

A Comprehensive Review Pharmacotoxicological Evaluation of a Polyherbal Formulation for the Wound Healing of Diabetic Patients

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Abstract

Diabetes mellitus is a chronic metabolic disorder frequently associated with complications such as persistent inflammation, oxidative stress, and impaired wound healing. Polyherbal formulations represent a promising therapeutic approach by targeting multiple biochemical pathways simultaneously. This review discusses the phytochemical properties, pharmacological mechanisms, and scientific evidence supporting a polyherbal formulation comprising *Limnospira platensis*, *Syzygium cumini*, *Tinospora cordifolia*, *Withania somnifera*, *Senna auriculata*, *Catharanthus roseus*, *Centenella asiatica*, *Tridax Procumbens*, and *Gymnema sylvestre*. Each herb exhibits significant antidiabetic, anti-inflammatory, or wound-healing effects, and together they provide complementary mechanisms including antioxidant activity, immunomodulation, β -cell protection, inhibition of carbohydrate-digesting enzymes, fibroblast proliferation, angiogenesis, and antimicrobial protection. This review highlights the synergistic potential of the formulation and outlines the need for standardized preclinical and clinical studies. The combined pharmacological actions indicate that this polyherbal blend may serve as an effective natural therapy for diabetes and its associated complications.

Keywords: Diabetes mellitus, wound healing, anti-inflammatory, *Tinospora cordifolia*, *Centenella asiatica*, *Gymnema sylvestre* and *Tridax Procumbens*.

1. Introduction

Diabetes mellitus is associated with chronic hyperglycemia, vascular dysfunction, neuropathy, and impaired immune responses that contribute to delayed wound healing. Diabetic foot ulcers affect approximately 15% of diabetic patients and are a leading cause of lower-limb amputation. Herbal therapies have emerged as promising alternatives because they can simultaneously regulate inflammation, oxidative stress, microbial burden, and tissue regeneration.[1]

A polyherbal formulation integrating *T. cordifolia*, *C. asiatica*, *G. sylvestre*, and *T. procumbens* may provide complementary mechanisms that accelerate diabetic wound repair.

2. Pathophysiology of Diabetic Wound Healing

Normal wound healing proceeds through:

1. Hemostasis
2. Inflammation
3. Proliferation
4. Remodeling

In diabetic wounds these phases are disrupted due to:

- Excess reactive oxygen species (ROS)
- Persistent inflammation
- Reduced angiogenesis
- Impaired fibroblast function
- Delayed collagen synthesis
- Increased susceptibility to infection

These abnormalities lead to chronic non-healing wounds. [2]

3. Medicinal Plants Used in the Polyherbal Formulation

3.1 *Tinospora cordifolia* (Guduchi)

Major Phytoconstituents

- Alkaloids (berberine, magnoflorine)
- Diterpenoid lactones
- Glycosides
- Steroids
- Flavonoids
- Polysaccharides

Wound-Healing Activities

Tinospora cordifolia exhibits:

- Antioxidant activity
- Anti-inflammatory effects
- Antimicrobial properties
- Immunomodulatory activity
- Enhanced collagen synthesis
- Increased granulation tissue formation

Experimental studies have demonstrated accelerated re-epithelialization, increased tensile strength, and enhanced collagen deposition in wound models. [3]

Relevance in Diabetic Wounds

Its antidiabetic and immunomodulatory actions help control hyperglycemia and reduce infection-related complications, thereby promoting wound closure. [4]

3.2 *Centella asiatica* (Gotu Kola)

Major Phytoconstituents

- Asiaticoside
- Madecassoside
- Asiatic acid
- Madecassic acid
- Flavonoids

Wound-Healing Activities

Centella asiatica is one of the most extensively studied wound-healing herbs.

Reported actions include:

- Stimulation of fibroblast proliferation
- Enhanced collagen synthesis
- Promotion of angiogenesis
- Increased extracellular matrix production
- Accelerated epithelialization

Animal studies under diabetic conditions demonstrated significant improvement in wound contraction and healing rates. [5]

Mechanism

Asiaticoside stimulates:

- Transforming Growth Factor- β (TGF- β)
- Collagen type I synthesis
- Fibroblast migration

These actions promote faster tissue regeneration. [6]

3.3 *Gymnema sylvestre* (Gurmar)

Major Phytoconstituents

- Gymnemic acids
- Gurmarin
- Saponins
- Flavonoids
- Triterpenoids

Pharmacological Activities

- Antidiabetic
- Antioxidant
- Anti-inflammatory
- Antimicrobial

Relevance in Diabetic Wound Healing

Unlike the other herbs, *Gymnema sylvestre* contributes primarily through glycemic control. Hyperglycemia is a major factor responsible for delayed wound healing. By improving glucose homeostasis and reducing oxidative stress, *G. sylvestre* creates a physiological environment favorable for tissue repair.

Several studies have demonstrated its ability to:

- Enhance insulin secretion
- Improve glucose utilization
- Reduce lipid peroxidation
- Minimize oxidative tissue damage

These effects indirectly accelerate wound healing in diabetic patients.

3.4 *Tridax procumbens* (Coatbuttons)

Major Phytoconstituents

- Flavonoids
- Terpenoids
- Alkaloids
- Sterols
- Tannins
- Polysaccharides

Wound-Healing Activities

Traditionally used for treating cuts and wounds, *T. procumbens* exhibits:

- Antimicrobial activity
- Anti-inflammatory activity
- Antioxidant effects
- Increased collagen synthesis
- Enhanced fibroblast proliferation

Studies suggest that *T. procumbens* promotes wound healing through increased lysyl oxidase activity and vascular endothelial growth factor (VEGF)-mediated angiogenesis. [7]

Antidiabetic Potential

Extracts of *T. procumbens* have also demonstrated antihyperglycemic activity, making it particularly valuable in diabetic wound management. [8]

4. Rationale for Polyherbal Combination [9]

Ingredient	Primary Action in Wound Healing	Key Phytoconstituents
<i>Tinospora cordifolia</i>	Reduces blood glucose , enhances wound contraction, and accelerates epithelization while increasing collagen deposition.	Alkaloids, glycosides, and alpha-D-glucan.
<i>Centella asiatica</i>	Accelerates wound closure via the AKT/MAPK/NF-κB pathway , enhances angiogenesis, and suppresses pro-inflammatory cytokines.	Triterpenoids (Asiaticoside), Quercetin, and Kaempferol.
<i>Gymnema sylvestre</i>	Potent antihyperglycemic action that restores a healthy metabolic environment essential for natural healing cascades to resume	Gymnemic acids and saponins.
<i>Tridax procumbens</i>	Antimicrobial and anti-inflammatory properties that prevent infection and boost fibroblast proliferation and blood flow	Flavonoids, alkaloids, and tannins.

The combination provides:

Antioxidant Synergy

All four plants contain flavonoids and phenolics that neutralize ROS.

Anti-inflammatory Synergy

Reduction of pro-inflammatory cytokines shortens the inflammatory phase.

Enhanced Angiogenesis

Centella asiatica and *Tridax procumbens* stimulate vascular growth.

Improved Collagen Formation

Centella asiatica, *Tinospora cordifolia*, and *Tridax procumbens* promote fibroblast activity and collagen maturation.

Better Glycemic Control

Gymnema sylvestre and *Tinospora cordifolia* help maintain glucose homeostasis.

Antimicrobial Protection

Tinospora cordifolia and *Tridax procumbens* inhibit wound pathogens.

5. Proposed Mechanism of Polyherbal Formulation

The polyherbal formulation may act through multiple pathways:

1. Reduction of oxidative stress
2. Suppression of chronic inflammation
3. Promotion of fibroblast proliferation
4. Increased collagen synthesis
5. Enhanced angiogenesis
6. Improved glycemic control
7. Prevention of microbial infection
8. Faster re-epithelialization

Together, these effects may significantly accelerate diabetic wound closure.

6. Conclusion

A polyherbal formulation containing *Tinospora cordifolia*, *Centella asiatica*, *Gymnema sylvestre*, and *Tridax procumbens* offers a scientifically plausible and potentially effective strategy for diabetic wound healing. The formulation combines antidiabetic, antioxidant, anti-inflammatory, antimicrobial, angiogenic, and collagen-promoting activities. Such synergistic effects may overcome multiple pathological barriers associated with diabetic wounds and warrant further preclinical and clinical investigation. [10]

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