronic wounds worldwide (7,8), while in the US, traumatic wounds result in >300,000 hospitalizations annually (7,8).

The restoration of the affected area is the main aim of quality wound rehabilitation. Surgical wounds account for the vast majority of skin injuries, with ~80% of these wounds requiring the use of some form of closure product, such as sutures, staples or tape, while numerous wound management strategies use hemostasis products, fabric bandages and surgical dressings (9,10).

Wound healing is a normal biological process in the human body that is achieved via four rigidly coordinated phases: Hemostasis, inflammation, proliferation and remodeling (4,6). Wound healing, therefore, involves a number of processes, including inflammation, cell proliferation and contraction of the collagen lattice (11-13). In addition, the healing process

may be hampered by the presence of oxygen free radicals or microbial infection (5,6). Over the last 15 years, the *in vitro* tests developed to investigate wound healing have exploited all of these processes as targets for enhancing its management. Since the different phases of the wound healing process overlap, an ideal plant-based remedy should affect at least two phases before it can be considered to have scientific support for its use (12-14). Despite significant advances in the pharmaceutical industry, the pursuit of effective and low cost therapies for wound healing remains a challenge for modern medicine due to the potentially chronic nature of injuries and the side effects associated with current therapies (15-19). In the search for novel therapeutic options, plants and their metabolites represent an important potential source of biomolecules.

2. Plant-derived wound healing agents

Numerous medicinal plants have been reported to possess wound healing activity (20-28). During the 20th century, 80% of the world population depended on traditional medicine for their primary healthcare requirements (29). Medicinal plants continue to serve an important role in healthcare as a source of novel drugs, and herbal and food supplements. However, several ethnic groups have failed to retain their historical collective knowledge of such medicinal plant use (30); the disappearance of traditional cultural and natural resources due to population growth, urbanization, and the erosion of botanical knowledge in developing countries may result in the potentially permanent loss of such unrecorded knowledge and information (31). Folk and tribal medicine practices employ numerous plants and animal products for the treatment of cuts, wounds and burns (12). Some of these plants have been screened scientifically to evaluate their wound healing activity in different pharmacological models and human subjects; however, the potential of most of these plants remains unexplored (29-31). It is, therefore, critical to ensure that the agents that are currently used in traditional systems of medicine do not disappear from use before they can be fully assessed and documented (32).

Research on wound healing agents is one of the emerging areas in modern biomedical sciences (33-37). For medicinal plants to properly contribute to affordable healthcare, they must be scientifically assessed; phytochemical screenings are often considered as the first step towards the discovery of useful drugs (38,39). Successive solvent extraction techniques, as well as chromatographic separations and spectroscopic methods, have been used to determine the chemical constituents of plants and study their bioactivity as it applies to traditional medicine (32,37). A number of secondary metabolites and active compounds isolated from plants have been demonstrated as active facilitators of wound healing in animal models. Important examples include: Tannins from *Terminalia arjuna* (40); oleanolic acid from *Anredera diffusa* (41); polysaccharides from *Opuntia ficus-indica* (42); gentiopicroside, sweroside and swertiamarin from *Gentiana lutea* (43); shikonin derivatives (deoxyshikonin, acetyl shikonin, 3-hydroxy-isovaleryl shikonin and 5,8-odimethyl acetyl shikonin) from *Onosma argentatum* (44); asiaticoside, asiatic acid and madecassic acid from *Centella asiatica* (45-47); quercetin, isorhamnetin and kaempferol from *Hippophae rhamnoides* (48); curcumin from *Curcuma longa* (49); oleoresin from *Copaifera langsdorffii* (50); proanthocyanidins and resveratrol from grapes (51,52), acylated iridoid glycosides from *Scrophularia nodosa* (53); phenolic acids (protocatechuic, p-hydroxybenzoic, p-coumaric, ferulic and vanillic acids) from *C. odorata* (54,55); glycoprotein fraction of *Aloe vera* (56); (+)-epi-alpha-bisabolol from *Peperomia galioides* (57); fukinolic and cimicifugic acids from *Cimicifuga* spp. (58); and xyloglucan from *Tamarindus indicus* (59).

A major challenge to the pharmacological validation of wound healing plants, is that the exact mechanism of the process of wound healing is not clearly understood; wound healing is known to be a complicated process involving a number of stages, including inflammation, epithelization, antioxidant defense and biochemical changes (hydroxyproline), granulation, neovascularization and wound contraction (60), however, the precise mechanistic details remain unclear. The majority of research studies into medicinal plants are, therefore, restricted to screening plants to simply evaluate their wound healing effects and investigate the mechanistic details. This review aims to evaluate the current knowledge and information available regarding the underutilized and neglected medicinal plant *C. odorata*, including its mechanism of action *in vitro* and *in vivo,* and to examine the ethnopharmacological claims of the usefulness of this plant. This may contribute to encouraging the global acceptance of wound healing agents of plant origin and the recognition of their important natural role in wound healing. To support this, a study reported that ~31% of these medicinal plants have been used to treat wounds, 29% have been used to treat cuts, 10% to treat burns, and 22% to treat cuts and wounds (27,61).

3. *Chromolaena odorata* as nature's wound healer

C. odorata [Linn (L.)] King and Robinson (formerly known as *Eupatorium odoratum* L. Table I), belongs to the kingdom Plantae, subkingdom Tracheobionta (vascular plants), superdivision Spermatophyta (seed plants), division Magnoliophyta (flowering plants), class Magnoliopsida (dicotyledons), subclass Asteridae, order Asterales, family Compositae, genus *Chromolaena* DC (Thoroughwort), and species *C. odorata* (L.) (62-67). It belongs to the largest family of flowering plants, which contains about 900 genera and 13,000 species (62-67). *C. odorata* is also known as *Eupatorium conyzoides* Vahl, *Eupatorium brachiatum* Siam weed. ex Wiestr, *Eupatorium atriplicifolium* Vahl and *Osmia odorata* (L.) Schultz-Bip. It is colloquially known in English by names including Siam weed, triffid weed, bitter bush, Jack in the Bush, Christmas bush and baby tea, and by numerous other names in other countries and languages (68).

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 (54,55,67,69,70). *C. odorata*, and closely related *Eupatorium spp.,* have been discovered in Europe including France, Thailand, China and Indo-China (54,55,66,69,71). Compared with other large families, such as Leguminosae, the number of important economic products derived from the family Compositae is relatively small (62,65). *C. odorata* is a diffuse and scrambling perennial shrub that grows to a height of 3-7 m in the open (72-75).

Table I. General information about *C. odorata*.

Scientific name	*Chromolaena odorata*
Taxonomic name	*Chromolaena odorata* (Linn) King & Robinson
Family	*Asteraceae (Compositae)*
Genus	*Chromolaena*
Synonym	*Eupatorium odoratum*
Organism type	Herb (54,64)
Habitat	Agricultural areas, natural forests, planted forests, range/grasslands, riparian zones, ruderal/disturbed, scrub/shrublands (74).
Common names	Siam weeds (64,65,66,67,69,80); Triffed weeds (64,65); Bitter bush/ Jack in the bush (64,65); Pokok kapal terbang or aeroplane plant (69,80); Pokok Jerman (69)

It is a prolific weed that thrives in the majority of soil types, is found in abundance on open wasteland and along roadsides, and prevents the establishment of other flora (76,77). *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 (78). It is considered a menace because it affects plantations and other ecosystems due to its invasive nature (66,79).

As outlined in Fig. 1, *C. odorata* has been reported to exhibit antibacterial, antiplasmodic, antiprotozoal, antitrypanosomal, antifungal, antihypertensive, anti-inflammatory, astringent, diuretic, hepatotropic (54,55,66,80-82), immunomodulatory (83) and anticancer effects (84-90). It is also applied topically as an antidote to the sting of the spine of the common sea catfish (86). Traditionally, fresh leaves or a decoction of *C. odorata* have been used throughout Vietnam and other tropical countries for the treatment of leech bites, soft tissue wounds, burn wounds, skin infections, rashes, diabetes and periodontitis, and as an insect repellent (54,55,91-93). A poultice of the leaves is traditionally applied to cuts or wounds to stop bleeding and promote healing (69,76,93). Eupolin, a product made from *Chromolaena* spp., has already been licensed for use in Vietnam for the treatment of soft tissue burns and wounds (69,94-97). An aqueous decoction of the roots is used as an antipyretic and analgesic remedy, and a leaf extract with salt is used as a gargle for sore throats and colds (69). The fresh leaves and extracts of *C. odorata* are traditional herbal treatments in certain developing countries, including Thailand, India and Vietnam, for burns, soft tissue wounds, and skin infections (81,94,96).

4. Chemical constituents of *Chromolaena odorata*

Several chemical analyses of *C. odorata* L. have been undertaken that have identified constituents including monoterpenes, sesquiterpenes hydrocarbons, triterpenes/steroids, alkaloids and flavonoids (98-100). The leaves of this plant have been found to be a rich source of flavonoids including quercetin, sinensetin, sakuranetin, padmatin, kaempferol and salvagenin (86,98). The leaves of *C. odorata* also contain the highest concentration of allelochemicals isolated from a plant (98). 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 (99). Another study by Heiss *et al* (100) demonstrated that 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). To 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-methylanthraquinone, 3-hydroxy-1,2,4-trimethoxy-6-methylanthraquinone, 3-hydroxy-1,2-dimethoxy-6-methylanthraquinone 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'-trimethoxychalcone, (-)-pinoresinol, austrocortinin, tianshic acid, cleomiscosin D, (-)-medioresinol, (-)-syringaresinol, and cleomiscosin A (99). Fig. 2 presents the chemical structures of a few of the important bioactive compounds in *C. odorata*, including stigmasterol, scutellarein tetramethyl ether (Scu; 4',5,6,7-tetramethoxy-flavone), flavonoids (98,99,101,102), and the phytoprostane compound chromomoric acid C-1 (100).

5. Pharmacological activities and wound healing mechanism

Wound healing is an intricate process by which the skin or other organs and tissues self-repair following injury (103). In normal skin, the epidermis and dermis form a protective barrier against the external environment. The moment the injury occurs and this protective barrier breaks, the process of wound healing is immediately activated, and can continue for months or years (3). Wound healing involves continuous cell-cell and cell-matrix interactions (104), and requires the collaborative efforts of numerous different tissues and cell types, including platelet aggregation and blood clotting, fibrin formation, inflammation, angiogenesis and reepithelialization (105,106). Healing is considered complete once the disrupted surfaces are firmly knitted together by collagen (107). Optimal wound healing involves minimizing tissue damage and providing adequate tissue perfusion and oxygenation, proper nutrition and a moist wound healing environment to restore function to the injury site (108).

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 stages. Extracts of the leaves and other plant parts of *C. odorata* (Table II) have been demonstrated to be beneficial in the treatment of wounds and other disorders (54,55,69,71-73,92,109-112). For its traditional usage in wound healing, a paste of ground leaves is applied topically to the affected area (97,113). *In vitro* and *in vivo* studies of these extracts have demonstrated that they enhanced fibroblast,

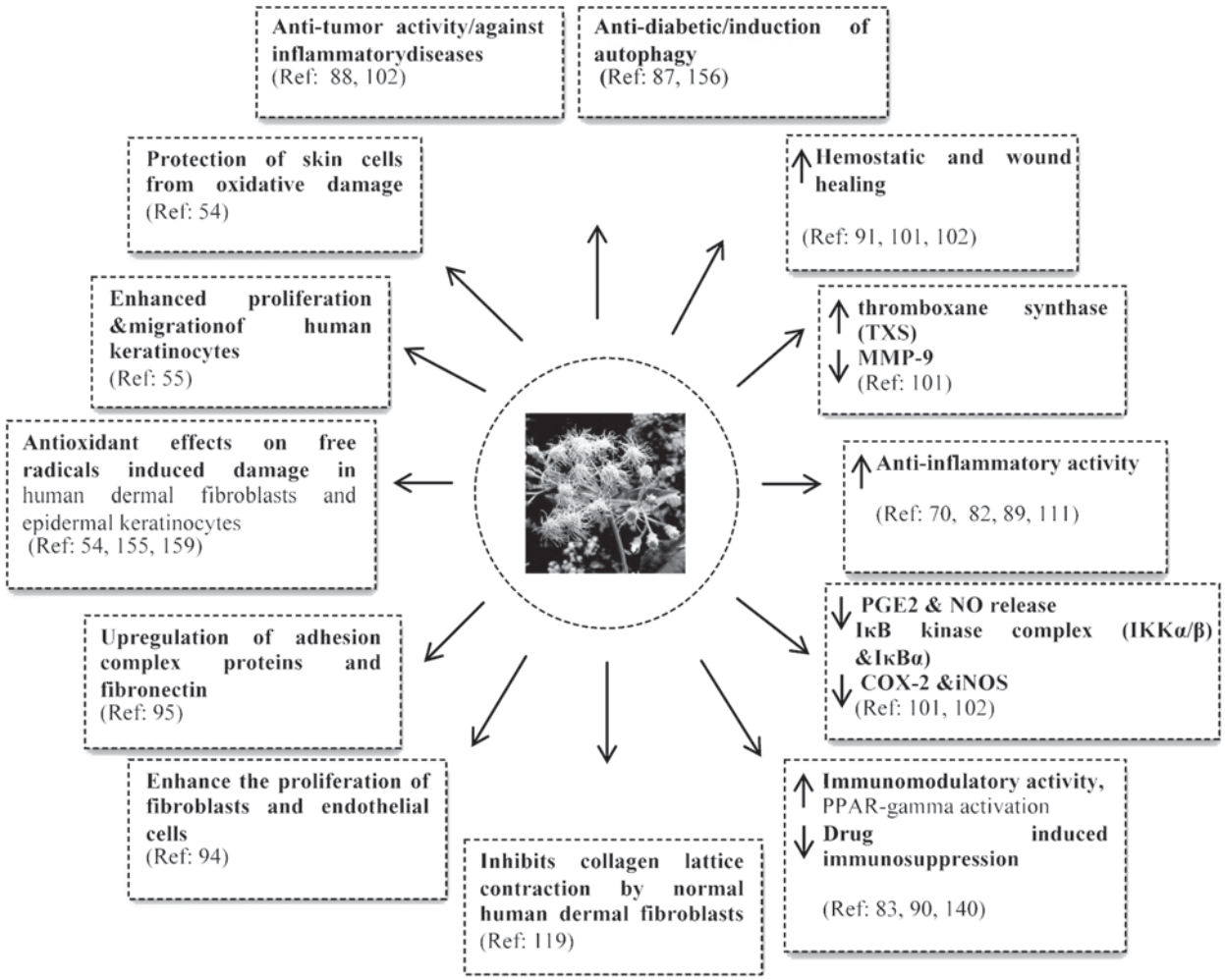

Figure 1. Cellular and bio-physiologic events associated with treatment with *Chromolaena odorata* extract.

endothelial cell and keratinocyte proliferation; stimulated keratinocyte migration *in vitro* (54,55); upregulated the keratinocyte-induced production of extracellular matrix (ECM) proteins and basement membrane components; and inhibited collagen lattice contraction by fibroblasts (85,90,94,95).

The process of wound healing involves four overlapping phases: Hemostasis (cessation of bleeding), inflammation, proliferation and remodeling (114-116). Thromboxane synthase is the primary regulator of hemostasis; the enzyme that converts prostaglandin H_2 to thromboxane A_2, which has potent vasoconstriction and platelet aggregation activity (117). Plasminogen activator inhibitor type 1 is also involved in hemostasis by inhibiting fibrinolysis, which prevents failure of the hemostasis (118). Subsequently, during the inflammatory phase, free radicals are released from neutrophils to kill bacteria (119,120), and heme and heme proteins locally accumulate at the wound site. Heme and heme proteins exert prooxidative and proinflammatory effects via increasing the expression level of adhesion molecules, increasing vascular permeability and increasing leukocyte infiltration, which induce wound healing. Heme oxygenase-1 (HO-1) is anti-inflammatory and is an antioxidant involved in a variety of wound healing processes. HO-1 produces biliverdin/bilirubin, iron, and carbon monoxide from heme, which have potent antioxidant effects. HO-1 overexpression accelerates wound healing by reducing inflammation, increasing proliferation, and inhibiting endothelial cell apoptosis (121). Matrix metalloproteinases (MMPs) are also important in wound healing via effects on remodeling of the ECM (122). MMP-9 is key effector among MMP proteins (123). Various reports have demonstrated that *C. odorata* extract accelerates hemostasis (124-126) and wound healing (54,94,95). In addition, Scu and stigmasterol also exhibit hemostatic (127) and anti-inflammatory activities (101,102,128). The phytoprostane compound chromomoric acid C-I has been identified in *C. odorata* as a strong inducer of nuclear factor, erythroid 2 like 2 (Nrf2) activity, which is a major regulator of various genes, including NADPH:quinone reductase, glutathione S-transferase, γ-glutamylcysteine synthetase, UDP-glucuronosyltransferases and epoxide hydrolase, with defensive, anti-inflammatory and detoxifying functions (100). The mechanisms of the wound healing phases of *C. odorata* are briefly demonstrated in Fig. 3.

Inflammation is a response to tissue injury caused by infection, trauma, chemicals, heat, or unrecognized particles (129). During the acute response, inflammation causes an influx of neutrophils to the wound area. Free radicals are produced from these cells as part of the characteristic 'respiratory burst' activity (130). Free radicals are also generated by

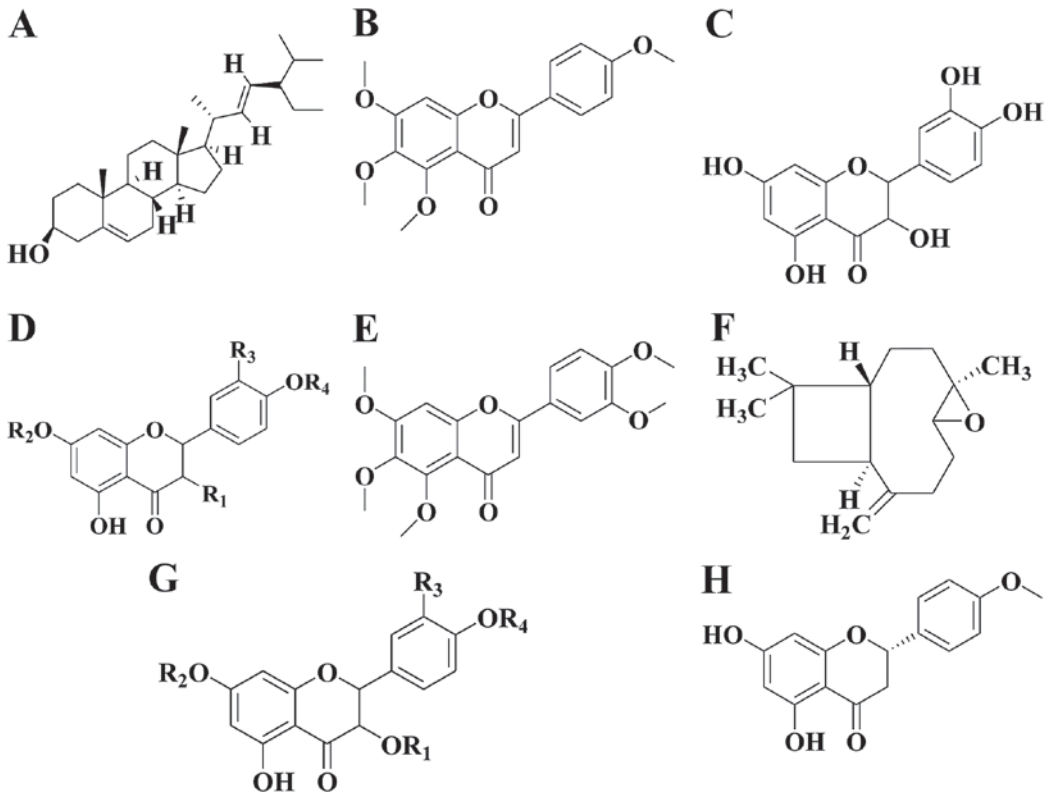

Figure 2. Chemical structures of bioactive components of *Chromolaena odorata*. (A) Stigmasterol, (B) Scutellarein tetramethyl ether, (C) Quercetin, (D-1) Aromadendrin 4'-methyl ether: R_1 = OH; R_2, R_3 = H; R_4 = CH_3, (D-2) Eriodictyol 7,4'-dimethyl ether: R_1 = H; R_2, R_4 = CH_3; R_3 = OH, (D-3) Naringenin 4'-methyl ether: R_1, R_2, R_3 = H; R_4 = CH_3, (D-4)Taxifolin 4'-methyl ether: R_1, R_3 = OH; R_2 = H; R_4 = CH_3, (D-5)Taxifolin 7'-methyl ether: R_1, R_3 = OH; R_2 = CH_3; R_4 = H, (E) Sinensetin, (F) Caryophyllene oxide, (G-1) Quercetin 7,4'-dimethyl ether: R_1, R_3 = H; R_2, R_4 = CH_3, (G-2)Kaempferol 4'-methyl ether: R_1, R_2, R_3 = H; R_4 = CH_3, (G-3)Quercetin 3-*O*-rutinoside: R_1 = glu (6-1)rham; R_2, R_4 = H; R_3 = OH, (G-4)Kaempferol 3-*O*-rutinoside: R_1 = glu (6-1)rham; R_2, R_3, R_4 = H, (G-5)Quercetin 4'-methyl ether: R_1, R_2 = H; R_3 = OH; R_4 = CH_3, (G-6) Quercetin 7'-methyl ether: R_1, R_4 = H; R_2 = CH_3; R_3 = OH, (H) Isosakuranetin.

wound-associated non-phagocytic cells by mechanisms involving non-phagocytic NADPH oxidase (131). Therefore, the wound area has high levels of oxygen- and nitrogen-centered reactive species, and their derivative molecules. Oxidative stress is caused by these radicals and causes lipid peroxidation, DNA damage and enzyme inactivation, including free-radical scavenging proteins. Reports of the effects of oxidants in the pathogenesis of various diseases suggests that antioxidants may be useful as therapeutics in such conditions. In patients, topical application of free-radical-scavenging molecules has been reported to markedly improve wound healing and prevent from oxidative damage to tissues (132).

Inflammation upregulates several proinflammatory cytokines. Cyclooxygenase-2 and inducible nitric oxide synthase are important proinflammatory enzymes in inflammation (133,134). They produce proinflammatory mediators, prostaglandin E2 and nitric oxide, which enhance the expression of proinflammatory cytokines including tumor necrosis factor-α and interleukin-1β. *C. odorata* is capable of anti-inflammatory activity *in vitro* and *in vivo* (135-138). The Scu, isosakuranetin and stigmasterol have also been reported to possess anti-inflammatory activity (69,127,128,139-141).

Wound repair involves an immune-mediated physiological mechanism (4), and several plants and herbs have been traditionally and experimentally used to treat skin disorders, including wounds (142,143). Enhanced healing activity has been attributed to increased collagen formation and angiogenesis (144,145). Collagen is a principal component of connective tissue, and provides a structural framework for the regenerating tissue (146). Furthermore, angiogenesis is required to improve circulation to the wound site, thus, providing oxygen and nutrients for the healing process (147-149). Histological analysis of healed wounds treated with *C. odorata* extract revealed increased fibroblast proliferation, collagen synthesis and neovascularization, resulting in an increased wound tensile strength and accelerated healing wound, compared with untreated wounds (100-102). The proliferative phase of wound healing follows, and usually overlaps with, the inflammatory phase, and is characterized by epithelial cell proliferation and migration over the provisional matrix within the wound (re-epithelialization) (4,21). 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 (54,55,85,86,94,95,101,102).

Reactive oxygen species (ROS) disrupt wound healing due to their damaging effects on cells and tissues. ROS are able to degrade absorbable synthetic biomaterials (150,151). Free-radical-scavenging enzymes are cytoprotective and are essential for the reducing, deactivating and removing of ROS, and for wound healing regulation. Inflammatory disease pathology involves excessive ROS generation by polymorphonuclear leukocytes (PMNLs). Natural compounds with

Table II. Biological activity of different parts of *C. odorata*.

Serial no.	Part of plant	Biological activity	Refs.
1	Aqueous extract of aerial part and essential oil	Anti-malarial, anti-inflammatory, antibacterial	70,135
2	Ethanol, dichloromethane and methanol extract of whole plant	Analgesic, anti-inflammatory, antipyretic, antibacterial	73,82,101,102,110,111
3	Methanol, ethanol and aqueous extract of the leaf	Antioxidant, anti-inflammatory, wound healing properties, anti-staphylococcal, induces apoptosis and autophagy	54,55,66,85,87,109
4	Flower	Antibacterial, Mycobacterium tuberculosis, anticancer	87,92
5	Methanol extract of whole plant	Platelet activating factor receptor binding inhibitory activity	69

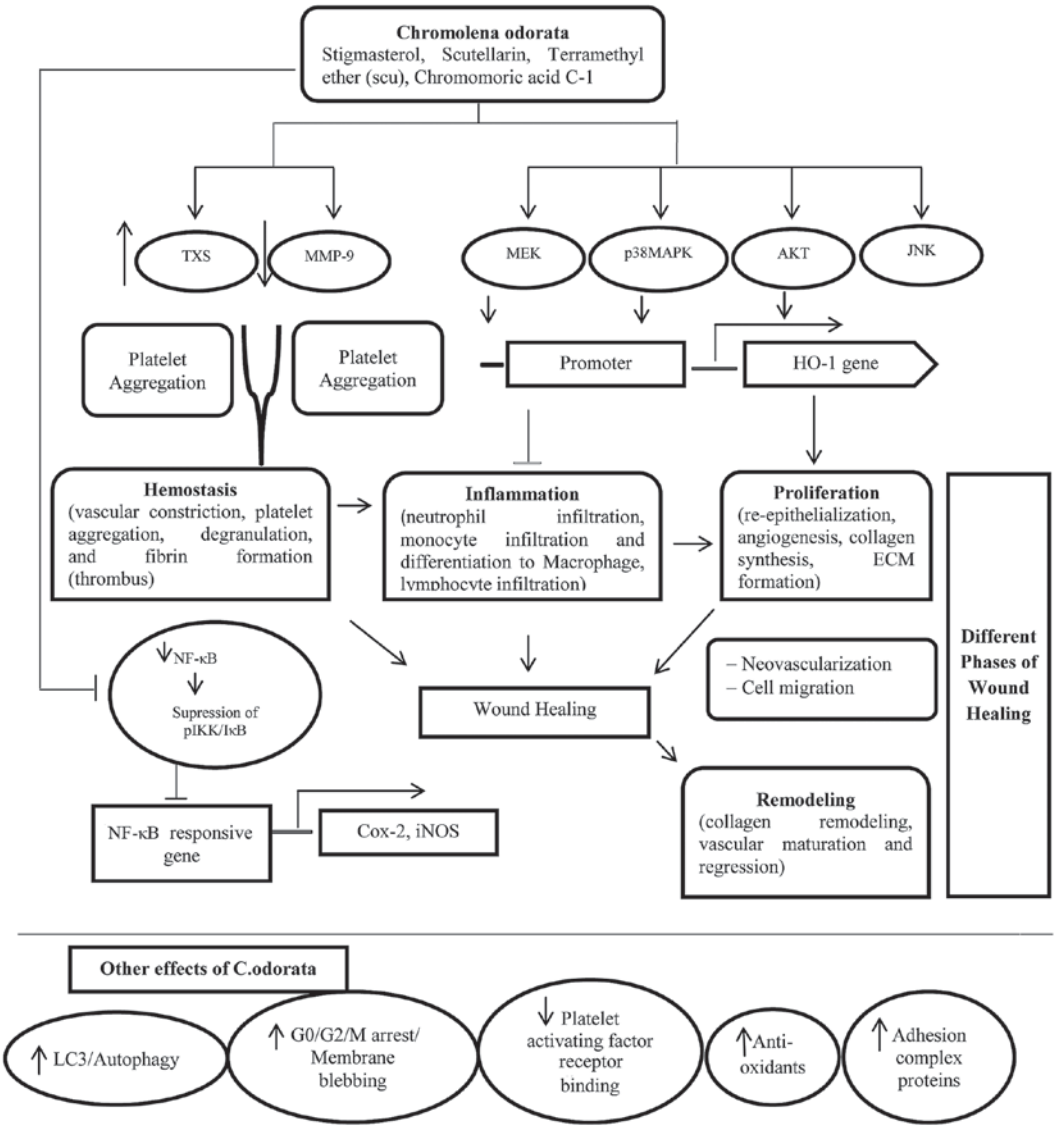

Figure 3. Schematic diagram showing the cellular and bio-physiologic events associated with the *Chromolaena odorata* wound healing mechanism of action and other pharmacological activities. *C. odorata* extract or its bioactive principles stimulate hemostatic activity by stimulation of TXS and repression of MMP-9 expressions. It also activates MEK, p38 MAPK, AKT and JNK kinase pathways which initiated the expression of HO-1. The induction of HO-1 will inhibit an inflammation and stimulate cell proliferation, thereby enhancing neovascularization and cell migration that helps to accomplish wound healing. *C. odorata* also increase antioxidant, antidiabetic activity, adhesion complex proteins expression and induce apoptosis and autophagy in tumor cells (modified from Pandith *et al*, 2013). TXS, thromboxane synthase; MMP, matrix metalloproteinase; MEK, MAPK kinase; MAPK, mitogen-activated protein kinase; AKT, protein kinase B; JNK, c-Jun N-terminal kinase; HO, heme oxygenase; ECM, extracellular matrix; NF-κB, nuclear factor κ-light-chain-enhancer of activated B cells; pIKK, phosphatidylinositol 3-kinase-related-kinase; Cox-2, cyclooxygenase-2; iNOS, inducible nitric oxide synthase; LC3, light chain 3; PAF, platelet activating factor.

antioxidant activity may be useful in reducing or regulating the oxidative damage caused by ROS produced from PMNLs. A previous study reported that *Chromolaena* species inhibit ROS generation via opsonized zymosan-stimulated PMNLs (83).

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 (145). The antioxidant enzymes superoxide dismutase and catalase are known to quench the superoxide radical and prevent free radical-mediated damage to cells (152). Other active compounds within *C. odorata,* including triterpenes, alkaloids, flavonoids, and biomolecules (153) have been reported to have antioxidant activity and may, therefore, support wound healing (154). Thus, the enhanced wound healing stimulated by *C. odorata* may be due to the free radical scavenging action of the plant, as well as enhanced antioxidant enzyme levels. Similarly, *Tephrosia purpurea* has been reported to contain same flavonoids, which may be one of the potential mechanisms contributing to its enhancement of wound healing (153). In conclusion, flavonoids can scavenge ROS and free radicals, which are reactive intermediates that are potentially implicated in delaying wound healing (155-159).

6. Conclusion

Although *C. odorata* exhibits a wide spectrum of pharmacological activities, the field of wound healing is fraught with challenges, including understanding wounds themselves, and investigating the known and unknown constituents of natural products. For >30 years, researchers have investigated the healing efficacy of *C. odorata* in attempts to justify the inclusion of this plant in the management strategy of wound healing. This review has aimed to summarize these findings, in the hopes of enhancing the understanding of the benefits of *C. odorata* and contributing to assessments of its usefulness as claimed by the communities that use it for its wound healing properties. While the plant is commonly available, it is primarily known worldwide as a harmful weed. However, due to the increasing global interest in medicinal herbs, it has been predicted that medicinal herbs and plants are likely to be the focus of medicinal practice in the future. *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. This envisaged preclinical research may ultimately progress to translational clinical trials. *C. odorata* has been proven safe for application (84-85) 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.

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