ISSN: 1672 - 6553

JOURNAL OF DYNAMICS AND CONTROL

VOLUME 10 ISSUE 07: P157-186

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JOURNAL OF DYNAMICS AND CONTROL
https://doi.org/10.71058/jodac.v10i0708

EXPERIMENTAL STUDIES ON WOUND HEALING ACTIVITY OF *Trichosanthes dioica* LEAVES: A REVIEW

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Abstract: *Wound healing is a complex biological process involving hemostasis, inflammation, proliferation, and tissue remodeling to restore the structural and functional integrity of damaged tissues. Medicinal plants have gained considerable attention in wound management because of their diverse pharmacological properties and relatively safer therapeutic profile compared to synthetic agents. Among various medicinal plants, the* Trichosanthes dioica *species belonging to the family Cucurbitaceae possesses several bioactive phytoconstituents that may contribute significantly to tissue repair and regeneration. The present review focuses on the phytochemical constituents, pharmacological activities and potential wound healing mechanisms associated with* Trichosanthes *dioica leaves. Various secondary metabolites including flavonoids, alkaloids, tannins, saponins, phenolic compounds, glycosides, terpenoids and phytosterols reported in the leaves exhibit antioxidant, anti-inflammatory, antimicrobial and collagen-promoting activities that are closely associated with different phases of wound healing. The review further discusses in vitro and in vivo experimental approaches such as fibroblast proliferation assay, scratch wound assay, excision wound model, incision wound model, burn wound model and diabetic wound model for evaluating wound healing efficacy. Histopathological, biochemical and molecular parameters including re-epithelialization, granulation tissue formation, collagen deposition, hydroxyproline estimation, antioxidant enzyme activity, cytokine analysis and growth factor expression are also highlighted to explain tissue regenerative mechanisms. In addition, important molecular pathways such as NF-κB, MAPK and TGF-β signaling involved in wound repair are discussed in relation to phytoconstituents present in* Trichosanthes *dioica leaves. Although direct scientific evidence regarding wound healing activity of* Trichosanthes *dioica leaves remains limited, the available phytopharmacological information suggests promising therapeutic potential for tissue regeneration and wound management. Therefore, further experimental, molecular, and formulation-based investigations are necessary to establish the clinical significance and therapeutic applicability of* Trichosanthes *dioica leaf extract in regenerative medicine.*

Keywords: Trichosanthes *dioica leaves; wound healing; phytoconstituents; antioxidant activity; anti-inflammatory activity; antimicrobial activity; collagen synthesis; fibroblast proliferation; angiogenesis; tissue regeneration; NF-κB pathway; MAPK signaling; herbal formulations*

1. Introduction

1.1 Overview of Wound Healing

Wound healing is a dynamic and complex biological process whereby the body can restore structure and function to damaged tissue. (Ferro et al., 2017) Wounds can result from injury, burns, surgery, infection by microorganisms, or diabetes, traumatic or other pathological conditions that affect the normal structure of skin and underlying tissues. (Miller et al., 2024) The healing of wounds is essential for maintaining tissue homeostasis and protecting the body from microbial invasion, fluid loss, and further tissue damage.

Several cell types, components of the extracellular matrix, cytokines, chemokines, and growth factors are involved in a coordinated interaction for wound healing. (Jin et al., 2021)

https://doi.org/10.71058/jodac.v10i0708

This process typically takes place in a sequential way, in four overlapping phases: hemostasis, inflammation, proliferation, and remodeling. The hemostatic phase initiates right after an injury to the tissues, to prevent excessive blood loss through clot formation. (Abrams et al., 2018)

This is followed by inflammation, which involves immune cells clearing cellular debris and invading microorganisms from the wound. The proliferative phase is characterised by fibroblast proliferation, collagen synthesis, angiogenesis and granulation tissue formation, which results in tissue regeneration and contraction of the wound. Lastly, during remodeling, tissue strength and organization are restored by collagen maturation and ECM remodeling. (Ng et al., 2019)

Various local and systemic factors can affect wound healing, such as oxidative stress, vascular insufficiency and immune status, diabetes, nutrition and infection, and age. Chronic wounds, unwanted scar formation, or tissue decay can occur because of delayed or impaired wound healing, and can put a heavy burden on health care resources around the world. (Hatzopoulos & Ciorba, 2018)

In recent years, medicinal plants have attracted much interest in wound management due to their numerous pharmacological activities like antioxidants, anti-inflammatory, anti-microbial, and collagen-promoting activity. (El-Shemy, 2018)

Trichosanthes dioica is considered antipyretic, diuretic, laxative, cardio-tonic, anti-ulcer, etc (Sarkar et al., 2017). Leaves of *T. dioica* are used traditionally to treat jaundice, oedema, and alopecia. It also has antioxidant and sedative effects (Khare et al., 2004). Various phytoconstituents from plants have been reported to enhance various stages of wound healing, such as flavonoids, tannins, terpenoids, phenolic compounds, and alkaloids. Trichosanthes *dioica* spp. are among the various medicinal plants traditionally employed for different therapeutic uses, which have been reported to contain a variety of bioactive compounds that can be related to tissue repair and regeneration. Hence, it is essential to have knowledge of the wound healing process to assess the therapeutic efficacy of Trichosanthes *dioica* leaves in wound healing experiments. (Dhawal et al., 2023; Ghaisas et al., 2008; Bhattacharya & Haldar et al., 2012d)

Therapeutic properties of Trichosanthes dioica- It has anti-tumour, antioxidant, antibiotic, laxative, antidiabetic, antidiarrheal, immunomodulatory, anti-inflammatory, cytotoxic, hepatoprotective and thrombolytic effects. (Adiga et al., 2010; Bhattacharya et al., 2011)

1.2 Phases of Wound Healing

Wound healing is a biological process that is coordinated and takes place in a series of overlapping phases to restore the integrity and function of damaged tissues. The phases are hemostasis, inflammation, proliferation, and remodeling. (Wang et al., 2024)

There are multiple cellular and molecular mechanisms that regulate each phase, which are important for tissue repair and regeneration.

Hemostasis

The first and immediate stage of wound healing that occurs immediately after tissue injury is hemostasis. The goal of this stage is to prevent excessive bleeding and to preserve the blood vessels. When injured, blood vessels constrict (vasoconstriction) to limit bleeding from the injury. At the same time, platelets clump together and stick to the damaged blood vessels, creating a temporary plug. ((Pourshahrestani et al., 2020)

https://doi.org/10.71058/jodac.v10i0708

In this process, several blood-clotting factors are activated that convert the blood clotting protein fibrinogen to fibrin, which strengthens the blood clot. During later stages of healing, inflammatory cells, fibroblasts, and keratinocytes migrate through the fibrin clot, which serves as a temporary extracellular matrix that supports their migration. (Mamun et al., 2024)

Platelets also produce several growth factors and cytokines, including platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), and vascular endothelial growth factor (VEGF), which trigger cellular signaling pathways crucial for tissue repair.

Therefore, the hemostasis stage not only helps to prevent bleeding but also helps to set the stage for the inflammatory and proliferative stages of wound healing.

Inflammation

The inflammatory phase starts a few days after hemostasis and usually lasts for several days depending on the severity of the injury. This phase is very important in the process of wound protection from microbial infections and elimination of damaged tissues and cellular debris. Inflammation causes vasodilation, leading to increased blood flow and vascular permeability at the site of the wound. This results in the classical signs of inflammation, including redness, heat, swelling, and pain. (Schneider et al., 2021; (Koh & DiPietro, 2011)

The first inflammatory cells to migrate to the wound area are neutrophils. These cells act as phagocytes and destroy bacteria, foreign matter, and dead tissue. Neutrophils also release reactive oxygen species, proteolytic enzymes, and inflammatory mediators that help in wound decontamination. Then, during the inflammatory phase, macrophages are the predominant cells. Macrophages remain phagocytic and secrete various cytokines and growth factors, which control fibroblast proliferation, collagen synthesis, angiogenesis, and tissue remodeling. (Zhao et al., 2021)

While inflammation is part and parcel of the normal wound healing process, excessive or prolonged inflammation may postpone the healing process and may promote chronic wound formation. Consequently, control of inflammatory mediators is important for the proper repair of tissue. A large number of medicinal plants contain anti-inflammatory and antioxidant phytoconstituents which can regulate inflammatory responses and promote wound healing processes. (Shukla et al., 2019)

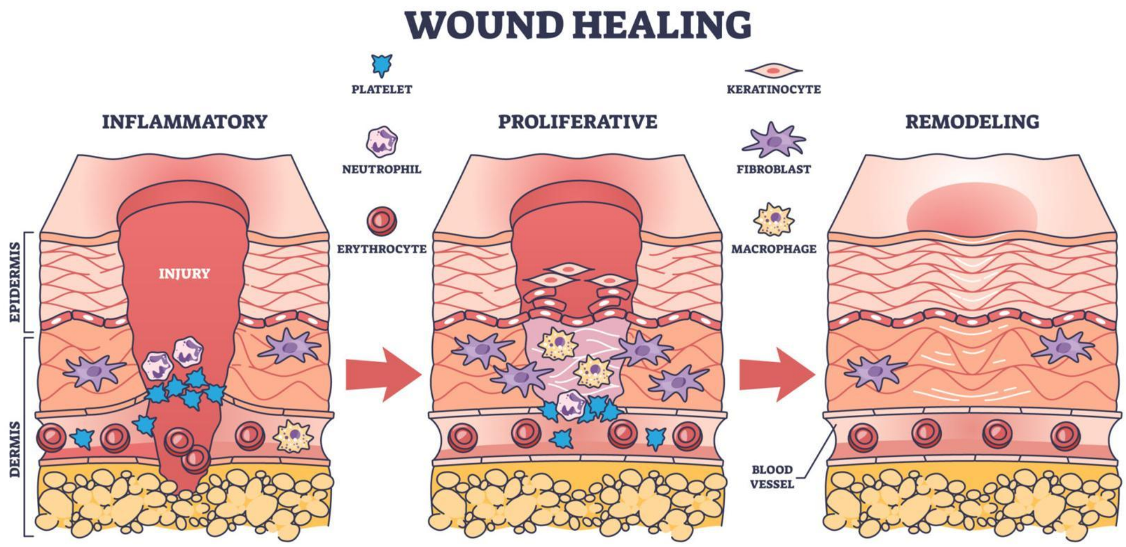
Proliferation

The third phase of wound healing is known as the proliferative phase, which typically starts a few days after the wounding. This phase is mainly responsible for tissue regeneration, wound contraction, and restoration of the damaged tissue structure. At this time, fibroblasts at the wound site migrate and actively produce collagen and other proteins of the extracellular matrix and granulation tissue to support new tissue growth. (C. Wang et al., 2018)

The formation of new blood vessels from pre-existing blood vessels, called angiogenesis, is one of the key events of the proliferative phase. The newly-formed blood vessels provide oxygen and nutrition to the healing tissue and stimulate the growth and metabolism of the cells. Fibroblasts also make collagen fibers, particularly type III collagen, that add to the strength of wounds and repair of tissue. (C. Wang et al., 2018b)

At the same time, cells in the epithelial layers regenerate and spread over the surface of the wound, a process called re-epithelialization. This process can restore the barrier function of the skin. Myofibroblasts derived from fibroblasts are involved in wound contraction and are responsible for wound contraction, which will reduce wound size. (Khalil et al., 2017)

The role of various growth factors during this phase is important, including transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF). Therefore, the proliferative phase is regarded as a critical time when successful wound healing is occurring, since it determines the formation of healthy granulation tissue and tissue regeneration. (Duarte et al., 2024;Velnar et al., 2009)



Source: Adapted from [National Centre for Biotechnology Information (NCBI)] and published wound healing literature.

Figure 2. Major phases of wound healing including hemostasis, inflammation, proliferation and remodeling.

1.3 Role of Medicinal Plants in Wound Management

Since ancient times, medicinal plants have been applied in traditional medicine to heal and control wounds, burns, and skin diseases. Plant-based therapies are regarded as one of the most valuable sources of bioactive compounds with substantial pharmacological activities that are associated with tissue repair and regeneration. Increasing incidence of chronic wounds, microbial resistance, and adverse effects of synthetic drugs have led medicinal plants to receive tremendous scientific interest to be used as an alternative therapeutic agent against wounds. (Duarte et al., 2024; (Nagori & Solanki, 2011)

The healing activities of medicinal plants are largely due to the presence of several phytoconstituents like flavonoids, alkaloids, tannins, terpenoids, saponins, glycosides, and phenolic compounds. These bioactive compounds have antioxidant and anti-inflammatory activities as well as antimicrobial and collagen-promoting properties, playing a role in various stages of wound healing. Antioxidants decrease oxidative stress and tissue damage caused by free radicals, and anti-inflammatory agents control inflammatory mediators and cytokines at the wound site. Likewise, antimicrobial phytochemicals keep microbes away and prevent their infection, leading to quicker wound healing and tissue repair. (Bhadra et al., 2025;Kavitha, 2021)

Several medicinal plants are also known to have the ability to promote fibroblast proliferation, collagen synthesis, angiogenesis, and re-epithelialization, which are all important processes during the regeneration of tissue. Experimental studies on wound healing are widely conducted on herbal formulations like medicinal plant extract-based ointments, creams, gels, hydrogel dressings, etc. (Kasprzak-Drozd et al., 2024)

Medicinal plants are generally considered safe, easily accessible, and inexpensive when compared to synthetic wound healing agents. So, medicinal plants have continued to be a key source in the formulation of new therapeutic options for wound management and tissue regeneration. (Satchanska et al., 2024; Pathak & Mazumder et al., 2024)

1.4 Scope and Objective of the Review

The present review is meant to give a comprehensive idea about the phytochemical constituents and pharmacological activities of *Trichosanthes dioica* leaves with special emphasis on the use of leaves in wound healing and tissue regeneration. The healing process is a complex biological event that includes control of inflammation, suppression of microorganisms, collagen formation, angiogenesis, and proliferation of cells. Therefore, medicinal plants with antioxidant, anti-inflammatory, and antimicrobial activities are regarded as important therapeutic agents for wound management. (Szekalska et al., 2016)

The literature on the phytochemistry, traditional applications, and biological activities of *Trichosanthes dioica* leaves relevant to wound healing processes was collected and critically analysed in this review. Experimental studies related to wound repair mechanisms such as antioxidant activity, proliferation of Fibroblasts, collagen production, tissue remodeling, and antimicrobial effects are also taken into consideration during the review.

Furthermore, the present review explores the possible molecular pathways involved in tissue regeneration and also brings out the significance of bioactive phytoconstituents present in the leaves of *Trichosanthes dioica*. Some of the formulation approaches, safety evaluation, and

https://doi.org/10.71058/jodac.v10i0708

future therapeutic applications are also briefly discussed to give a wider knowledge of the medicinal importance of the plant.

This review aims to capture and compile the existing scientific knowledge on the wound healing properties of *Trichosanthes dioica* leaves and highlight the potential of the leaves as a natural therapeutic agent for wound healing and regeneration.

2. Botanical and Phytochemical Profile of *Trichosanthes dioica* Leaves

2.1 Taxonomical Classification

The genus *Trichosanthes* is associated with the family Cucurbitaceae, which includes several climbing and creeping plants that are of medicinal importance and widely distributed in tropical and subtropical regions. The genus *Trichosanthes dioica* is widespread in India, China, Sri Lanka, and SE Asia and is widely used in traditional medicine for a variety of therapeutic purposes. (Sheshadri et al.,1990)

Below is the taxonomical classification of Trichosanthes:

- Kingdom: Plantae
- Subkingdom: Tracheobionta
- Division: Magnoliophyta
- Class: Magnoliopsida
- Order: Cucurbitales
- Family: Cucurbitaceae
- Genus: *Trichosanthes*
- Species: *dioica*

The family Cucurbitaceae is commonly referred to as the gourd family, which contains some medicinal and edible plants with high phytoconstituent bioactive compounds. Climbing herbs with tendrils and lobed leaves and elongated fruits are the distinguishing features of the genus *Trichosanthes*. Traditionally, this genus of plants has been used to treat inflammation, skin diseases, fever, diabetes, and digestive ailments. (Bussmann et al., 2018)

Trichosanthes dioica is among the various species, which is one of the most commonly studied medicinal plants due to its pharmacological significance. Some secondary metabolites like flavonoids, tannins, phenolics, glycosides, and terpenoids have been identified in the leaves of the plant, which may have antioxidant, antimicrobial, and hemostatic effects.

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2.2 Morphological Characteristics

Trichosanthes dioica. is an annual climbing herb with rapid growth and belongs to the family Cucurbitaceae. Commonly known as parwal or pointed gourd. It is a natural plant of tropical and subtropical regions and is cultivated throughout the plains of Northern India, extending to Assam and East Bengal.

The plant has an about 1cm thick stem and simple tendrils which may be used for climbing over supporting structures. (Kumar et al., 2008)The stem is green, angular, and somewhat pubescent. Its leaves are cordate, oblong, acute, sinuate-dentate, not lobed, and dark green with a rough texture, having a heart-shaped lamina. Leaves are dark green and bitter-tasting. (Wäldchen & Mäder, 2017; (Kumar et al., 2008)

Trichosanthes dioica has whitish green flowers, with racemose inflorescence, and flowers are sessile, solitary, bracteate, with an oblong-cylindrical calyx tube. The fruit is generally globose, smooth, with dark green to pale green stripes. The root system is well developed and composed of tuberous tap roots. Traditionally, parts of this plant, particularly the leaves, fruits, and roots, are used medicinally. Morphological features of the plant are helpful for the proper identification, authentication, and standardization of Trichosanthes for investigation in the field of pharmacology and phytochemistry.

Source: Adapted from Plants of the World Online and published botanical resources.

Figure 1. Morphological characteristics of Trichosanthes dioica leaves showing lobed leaf structure and climbing plant habit.

2.3 Geographical Distribution

Trichosanthes dioica. is distributed in tropical Asia, Polynesia, and Australia. The plant is widely cultivated in Tripura, Assam, Orissa, West Bengal, Uttar Pradesh, Bihar, and Tamil Nadu. The plant is typically grown for medicinal and food use in kitchen gardens, agricultural fields, and in rural areas. (Gupta et al., 2012)

The climate requirements for the species of *Trichosanthes dioica* are generally tropical, in the temperature range of 25°C to 35°C. It thrives in organic-rich, sandy loam soils with good drainage. Due to its climbing habit, it is often found growing on fences and other plants or structures in the cultivated areas.

2.4 Phytochemical Constituents of *Trichosanthes dioica* Leaves

Phytochemicals are bioactive naturally occurring compounds found in medicinal plants that make them therapeutic and pharmacological. (Q. Zhao et al., 2016)

The leaves of *Trichosanthes dioica* are rich in many bioactive secondary metabolites, which are responsible for different biological activities like anti-inflammatory, anti-oxidant, anti-microbial, and tissue regenerative activity. These phytoconstituents play an important role in wound healing by promoting collagen synthesis, reducing oxidative stress, and regulating inflammatory responses at the wound site. (Kavitha, 2021)

There are a number of phytochemical investigations conducted on the *Trichosanthes* species that revealed the presence of flavonoids, alkaloids, tannins, saponins, glycosides, phenolic compounds, terpenoids, and steroids. All these compounds play a role in the medicinal importance of the plant. (Sultan et al., 2004; Cedillo-Cortezano et al., 2024)

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Alkaloids

Alkaloids are secondary metabolites that contain nitrogen and are found in medicinal plants and have various biological activities. Alkaloids are found in *the leaves of Trichosanthes dioica, enhancing the plant's medicinal properties* in traditional medicine. The antimicrobial, analgesic, anti-inflammatory, and antioxidant properties of Alkaloids are beneficial in the wound healing process. (Tounekti et al., 2019) (Singh et al., 2010)

Tannins

Tannins are the polyphenolic compounds that occur naturally in medicinal plants, such as leaves of *Trichosanthes dioica*. These compounds display marked antioxidant, antimicrobial, and astringent activity, thus making them therapeutically important in wound healing and tissue repair. Tannins can precipitate proteins and to form protective coatings

over damaged tissues, thereby lowering susceptibility to infection and further tissue damage at the wound site. (H. Wang, 2023;Shah et al., 2026)

Saponins

Saponins are glycosidic compounds widely distributed in medicinal plants with foaming properties. The leaves of *Trichosanthes* are rich in saponins with different biological properties such as antioxidant, antimicrobial, anti-inflammatory, and immunomodulatory properties. The pharmacological activities described above make saponins important bioactive compounds for wound care and tissue repair.

It has been reported that saponins increase collagen formation and proliferation of fibroblasts during the proliferative phase of wound healing. They can also stimulate angiogenesis and epithelialization, aiding in tissue regeneration and wound healing. Moreover, the antimicrobial property of saponins helps to shield wounds from bacterial invasion and infection by microbes. (Liwa et al., 2017; Aba & Asuzu et al., 2018; Ezzat et al., 2021)

S. No.	Phytoconstituent	Chemical Class	Reported Pharmacological Activity	Role in Wound Healing
1	Alkaloids	Nitrogen-containing compounds	Antioxidant, anti-inflammatory	Reduces oxidative stress and inflammation
2	Flavonoids	Polyphenols	Antimicrobial, antioxidant	Promotes collagen synthesis
3	Glycosides	Phenolic compound	Antioxidant, anti-inflammatory and cardioprotective	Promotes tissue repair and cellular regeneration
4	Coumarins	Phenolic compounds	Anti-inflammatory, antimicrobial and antioxidant	Improves wound contraction and reduce inflammation
5	Phenols	Aromatic compounds	Anti-inflammatory, antimicrobial and antioxidant	Prevents oxidative damage and support healing

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6	Tannins	Polyphenolic compounds	Astringent, antimicrobial	Promotes wound contraction and reduces bleeding
7	Saponins	Glycosides	Fibroblast proliferative activity, immunomodulatory	Supports angiogenesis and collagen synthesis
8	Terpenoids	Isoprenoid compounds	Antioxidant, antimicrobial	Improves epithelialization and collagen deposition
9	Reducing sugars	Carbohydrates	Antioxidant and provides nutritional support	Provides energy for cellular growth and tissue repair
10	Fixed oils	Lipids	Anti-inflammatory	Maintains moisture
11.	Proteins and free amino acids	Macromolecules and Nitrogen-containing compounds	Antioxidant and provides nutritional support	Improves collagen formation and tissue remodeling
12.	Steroid	Triterpenoid	Anti-inflammatory and antioxidant	Promotes tissue regeneration and reduces inflammation
13.	Quinones	Cyclic compound	Antimicrobial, antioxidant and anti-inflammatory	Prevents microbial infection and supports tissue repair

Source: Compiled from published phytopharmacological studies on *Trichosanthes* species and wound healing literature. Use references from PubMed and NCBI.

3. Pharmacological Activities of Leaves Related to Wound Healing

The main factors attributed to the wound healing properties of medicinal plants are their antioxidant, anti-inflammatory, antimicrobial, and tissue regenerative properties due to the presence of biologically active phytoconstituents. The flavonoids, phenolic compounds, tannins, terpenoids, steroids, and glycosides are some of the important secondary metabolites of Trichosanthes leaves, which might be beneficial in various stages of wound healing. (Janmeda et al., 2025)

These phytoconstituents modulate inflammatory responses, decrease oxidative stress, prevent microbial infections, and promote collagen synthesis and proliferation of fibroblasts. These pharmacological effects are important for the proper repair of tissues, formation of granulation tissue, formation of new blood vessels, and contraction of the wound. Thus, the biological properties of Trichosanthes leaves could be used to promote wound healing and tissue regeneration processes. (Nagori & Solanki et al., 2011)

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S. No.	Pharmacological Activity	Major Phytoconstituents Involved	Possible Mechanism in Wound Healing
1	Anti-inflammatory activity	Flavonoids, terpenoids, phenolics	Inhibition of TNF-α, IL-1β, and COX pathways
2	Antioxidant activity	Quercetin, tannins	Free radical scavenging and oxidative stress reduction
3	Antimicrobial activity	Alkaloids, tannins, flavonoids	Inhibition of bacterial and fungal growth
4	Collagen-promoting activity	Triterpenoids	Enhanced collagen synthesis and extracellular matrix formation
5	Fibroblast proliferative activity	Saponins, flavonoids	Increased fibroblast migration and proliferation
6	Angiogenic activity	Phenolics, phytosterols	Stimulation of VEGF-mediated neovascularization
7	Tissue regenerative activity	Terpenoids	Accelerated epithelialization and wound contraction
8	Cytoprotective activity	Phenolic compounds	Protection of cells from oxidative injury

Source: Compiled from published pharmacological and wound healing studies available through PubMed Central (PMC) and ScienceDirect.

3.1 Anti-inflammatory Activity

Inflammation is a crucial part of wound repair that is essential to prevent infection from invading the wound and to clear away dead cells and other debris. (Kharbanda et al., 2015) But over-inflammation or chronic inflammation can slow tissue healing processes and lead to chronic wounds. So, it is significant to control inflammatory mediators for wound healing.

In T. dioica, flavonoids, phenolic compounds, terpenoids, and steroids are present in the leaves, which have a high anti-inflammatory potential. (Arora & Gill et al., 2020) The compounds could also block the production of cytokines and mediators that cause inflammation, such as tumour necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), cyclooxygenase (COX), and prostaglandins. The plant's ability to block these inflammatory pathways can help to minimize swelling, redness, and pain that can stem from wound damage. (Matei et al., 2025; Shukla et al., 2019)

The flavonoids in the leaves of Trichosanthes are found to have anti-inflammatory activity through inhibition of oxidative stress and inflammatory signaling pathways. Likewise, terpenoids and phytosterols can help maintain the integrity of cell membranes and limit the number of leukocytes at the wound site. All these actions together provide a good environment for new tissue growth and wound contraction.

Experimental research on other medicinal plants rich in the same phytoconstituents has shown that it leads to a decrease in inflammatory infiltrates, increased formation of granulation tissue, and accelerated epithelialization. Thus, the anti-inflammatory property of the leaves of *Trichosanthes dioica* could be very useful in wound healing and repair. (Mulisa et al., 2015)

3.2 Antioxidant Activity

One of the most important causes of delayed wound healing is oxidative stress, which results in damage to cells and hinders tissue regeneration. In tissue injury, excessive amounts of

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reactive oxygen species and free radicals can cause damage to proteins, lipids, and cell membranes, causing prolonged inflammation and delayed healing. Hence, antioxidants have an important role in the protection of tissues from oxidative damage and proper wound repair.

The leaves of the Trichosanthes are rich in various antioxidant phytochemicals like flavonoids, phenolics, tannins, and triterpenoids, which can play a pivotal role in tissue protection and regrowth. They help to neutralize free radicals and diminish oxidative stress at the wound site. The antioxidant phytochemicals may also increase the activity of endogenous antioxidants such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), which help prevent tissue damage due to oxidative stress.

Experimental research with medicinal plants with antioxidant activity has shown an increase in wound contraction, deposition of collagen, and enhancement of granulation tissue formation. Thus, the antioxidant property of the leaves of Trichosanthes can play a significant role in wound healing and tissue repair mechanisms. (Asif, 2015; Shah et al., 2026)

3.3 Antimicrobial Activity

Wounds can have many complications, including microbial infection, which can cause healing to take a long time. Pathogenic microorganisms at the wound site can cause chronic wound formation, necrosis of the tissue, and prolonged inflammation. As such, antimicrobial agents are significant in wound management in that they can help prevent infection and aid in tissue repair.

Flavonoids present in this plant have reported antimicrobial activity, which is important for wound healing. Leaf extract of this plant is effective against Staphylococcus sp., Klebsiella sp., Escherichia sp., Pseudomonas sp., and Mycobacterium sp. Thus, the antimicrobial activity of Trichosanthes leaf can play an important role in its wound healing activity. (Rai et al., 2010; Shah et al., 2026)

3.4 Collagen Promoting Activity

One of the major structural proteins in wound healing and tissue repair is collagen. It is used as a strengthening, elastic, and structural component of the skin and connective tissue. During the proliferative and remodeling phases of wound healing, collagen synthesis and deposition play a critical role in granulation tissue formation, wound contraction, and restoration of damaged tissues.

The leaves of Trichosanthes are rich in various bioactive phytoconstituents, including flavonoids, phenolic compounds, triterpenoids, and glycosides, which could stimulate collagen production and extracellular matrix accumulation. These compounds aid in stimulating the activity of fibroblasts and increasing the synthesis of collagen fibers in the wound area. The more collagen that is deposited, the stronger the tissue becomes and the faster the wound heals. (C. Wang et al., 2018c)

In conclusion, the collagen-promoting activity of Trichosanthes leaves could play a significant role in the healing process in tissue repair and wound contraction, in addition to normal skin architecture.

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3.5 Immunomodulatory effect

Aqueous extract of T. dioica shows immunomodulatory effect, biochemical and haematological effects. Enhances antibody formation, RBCs, WBCs, and haemoglobin, leaving the biochemical parameters unaltered. (Bhadoriyal & Mandoriya et al., 2012)

4. Experimental Studies on Wound Healing Activity

Experimental studies constitute a very important part of the assessment of the wound healing activity of medicinal plants and phytoconstituents. A range of in vitro and in vivo experimental models are widely used to study various mechanisms associated with tissue repair, such as the proliferation of fibroblasts, collagen synthesis, antimicrobial activity, and epithelialization. (Sangnim et al., 2024)

The bioactive phytoconstituents found in the leaves of Trichosanthes, such as flavonoids, phenolic compounds, tannins, and triterpenoids, can have a significant impact on various biological functions related to wound healing. (Sharma et al., 2023) Hence, experimental assessment of these activities is required to prove the therapeutic importance of this plant in the wound healing process. (Islam et al., 2018)

S. No.	Experimental Model	Type of Study	Major Parameter Evaluated	Significance
1	Fibroblast proliferation assay	In vitro	Cell viability and proliferation	Evaluates tissue regenerative potential
2	Scratch wound assay	In vitro	Cell migration and wound closure	Assesses epithelial regeneration
3	Keratinocyte migration assay	In vitro	Keratinocyte proliferation	Measures re-epithelialization
4	Excision wound model	In vivo	Percentage wound contraction	Determines wound closure rate
5	Incision wound model	In vivo	Tensile strength	Evaluates collagen maturation
6	Burn wound model	In vivo	Healing of thermal injury	Assesses tissue regeneration
7	Diabetic wound model	In vivo	Delayed wound healing	Evaluates healing under diabetic conditions
8	Histopathological analysis	Microscopic evaluation	Collagen deposition and granulation tissue	Validates tissue repair
9	Hydroxyproline estimation	Biochemical analysis	Collagen content	Measures extracellular matrix formation
10	Cytokine analysis	Molecular study	TNF-α, IL-6, IL-1β expression	Evaluates inflammatory response

Source: Compiled from experimental wound healing studies and pharmacological literature

4.1 Biochemical and Molecular Parameters

Various parameters are used to assess the efficacy of wound healing and tissue regeneration therapies; the biochemical and molecular parameters are among them. (Sani et al., 2023) These parameters provide scientific data on collagen synthesis, antioxidant status, inflammatory response, cellular proliferation, and remodeling of the extracellular matrix at various stages of wound healing.

Biochemical analysis plays a crucial role in experimental wound healing studies to evaluate the impact of medicinal plant extracts on the molecular mechanisms of wound healing. Common parameters for assessing healing progression and tissue regeneration include hydroxyproline content, activity of antioxidant enzymes, expression of cytokines and regulation of growth factors.

The phytoconstituents found in the leaves of *Trichosanthes dioica*, such as flavonoids, phenolic compounds, triterpenoids and phytosterols, could play a significant role in these biochemical and molecular pathways through their antioxidant, anti-inflammatory and collagen-boosting properties. The parameters, their biological significance, and interpretation in wound healing are well explained in the table below-

S. No.	Parameter	Biological Significance	Interpretation in Wound Healing
1	Re-epithelialization	Regeneration of epidermal layer	Indicates restoration of skin barrier
2	Granulation tissue formation	Development of connective tissue and blood vessels	Reflects active tissue repair
3	Collagen deposition	Extracellular matrix formation	Improves tensile strength of tissue
4	Hydroxyproline estimation	Marker of collagen content	Indicates collagen maturation
5	Fibroblast proliferation	Connective tissue regeneration	Promotes wound contraction
6	Angiogenesis	Formation of new blood vessels	Enhances oxygen and nutrient supply
7	Antioxidant enzyme activity	Oxidative stress regulation	Protects tissues from free radical damage
8	Cytokine analysis	Inflammatory mediator regulation	Evaluates inflammatory response
9	Growth factor expression	Cellular signaling and regeneration	Stimulates tissue remodeling
10	Neovascularization	Vascular regeneration	Supports granulation tissue development

Source: Compiled from histopathological and molecular wound healing studies available through PubMed Central (PMC), NCBI Bookshelf and published regenerative medicine literature.

5. The molecular mechanisms of wound healing

Several cell and molecular signaling pathways coordinate wound healing, including inflammation, cellular proliferation, collagen synthesis, angiogenesis, and tissue remodeling. The activity of the fibroblasts, keratinocytes, endothelial cells, and immune cells at various times in tissue repair is driven by these molecular pathways. These signaling mechanisms may become distorted, resulting in slow wound healing, chronic wounds, or hyperplastic scarring. (Velnar et al., 2009)

Some of these phytoconstituents found in medicinal plants can affect these molecular pathways via antioxidant, anti-inflammatory, and regenerative processes. The phytochemicals found in the leaves of Trichosanthes, such as flavonoids, phenolic compounds, terpenoids, and phytosterols, might regulate inflammatory mediators, cytokines, and growth factors that participate in wound healing. (Cedillo-Cortezano et al., 2024)

These molecular mechanisms are crucial for assessing the therapeutic potential of Trichosanthes leaves in tissue regeneration and wound healing. (Thakur et al., 2011)

S. No.	Molecular Pathway	Major Functions	Role in Wound Healing
1	NF-κB signaling pathway	Regulation of inflammatory mediators	Controls inflammation and immune response
2	MAPK pathway	Cell proliferation and migration	Promotes fibroblast activity and tissue regeneration
3	TGF-β pathway	Collagen synthesis and extracellular matrix formation	Enhances wound contraction and remodeling
4	VEGF signaling pathway	Angiogenesis and neovascularization	Improves blood supply to healing tissue
5	PDGF pathway	Fibroblast proliferation	Stimulates granulation tissue formation
6	FGF signaling pathway	Cellular growth and differentiation	Supports epithelialization and angiogenesis
7	ERK pathway	Cell survival and proliferation	Accelerates tissue regeneration
8	JNK pathway	Stress and inflammatory response	Regulates cellular repair mechanisms
9	p38 MAPK pathway	Cytokine regulation	Modulates inflammation and tissue remodeling
10	Smad signaling pathway	TGF-β mediated intracellular signaling	Controls collagen maturation and fibrosis

https://doi.org/10.71058/jodac.v10i0708

Source: Compiled from molecular wound healing studies available through PubMed, Nature Reviews Molecular Cell Biology, and NCBI.

5.1 NF-κB Signaling Pathway

One of the main transcription factors that regulates inflammatory responses in wound healing is the nuclear factor kappa B (NF-κB). The pathway is critical for the regulation of pro-inflammatory cytokines, chemokines, adhesion molecules, and enzyme expression related to tissue damage and immune activation.

While activation of NF-κB is a key step in the early inflammatory stage of wound healing, sustained NF-κB activation can lead to chronic inflammation, delayed epithelialization, and impaired tissue regeneration. Hence, the proper regulation of the NF-κB pathway is crucial to ensure a balanced inflammatory response during wound repair. (Henar, 2025)

The phytoconstituents such as flavonoids, phenolic compounds, and triterpenoids found in the leaves of *Trichosanthes dioica* can regulate NF-κB signaling by exerting antioxidant and anti-inflammatory effects. These compounds can help block activation of inflammatory cytokines and decrease cellular damage from oxidative stress, which may help promote collagen synthesis, cell proliferation, and tissue regeneration in fibroblasts.

Direct investigation of the molecular mechanisms of Trichosanthes leaves is still limited, and studies on NF-κB signaling can be considered as important molecular evidence about wound healing and anti-inflammatory potential of these leaves.

5.2 MAPK Pathway

Mitogen-activated protein kinase (MAPK) signaling pathway is another important molecular mechanism involved in wound healing and tissue regeneration. (H. Zhao et al., 2021b) During tissue repair, the MAPK pathway is responsible for controlling several processes such as cell proliferation, migration, differentiation, apoptosis, and inflammatory processes.

The MAPK signaling cascade mainly consists of extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK), and p38 MAPK pathways. Signaling molecules are activated by growth factors, oxidative stress, inflammatory cytokines, and tissue injury. The role of

https://doi.org/10.71058/jodac.v10i0708

activation of MAPK signaling in the wound healing process is of particular importance in the proliferation of fibroblasts, migration of keratinocytes, collagen production, and angiogenesis.

ERK signaling is primarily linked to cell growth and tissue regeneration, while JNK and p38 pathways are linked to inflammatory responses and stress-related activities in cells. Appropriate activation of MAPK signaling promotes granulation tissue formation, epithelialization, and remodeling of the extracellular matrix during wound healing. (Sawaya et al., 2020)

The phytoconstituents found in the leaves of *Trichosanthes dioica*, such as flavonoids and phenolic compounds, as well as triterpenoids, could affect the MAPK signaling pathways via an antioxidant and anti-inflammatory approach. Such compounds could have beneficial effects on the activities of fibroblasts, promote the movement of keratinocytes, and modulate the inflammatory mediators that are important for tissue repair.

Experimental investigation of medicinal plants with high flavonoid content showed that they modulate the MAPK-mediated cellular responses and promote wound healing and tissue regeneration. Thus, the investigation of MAPK signaling pathways could be helpful in providing valuable molecular insights into the wound healing associated with the leaf extract of *Trichosanthes dioica*.

5.3 TGF-β Mediated Collagen Formation

One of the most important growth factors in wound healing and tissue regeneration is transforming growth factor beta (TGF-β). It is important for controlling fibroblast proliferation, collagen synthesis, extracellular matrix formation, and remodeling in various stages of wound healing. There are several isoforms of TGF-β, but TGF-β1 is regarded as the main form involved in connective tissue repair and scar formation. (Zheng et al., 2026)

Platelets, macrophages, fibroblasts, and keratinocytes release TGF-β during wound healing at the site of tissue injuries. Once activated, TGF-β binds to specific cell surface receptors and activates intracellular signaling pathways that promote the migration and proliferation of fibroblasts. Activated fibroblasts then produce collagen fibres, fibronectin, and other components of the extracellular matrix required for the development of the granulation tissues and tissue repair.

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Differentiation of fibroblasts to myofibroblasts through TGF-β-mediated signalling is also involved in wound contraction and tissue remodeling. Collagen deposition increases tensile strength and structural stability of the healing tissue. But overactive activation of the TGF-β pathway could result in fibrotic scar formation, fibrosis, and keloid formation. Thus, maintaining a balance of TGF-β activity is crucial for adequate wound healing. (Dou et al., 2026)

The phytoconstituents in Trichosanthes leaves, specifically flavonoids, phenolic compounds, triterpenoids, and β-sitosterol, could affect the collagen-forming effect of TGF-β by antioxidant and anti-inflammatory effects. These compounds can help to activate fibroblasts and promote collagen production, and also shield connective tissue from damage caused by oxidative stress.

6. Formulation Approaches of *Trichosanthes* dioica Leaf Extract

Formulation development is a crucial step in enhancing the therapeutic efficiency, stability, and topical application of medicinal plant extracts used in wound management. (Huang et al., 2024) Herbal formulations made from plant extracts are much studied due to their extended contact time with the wound surface, ability to maintain a moist wound environment, and increased penetration of active phytoconstituents to damaged tissues.

Thus, various topical dosage forms like ointments, creams, gels, and hydrogel-based formulations can be formulated with the extract of the leaves of Trichosanthes and may be used for experimental wound healing studies and future therapeutic applications.

6.1 Herbal Ointments

Herbal ointment is a semi-solid topical formulation that is used in wound healing studies due to its ability to retain medicinal agents at the wound site and prevent microbial invasion and dehydration of the damaged tissue. Ointments are typically made from appropriate ointment bases like petroleum jelly, beeswax, paraffin, or polyethylene glycol with plant medications.

The Trichosanthes leaves contain phytochemicals such as flavonoids, tannins, and triterpenoids, which could play a role in wound healing by their antioxidant, anti-inflammatory, and antimicrobial properties. Herbal ointments applied topically can then help to diminish inflammation, promote collagen deposition, stimulate granulation tissue proliferation, and repair epithelial regeneration. (Saithi & Pashikanti, 2022)

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Herbal ointments are also beneficial as they keep the area moist, which is an ideal condition for tissue repair, and reduce any external irritation or microbial invasion. Very few limited wound healing compositions have been formulated using *Trichosanthes dioica* leaves, so formulation of herbal ointment might be a great point to further experimental and pharmacological research.

6.2 Creams and Gels

The topical application of creams and gels is preferred in wound management due to the ease of use, patient acceptance, and effective delivery of bioactive compounds to the site of the wound. These formulations have cooling, soothing, and moisturizing properties that may help to support tissue repair and reduce tissue irritation while healing. (Mohiuddin, 2019)

Phytoconstituents of *Trichosanthes* dioica leaves might retain their biological activity in the cream and gel formulation and might be responsible for antioxidant, antimicrobial, and anti-inflammatory activity at the wound site. The formulations can increase deposition of collagen and regeneration of tissue and improve the process of epithelialization by enabling a more targeted delivery of bioactive compounds. (Seddiqi et al., 2021)

Gel formulations are especially useful for burn wounds and inflamed tissues as they help to keep them hydrated, cool, and absorptive. In addition, cream formulations can be used to increase the permeability of the skin and the ability to release the phytochemicals into the regenerating tissue.

Although there is still a limited number of direct formulation studies involving Trichosanthes leaves, the development of creams and gels would present great research opportunities for assessing the therapeutic value of these formulations in wound healing and regenerative medicine.

7. Future perspectives and research opportunities

While the *Trichosanthes* leaves have proven to have wound healing potential, scientific studies that target the tissue repair properties of the leaves are yet to be investigated deeply. Thus, a large number of experimental and molecular investigations are needed to prove their therapeutic effectiveness and mechanism in wound management. (Habib et al., 2015)

In vitro and in vivo wound healing studies will be required to assess the effect of Trichosanthes leaf extract on the proliferation of fibroblasts, movement of keratinocytes, angiogenesis, collagen synthesis and remodeling of the extracellular matrix. The study of their role in tissue regeneration and inflammatory regulation will be facilitated by molecular investigations of these pathways, including NF-κB, MAPK and TGF-β.

These novel topical formulations, which are comprised of herbal ointments, hydrogels, nano formulations and nanofiber-based wound dressings, could further enhance the stability, bioavailability and sustained release of phytoconstituents at the wound site. Nanotechnology delivery systems could provide better delivery of bioactive compounds to damaged tissues, and may increase therapeutic efficacy in chronic and diabetic wounds. (Huang et al., 2024b)

There is a huge research potential for pharmacological validation and formulation development of the scientific evidence directly related to wound healing activity of the Trichosanthes leaves, which are comparatively less explored. Hence, detailed experimental explorations can be helpful in establishing the potential of the leaves of Trichosanthes as natural therapeutic agents for wound management and for regenerative medicine.

8. Conclusion

Wound healing is a complex and well-regulated biological process comprising control of inflammation, proliferation of cells, collagen deposition, angiogenesis, and remodeling of tissues. In wound management, medicinal plants have been studied in a significant amount of scientific research due to their various pharmacological properties and relatively safe therapeutic profile. Of these medicinal plants, the leaves of Trichosanthes have important phytochemical components which could be useful for tissue repair and regeneration. (Mulisa et al., 2015b)

In vitro cellular assays, in vivo wound models, histopathological evaluation, and molecular studies are valuable scientific methods to explore the wound healing potential of the leaf extract of Trichosanthes. The molecular pathways like NF-κB, MAPK, and TGF-β signaling could be involved in tissue regeneration and inflammatory regulation in addition.

While there are some indications from traditional medicine in relation to the medicinal uses of Trichosanthes leaves in skin ailments and wound healing, there is less solid scientific evidence

https://doi.org/10.71058/jodac.v10i0708

relating to the latter area. Thus, additional phytochemical, pharmacological, and molecular studies are required to determine their therapeutic efficacy and safety. (Chaachouay & Zidane, 2024)

To conclude, the leaves of Trichosanthes are a promising source of bioactive phytoconstituents that can be used in wound healing and regenerative medicine. Their medicinal values can be further substantiated by future experimental and formulation-based studies, and these findings may help in the formulation of new wound healing medicines using plants.

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