

# Phytochemical and Pharmacological Properties of *Tinospora cordifolia* (Giloy)

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## ABSTRACT

*Tinospora cordifolia* (commonly known as Giloy or Guduchi) is a revered herb in traditional Ayurvedic medicine, widely recognized for its rejuvenating properties. The plant's therapeutic effects stem from a rich profile of phytochemicals-alkaloids, terpenoids, lactones, and polysaccharides-responsible for diverse pharmacological activities such as immunomodulation, antioxidant, anti-inflammatory, antidiabetic, antimicrobial, and hepatoprotective effects. This paper explores the phytochemical constituents, pharmacological potentials, and clinical relevance of *T. cordifolia*, with a focus on its mechanisms of action and its growing role in integrative medicine, particularly post-COVID-19. The review also highlights the necessity of more rigorous scientific studies and standardization to bridge traditional uses and modern therapeutic applications.

**Keywords:** *Tinospora cordifolia*, Giloy, Immunomodulatory Activity of Giloy, Anti-inflammatory of Giloy, Pharmacological Properties of Giloy, COVID-19 Adjunct Therapy.

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**Received:** 14-05-2025;

**Revised:** 24-07-2025;

**Accepted:** 08-09-2025.

## INTRODUCTION

*Tinospora cordifolia* (Willd.) Miers, commonly known as Giloy or Guduchi, is a climbing shrub belonging to the family Menispermaceae. Renowned as a "Rasayana" (rejuvenating herb) in Ayurveda, it has been a cornerstone of traditional medicine systems across South Asia for centuries, revered for its multifaceted therapeutic potential. Its Sanskrit name, Guduchi ("one that protects the body"), underscores its historical use in treating fever, inflammation, metabolic disorders, and immune dysfunction.<sup>[1]</sup>

The plant's therapeutic efficacy is attributed to its rich repertoire of bioactive phytochemicals, including alkaloids (berberine, tinosporin), terpenoids (cordifoliosides), diterpenoid lactones, phenolic compounds, and polysaccharides. These compounds exhibit a wide spectrum of pharmacological activities, such as immunomodulation, antioxidant, anti-inflammatory,

antidiabetic, and hepatoprotective effects. Notably, during the COVID-19 pandemic, Giloy gained widespread attention as a potential adjunct therapy for immune support, further driving demand for evidence-based validation of its safety and efficacy.<sup>[2]</sup>

Despite its prominence, critical gaps persist in understanding the mechanistic pathways of its bioactive compounds, standardization of extracts, and clinical translation of preclinical findings. Additionally, rising commercial exploitation and habitat loss necessitate sustainable cultivation strategies to preserve its genetic diversity. Overview of major phytochemical constituents and pharmacological activities of *Tinospora cordifolia*. The plant contains alkaloids, terpenoids, and polysaccharides, contributing to its immunomodulatory, antioxidant, anti-inflammatory, antidiabetic, antimicrobial, and hepatoprotective effects (Figure 1). This review aims to consolidate current knowledge on the phytochemical and pharmacological properties of *T. cordifolia*, critically evaluate its therapeutic potential across diverse disease models, and highlight emerging challenges in its integration into modern healthcare systems. By bridging traditional wisdom with contemporary science, this work seeks to inform future research and policy frameworks for harnessing Giloy's full medicinal potential.<sup>[3]</sup>



DOI: 10.5530/pres.20252350

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## Distribution of *Tinospora cordifolia* (Giloy)

*Tinospora cordifolia*, commonly known as Giloy, is a herbaceous vine of the family Menispermaceae. Its distribution is primarily concentrated in tropical regions of the Indian subcontinent, including India, Sri Lanka, and Myanmar. The plant thrives in tropical and subtropical climates and is found in forests, hedges, and other natural habitats where it can climb on trees or spread extensively as a vine.<sup>[4]</sup>

**Native Range:** Indigenous to the Indian subcontinent.

**Habitat:** Found in tropical forests and areas with adequate sunlight and moisture. It grows as a climbing vine on trees or other structures

**Ecological Adaptation:** The plant is well-suited to a variety of tropical conditions and can grow in diverse soil types. It is often associated with endophytic fungi that colonize its tissues without causing harm, which may contribute to its ecological success

## Conservation Status

Due to its extensive use in Ayurvedic medicine for its pharmacological properties (e.g., anti-diabetic, anti-inflammatory, and immuno-modulatory effects), there is concern over its conservation. Efforts are being made to ensure sustainable harvesting and cultivation to meet increasing demand while preserving natural populations.<sup>[4]</sup>

## Morphological Features of *Tinospora cordifolia* (Giloy)

*Tinospora cordifolia*, commonly known as Giloy, is a large, deciduous, climbing shrub belonging to the family Menispermaceae. *Tinospora cordifolia* is a climbing shrub traditionally used in immunomodulatory properties. It belongs to the family Menispermaceae and is taxonomically classified as shown in Table 1. It is widely recognized for its medicinal properties in traditional systems like Ayurveda. Below are its detailed morphological characteristics:

### Growth Habit

**Type:** A climbing, extensively spreading vine.

**Branches:** Elongated, twining branches that climb over trees or other supports.

**Stem:** Succulent, greenish-gray, cylindrical, and rough in texture. Contains prominent lenticels and a spongy internal structure.

The stem is rich in bioactive compounds like alkaloids and glycosides.

### Leaves

**Type:** Simple, alternate, and exstipulate (lacking stipules).

**Shape:** Broadly ovate or heart-shaped (cordate), giving the plant its name "heart-leaved moonseed." show in Figure 2.

**Size:** Leaves measure 10-20 cm in length and 8-15 cm in width.

**Surface Texture:** Upper surface: Pubescent (slightly hairy).

**Lower surface:** Whitish-tomentose with a prominent reticulum (network of veins).

### Petioles

Long petioles (up to 15 cm) that are pulvinate (swollen) at both ends.

The basal end is twisted halfway around.

### Flowers

**Type:** Unisexual (male and female flowers are on separate plants).

**Size:** Small, inconspicuous flowers.

**Color:** Greenish-yellow. Show in Figure 3.

### Arrangement

Male flowers are clustered in axillary racemes.

Female flowers are solitary or sparsely arranged.

### Structure

**Sepals:** Six sepals arranged in two whorls of three each; the outer sepals are smaller than the inner ones.

**Petals:** Six obovate, membranous petals that are smaller than the sepals.

### Fruits

**Type:** Aggregate of small drupelets.

**Shape:** Ovoid and smooth.

**Colour:** Scarlet or orange when ripe.

**Arrangement:** Fruits grow in clusters of one to three on thick stalks with sub-terminal style scars show in Figure 4.

### Roots

Aerial roots develop along the climbing branches.

Roots are threadlike and play a significant role in nutrient absorption.

### Anatomical Features

The plant exhibits unique anatomical traits that distinguish it from related species like *Tinospora sinensis*: show in Figure 5.

Presence of secretory sacs and calcium oxalate crystals in the stem tissues.

A complex arrangement of vascular bundles with diffuse porous wood anatomy.

**Figure 6:** Geographical distribution of *Tinospora cordifolia*. The plant is predominantly found in tropical and subtropical regions, including India, Sri Lanka, Myanmar, and other parts of Southeast Asia. It typically grows in dry and deciduous forests, often climbing on trees and shrubs

### Ethnopharmacological importance of *T. cordifolia*

*Tinospora cordifolia*, commonly known as Giloy or Guduchi, is a highly valued medicinal plant in traditional medicine systems, especially Ayurveda, Siddha, and folk medicine. Its ethnopharmacological significance stems from its diverse therapeutic applications, which are attributed to the presence of bioactive compounds like alkaloids, diterpenoid lactones, glycosides, steroids, and phenolics. Below are the detailed aspects of its importance:

#### Ayurvedic Medicine

In Ayurveda, *Tinospora cordifolia* (Giloy) is revered as a "Rasayana" herb, which promotes longevity, rejuvenation, and overall health. It is often referred to as "Amrita," meaning the "nectar of immortality," and is extensively mentioned in classical Ayurvedic texts like *Charaka Samhita* and *Sushruta Samhita*. The plant is used for its ability to balance the three doshas (Vata, Pitta, and Kapha) and is considered effective in treating a wide range of ailments. It is traditionally used to manage chronic fevers, especially those caused by infections like malaria or dengue, due to its antipyretic properties. Giloy is also employed as an immunomodulator to enhance the body's defense mechanisms against infections and diseases. Additionally, it is used for managing diabetes by regulating blood sugar levels, improving digestion through its "Agnideepana" (digestive fire-enhancing) property, and treating skin disorders like eczema and psoriasis. Other therapeutic applications include alleviating jaundice, anemia, arthritis, respiratory disorders like asthma, and urinary tract infections. Its adaptogenic properties make it a key remedy for stress-related conditions.<sup>[5]</sup>

**Table 1:** Taxonomic classification.

Taxonomic classification
Kingdom: <i>Plante</i>
Division: <i>Magnoliopsida</i>
Class: <i>Manoliopsida</i>
Order: <i>Ranunculales</i>
Family: <i>Menispermaceae</i>
Genus: <i>Tinospora</i>
Species: <i>cordifolia</i>

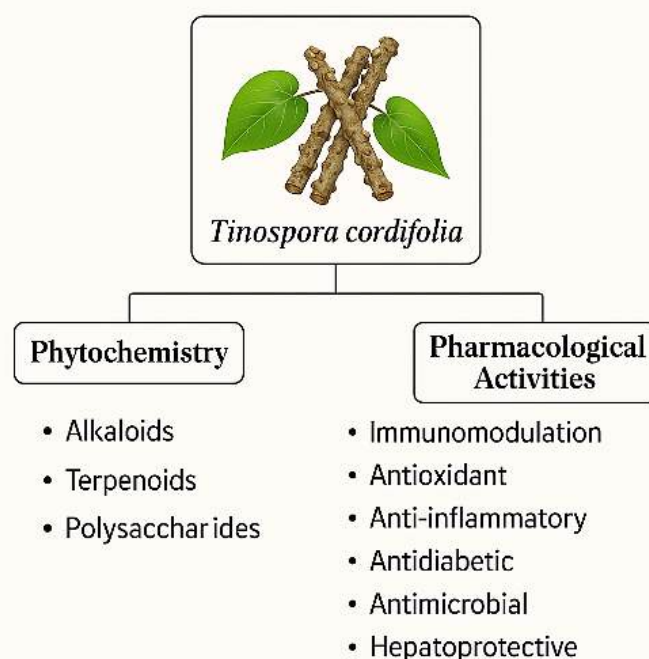
### Folk Medicine

In traditional folk medicine practices, *T. cordifolia* is widely used across rural communities in India and other tropical regions. The plant's stem extract is commonly administered as a remedy for general debility and fatigue, acting as a natural health tonic. It is also used as an antidote for snake bites and scorpion stings. The starch extracted from the plant's stem is employed to treat chronic fevers and improve appetite.<sup>[6]</sup> Folk practitioners use Giloy paste or decoction for wound healing, fractures, and skin inflammations. It is also applied to alleviate gastrointestinal issues such as diarrhea, dysentery, colitis, and abdominal pain. Furthermore, the roots of the plant are traditionally used as an emetic to relieve intestinal obstructions. In some regions, *T. cordifolia* is believed to enhance memory and cognitive functions, making it a popular choice for treating age-related cognitive decline.<sup>[7]</sup>

### Pharmacological Activities

#### Immunomodulatory Effects

The immunomodulatory effects of *Tinospora cordifolia* (Giloy) are significant and are primarily attributed to its rich array of bioactive compounds, including alkaloids, diterpenoid lactones, polysaccharides, glycosides, and phenolics. These compounds work synergistically to modulate immune responses through several mechanisms. For instance, *T. cordifolia* extracts have been shown to upregulate cytokines such as Interleukin-6 (IL-6), enhancing the activation of inflammatory responses and promoting the differentiation of B cells and cytotoxic T cells. Polysaccharides derived from the plant can modulate cytokine release and nitric oxide production in macrophages, thereby



**Figure 1:** Graphical abstract of *Tinospora cordifolia* (Giloy).



providing protection against endotoxic shock.<sup>[8]</sup> Moreover, aqueous extracts of *T. cordifolia* have demonstrated the ability to enhance macrophage activity by increasing lysosomal secretion and boosting nitric oxide production, which is crucial for pathogen elimination. In animal studies, the plant has been shown to elevate antioxidant enzyme levels, reducing oxidative damage in vital organs like the liver and spleen. Additionally, specific compounds within *T. cordifolia*, such as alpha-d-glucan, stimulate lymphocyte activation and suppress inflammatory mediators, further supporting its role in enhancing adaptive

immunity. Clinical applications have also been observed, with human studies indicating improved antibody production against various antigens and enhanced immune responses in children. Furthermore, bioactive constituents like syringin exhibit anti-inflammatory and antioxidant properties by inhibiting pro-inflammatory pathways such as NF- $\kappa$ B. Collectively, these findings highlight *Tinospora cordifolia* as a potent immunomodulator with promising applications in treating infections and chronic inflammatory conditions, though further research is needed to standardize dosages and validate its clinical efficacy in humans.<sup>[9,10]</sup>



**Figure 2:** Leaves of *Tinospora cordifolia* (Giloy).

### Anti-Diabetic Properties of *Tinospora cordifolia* (Giloy)

*Tinospora cordifolia* exhibits significant anti-diabetic properties, making it a valuable herb for managing diabetes mellitus, particularly type 2 diabetes. Its therapeutic effects are attributed to its ability to regulate blood glucose levels, enhance insulin secretion, improve glucose uptake, and mitigate oxidative stress. Studies have shown that oral administration of *T. cordifolia* extracts (100-200 mg/kg body weight) in diabetic animal models effectively reduces blood glucose levels by stimulating insulin secretion and inhibiting key enzymes involved in gluconeogenesis and glycogenolysis, such as glucose-6-phosphatase and fructose-1,6-diphosphatase. Additionally, it restores hepatic glycogen content, as evidenced by histopathological studies using periodic acid-Schiff staining.<sup>[11]</sup>

The plant also promotes glucose uptake in peripheral tissues through insulin-dependent and independent pathways. For instance, its stem extracts enhance the activity of glucose transporters GLUT1 and GLUT3 for basal glucose uptake



**Figure 3:** plant with flower.



and GLUT4 for insulin-mediated glucose transport in skeletal muscle cells. This mechanism is supported by increased Phosphorylation of Protein Kinase B (AKT) and AMP-Activated Protein Kinase (AMPK), which are critical regulators of glucose metabolism.<sup>[12]</sup> Moreover, *T. cordifolia* preserves pancreatic beta cells from damage caused by inflammatory cytokines like interleukin-1 $\beta$  and interferon- $\gamma$ , thereby maintaining endogenous insulin production.<sup>[13]</sup>

Oxidative stress is a major contributor to diabetic complications, and *T. cordifolia* counters this by enhancing antioxidant defenses. It suppresses oxidative stress markers such as Thiobarbituric Acid Reactive Substances (TBARS) while boosting antioxidant enzymes like Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx), and Glutathione (GSH). These effects not

only improve glucose metabolism but also reduce the risk of diabetes-related complications.

Several bioactive constituents isolated from *Tinospora cordifolia* have demonstrated potent pharmacological activities such as immunomodulation, anticancer, antidiabetic, and anti-inflammatory effects. Key compounds and their biological actions are summarized in Table 2.

Clinical studies suggest that *T. cordifolia* exhibits insulin-like activity, effectively lowering blood glucose levels without causing acute toxicity or behavioral changes. Additionally, its active compound tinosporaside improves insulin sensitivity and fasting blood glucose levels in diabetic mice while enhancing lipid profiles by reducing triglycerides and total cholesterol levels. These findings highlight its potential as a natural therapeutic agent for managing diabetes mellitus while minimizing the side effects associated with synthetic drugs.<sup>[14]</sup>

### Anti-Inflammatory and Antipyretic Properties of *Tinospora cordifolia* (Giloy)

*Tinospora cordifolia* (Giloy) has garnered significant attention for its potent anti-inflammatory and antipyretic properties, which are well-documented in both traditional and scientific literature.<sup>[15]</sup> The plant's extracts have been shown to effectively alleviate inflammation and reduce fever, making it a valuable resource in herbal medicine. In various studies, *T. cordifolia* extracts have demonstrated significant anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , and IL-6. For instance, *in vitro* studies using RAW 264.7 macrophage cells revealed that the chloroform extract of *T. cordifolia* significantly reduced the expression of Cyclooxygenase-2 (COX-2) and inhibited Nitric Oxide (NO) production when cells were stimulated with Lipopolysaccharides (LPS). This inhibition is crucial as COX-2 is an enzyme that plays



**Figure 4:** fruits *Tinospora cordifolia* (Giloy).



**Figure 5:** Aerial roots of *Tinospora cordifolia* (Giloy).

a key role in the inflammatory process. Additionally, the extract has been shown to prevent the phosphorylation of p38 MAPK and retain NF- $\kappa$ B in the cytoplasm, further contributing to its anti-inflammatory action.<sup>[16]</sup>

The antipyretic activity of *T. cordifolia* has also been validated through experimental models. Studies utilizing brewer's yeast-induced pyrexia in mice demonstrated that administration of *T. cordifolia* extract resulted in a significant reduction in body temperature, indicating its effectiveness in managing fever. The extract's ability to modulate inflammatory responses and reduce fever can be attributed to its rich phytochemical profile, which includes compounds like tinosporaside, stigmasterol, and  $\beta$ -sitosterol-each contributing to its therapeutic effects. Furthermore, the extract has been found to enhance wound healing processes by reducing inflammation at injury sites, thereby promoting faster recovery. Collectively, these findings underscore the potential of *Tinospora cordifolia* as a natural remedy for treating inflammatory disorders and fever, supporting its traditional use in various medicinal practices.<sup>[17]</sup>

## Hepatoprotective Properties of *Tinospora cordifolia* (Giloy)

*Tinospora cordifolia* exhibits remarkable hepatoprotective properties, making it a valuable herb for managing liver disorders and preventing hepatic damage caused by toxins. Its hepatoprotective effects are primarily attributed to its rich phytochemical composition, including alkaloids (e.g., berberine, palmatine, and jatrorrhizine), diterpenoids, glycosides, and polyphenols. These bioactive compounds work synergistically to protect the liver by mitigating oxidative stress, reducing inflammation, and promoting hepatic cell regeneration. Studies using Carbon tetrachloride (CCl<sub>4</sub>)-induced hepatotoxicity models in rats have demonstrated that *T. cordifolia* extract significantly reduces serum levels of liver enzymes such as SGOT, SGPT, ALP, and bilirubin-key markers of liver damage. This indicates its ability to restore liver function and prevent cellular injury. Additionally, the plant extract enhances antioxidant

defenses by upregulating enzymes like Superoxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (GPx), and Glutathione (GSH), which collectively neutralize Reactive Oxygen Species (ROS) and prevent lipid peroxidation.<sup>[18]</sup>

Berberine, one of the active constituents of *T. cordifolia*, plays a critical role in hepatoprotection by inhibiting pro-inflammatory cascades mediated by TNF- $\alpha$  and reducing nitrosative stress through suppression of Inducible Nitric Oxide Synthase (iNOS). This reduces inflammation and prevents necrosis of hepatocytes. Furthermore, compounds such as columbin and magnoflorine promote liver regeneration by activating Peroxisome Proliferator-Activated Receptor- $\alpha$  (PPAR $\alpha$ ) and optimizing dopamine receptor activity. Experimental studies have also shown that *T. cordifolia* extract can reverse damage caused by heavy metals like arsenic and cadmium as well as drug-induced hepatotoxicity from paracetamol or thioacetamide. The plant's ability to inhibit lipid peroxidation and normalize biomarkers like Malondialdehyde (MDA) further underscores its protective role against oxidative damage.<sup>[19]</sup>

In addition to its direct hepatoprotective effects, *T. cordifolia* is an active ingredient in polyherbal formulations used to treat jaundice and other liver disorders. Its safety profile is notable, with

**Table 2:** Bioactive compounds found in *Tinospora cordifolia*.

Compound	Biological Activity
Cordifolioside A	Immunostimulant, anticancer
Tinocordiside	Immunomodulatory, antidiabetic
Magnoflorine	Anticancer, antidiabetic, anti-inflammatory
Berberine	Antidiabetic, antimicrobial
Syringin	Antioxidant, immunomodulatory
N-formylannonain	Immunomodulatory, cytotoxic
11-hydroxymustakone	Immunomodulatory, cytotoxic
Arabinogalactan (G1-4A)	Immunomodulatory, anti-inflammatory



**Figure 6:** geographical obtain of plant.



studies indicating no adverse effects at doses up to 2000 mg/kg body weight. These findings highlight *T. cordifolia* as a promising candidate for developing novel therapeutic agents for managing hepatic ailments while minimizing side effects associated with synthetic drugs.<sup>[20]</sup>

**Figure 7:** Causes, effects, and treatments associated with *Tinospora cordifolia* (Giloy). The figure illustrates how environmental, physiological, and pathological stressors contribute to oxidative damage, inflammation, and immune suppression, which are mitigated through the pharmacological actions of *T. cordifolia* such as immunomodulation, hepatoprotection, and antioxidant activity.

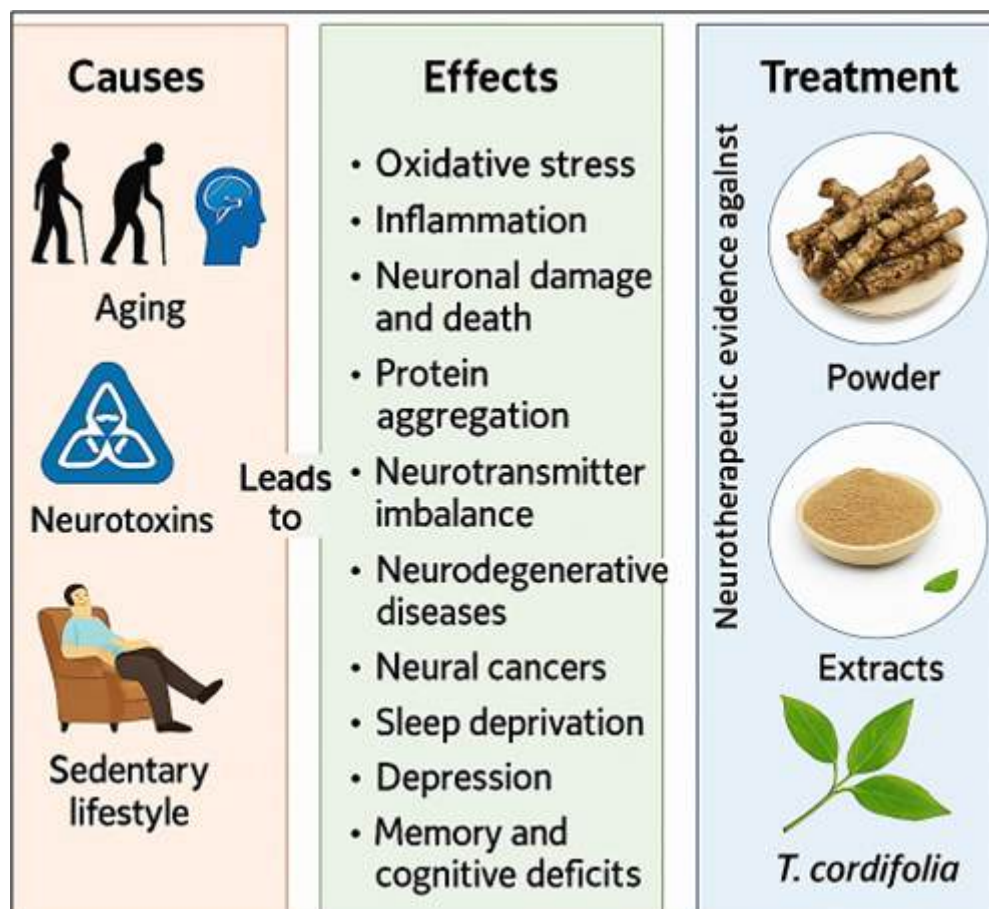
### Antioxidant Activity of *Tinospora cordifolia* (Giloy)

*Tinospora cordifolia* exhibits potent antioxidant activity, which is attributed to its rich composition of bioactive compounds such as phenolics, flavonoids, alkaloids, and diterpenoid lactones. These compounds effectively neutralize free radicals, reduce oxidative stress, and protect cellular structures from damage caused by Reactive Oxygen Species (ROS). Studies have demonstrated that extracts from various parts of the plant, including roots, leaves, and stems, exhibit significant antioxidant potential. For instance, aqueous root extracts of *T. cordifolia* administered to diabetic rats

reduced plasma levels of Thiobarbituric Acid Reactive Substances (TBARS), ceruloplasmin, and alpha-tocopherol while increasing levels of glutathione and vitamin C, indicating its ability to restore antioxidant balance in oxidative stress conditions.<sup>[21]</sup>

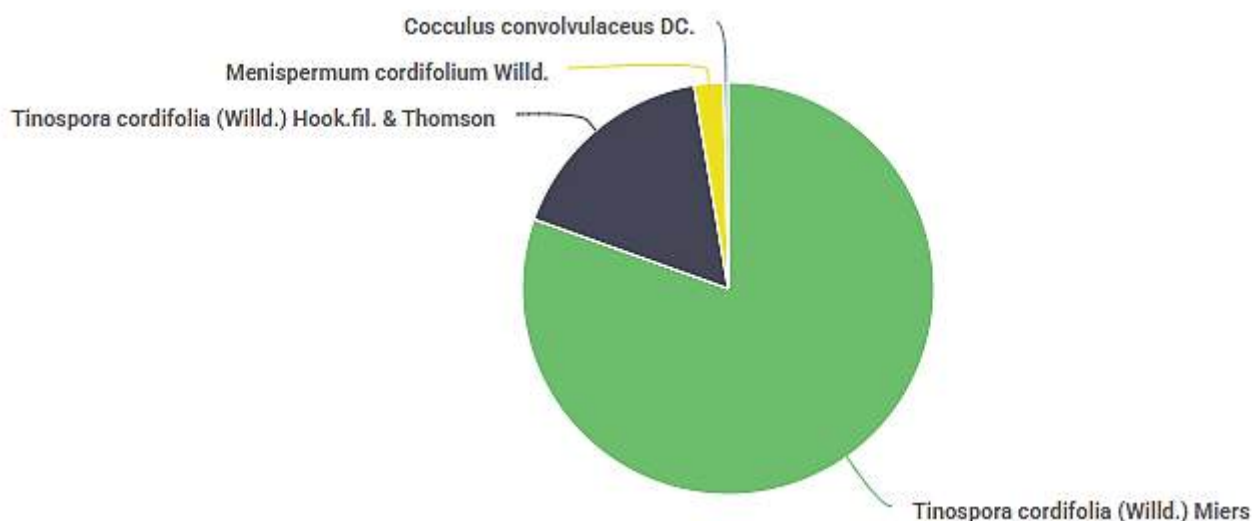
Additionally, leaf extracts have shown high radical scavenging activity in *in vitro* models. Ethanol extracts exhibited strong DPPH (2,2-Diphenyl-1-Picrylhydrazyl) radical scavenging with an EC<sub>50</sub> value of 0.5 mg/mL, outperforming other solvents like methanol and chloroform. The plant also demonstrated lipid peroxidation inhibition in liposome models induced by ferric ions. Furthermore, *T. cordifolia* stem extracts displayed substantial metal ion chelating activity (67-95%) at low concentrations (10-40 µg/mL), which is crucial in preventing oxidative damage caused by transition metals like iron.<sup>[22]</sup>

The total phenolic content in various extracts has been quantified between 8.75-52.50 catechol equivalents per gram (CE/g), correlating with its strong reducing power and antioxidant capacity. These findings suggest that *T. cordifolia* not only scavenges free radicals but also enhances endogenous antioxidant enzyme activity, such as superoxide dismutase (SOD) and catalase (CAT). Its antioxidant properties are further validated by its ability to protect against oxidative stress-related diseases like diabetes, cancer, and neurodegenerative disorders. Collectively,



**Figure 7:** Causes, effect and treatments for *T. cordifolia* (Giloy).

## Name usages applied to occurrences (Figure 8)



**Figure 8:** Name usages applied to occurrences of *Tinospora cordifolia*. The pie chart illustrates the frequency of various scientific names used for *T. cordifolia* in botanical and taxonomic records.

these studies establish *Tinospora cordifolia* as a promising natural antioxidant with therapeutic potential for managing oxidative stress-induced conditions.<sup>[23]</sup>

### Antimicrobial Properties of *Tinospora cordifolia* (Giloy)

*Tinospora cordifolia* exhibits significant antimicrobial properties, making it a valuable resource in the treatment of various infections. Numerous studies have demonstrated its effectiveness against a range of pathogenic microorganisms, including bacteria, fungi, and viruses. The antimicrobial activity is largely attributed to the presence of diverse bioactive compounds such as alkaloids, glycosides, saponins, and tannins, which contribute to its efficacy.<sup>[24]</sup> For instance, ethanolic extracts of *T. cordifolia* have shown potent antibacterial effects against common oral pathogens like *Streptococcus mutans*, with studies revealing substantial zones of inhibition when tested using the disc diffusion method. At a concentration of 3 mg, *T. cordifolia* produced a zone of inhibition measuring 25.6 mm against *S. mutans*, outperforming other herbal extracts.<sup>[25]</sup>

In addition to its antibacterial properties, *T. cordifolia* has demonstrated antifungal activity against strains such as *Candida albicans*. The plant's extracts have been shown to inhibit fungal growth effectively, with comparable results to standard antifungal drugs like nystatin. Furthermore, its methanolic extract has exhibited strong activity against opportunistic pathogens like *Pseudomonas aeruginosa*, highlighting its potential in treating multidrug-resistant infections. The mechanism behind its antimicrobial action may involve disrupting microbial cell

membranes or inhibiting essential metabolic pathways in these pathogens.<sup>[26],[27]</sup>

Moreover, research has indicated that *T. cordifolia* can enhance immune responses, further supporting its role in combating infections. For example, studies involving murine models have suggested that the plant can help re-establish immune function during systemic candidiasis and other infections. Overall, the antimicrobial properties of *Tinospora cordifolia* underscore its importance in traditional medicine and its potential as a source for developing new antimicrobial agents to address the growing challenge of antibiotic resistance.<sup>[28]</sup>

### Anti-Cancer Potential of *Tinospora cordifolia* (Giloy)

*Tinospora cordifolia*, commonly known as Giloy, has garnered significant attention for its anti-cancer potential, supported by a growing body of research demonstrating its efficacy against various cancer types, including breast, prostate, colon, and leukemia.<sup>[29]</sup> The plant's anticancer properties are primarily attributed to its rich phytochemical composition, which includes alkaloids, flavonoids, glycosides, and diterpenoid lactones. Studies have shown that extracts from *T. cordifolia* can inhibit cell proliferation and induce apoptosis in cancer cell lines through multiple mechanisms.<sup>[30]</sup> For instance, aqueous and ethanolic extracts have been reported to exhibit antiproliferative activity in various cancer models, including hepatocellular carcinoma and glioblastoma. *In vitro* studies have indicated that the extracts can arrest the cell cycle at specific phases (G0/G1 and G2/M), suppress the expression of cyclin D1 (a key regulator of cell cycle progression), and enhance the expression of pro-apoptotic



markers while downregulating anti-apoptotic proteins like Bcl-xL.<sup>[31]</sup>

Mechanistically, *T. cordifolia* exerts its anti-cancer effects by modulating various signaling pathways involved in cell growth, differentiation, and metastasis. For example, it has been shown to inhibit Epithelial-Mesenchymal Transition (EMT), a critical process in cancer metastasis, by reducing the expression of plasticity markers such as NCAM and MMP-2/9. Additionally, its active compounds like berberine have been identified to target multiple pathways associated with tumor growth and progression, leading to reduced expression of genes involved in colon cancer development. The synergistic effect of combining different phytochemicals from *T. cordifolia* has also been noted to enhance its overall anticancer efficacy.<sup>[32]</sup> Overall, the evidence supports *Tinospora cordifolia* as a promising candidate for developing natural therapeutic agents against cancer; however, further well-designed clinical trials are essential to validate these findings and establish standardized dosages for effective use in cancer treatment.<sup>[33]</sup>

### Stress and Ulcer Management with *Tinospora cordifolia* (Giloy)

*Tinospora cordifolia*, commonly known as Giloy, is recognized for its significant role in managing stress and ulcers, supported by both traditional use and scientific research. The herb is classified as an adaptogen, which means it helps the body adapt to stressors and promotes homeostasis.<sup>[34]</sup> Clinical studies have demonstrated that *T. cordifolia* effectively reduces symptoms associated with chronic stress, such as anxiety and depression, by modulating biochemical parameters linked to stress responses. For instance, a study involving patients with mental stress showed that treatment with *T. cordifolia* significantly lowered serum glucose levels, triglycerides, and cholesterol while improving psychological well-being, comparable to the effects of conventional anxiolytic medications like diazepam.<sup>[35]</sup> Additionally, its extracts have been found to reduce oxidative stress markers and enhance antioxidant defense, thereby mitigating the physiological impacts of stress.<sup>[36,37]</sup>

In terms of ulcer management, *T. cordifolia* has been shown to possess gastroprotective properties that help prevent and heal gastric ulcers. The plant's bioactive compounds exhibit anti-inflammatory effects that reduce gastric mucosal damage caused by irritants such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or alcohol. Studies indicate that *T. cordifolia* can significantly decrease the ulcer index in experimental models by promoting mucus secretion and enhancing the integrity of the gastric mucosal barrier. Furthermore, its ability to inhibit the secretion of gastric acid and stimulate mucosal healing processes contributes to its effectiveness in treating peptic ulcers. Overall, the adaptogenic and gastroprotective properties

of *Tinospora cordifolia* make it a valuable natural remedy for managing stress-related disorders and gastrointestinal health issues, reinforcing its longstanding use in traditional medicine systems.<sup>[38]</sup>

### Phytochemical constituents and active compounds isolated from *T. cordifolia*

*Tinospora cordifolia*, commonly known as Guduchi or Giloy, is a widely used medicinal plant in the Indian system of medicine (Ayurveda) due to its rich phytochemical profile and therapeutic properties. The plant contains a variety of bioactive compounds that contribute to its pharmacological activities, including immunomodulation, antioxidant effects, anti-inflammatory properties, and more.

#### Phytochemical Constituents

The major classes of compounds isolated from *T. cordifolia* include alkaloids, terpenoids, glycosides, steroids, phenolics, lignans, and polysaccharides. These compounds are distributed across different parts of the plant such as the stem, leaves, and roots. *Tinospora cordifolia* contains a diverse range of bioactive compounds, including alkaloids, glycosides, and long-chain aliphatic alcohols, which contribute to its pharmacological properties. A detailed list of these phytoconstituents is provided in Table 3.

#### Alkaloids

Key alkaloids include berberine, palmatine, magnoflorine, jatrorrhizine, and tembetarine.

These compounds exhibit diverse biological activities such as anti-inflammatory, antioxidant, and antimicrobial effects.<sup>[39,40]</sup>

#### Terpenoids

Terpenoids like tinosporide, tinosporaside, clerodane diterpenes, and furanolactones are prominent in the plant.

They are known for their anticancer, hepatoprotective, and anti-diabetic properties.

#### Glycosides

Important glycosides include cordifolioside A and B, syringin, amritoside A-D, and tinocordiside.

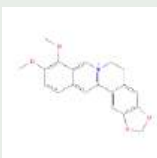
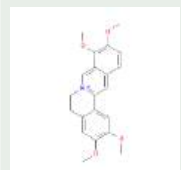
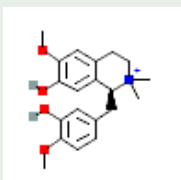
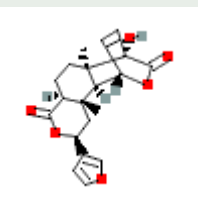
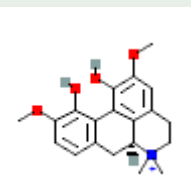
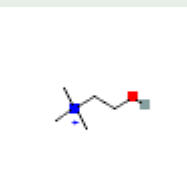
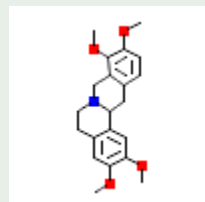
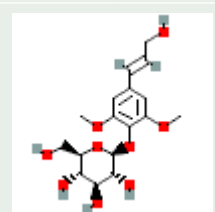
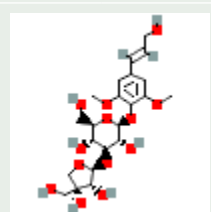
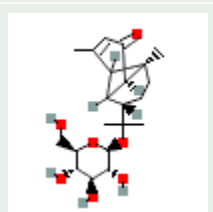
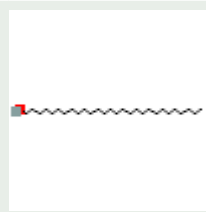
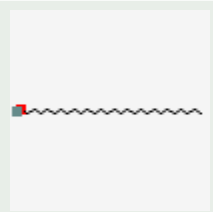
These compounds are primarily responsible for the immunomodulatory and cardioprotective effects of *T. cordifolia*.

#### Steroids

Steroidal compounds such as  $\beta$ -sitosterol and giloisterol are present in the stem.

They contribute to anti-inflammatory and cholesterol-lowering activities.

**Table 3: Classification of Phytochemical Compounds in *Tinospora cordifolia*.**

					
Berberine	Palmatine	Tembetarine	Isocolumbin	Magnoflorine	Choline
					
tetrahydropalmatine					
Glycosides containing compounds					
					
Syringin A	Cordifolioside	Tinocordiside			
Aliphatic containing compounds					
					
1-Octacosanol			1-Heptacosanol		

## Phenolics and Flavonoids

Phenolic compounds like lignans and flavonoids (e.g., apigenin and luteolin) are abundant.

These compounds act as antioxidants and play a role in reducing oxidative stress.

## Polysaccharides

Polysaccharides such as arabinogalactan (G1-4A) have been identified.

These high-molecular-weight compounds enhance immune responses by activating macrophages.

## Miscellaneous Compounds

Other notable constituents include aliphatic compounds (e.g., heptacosanol), diterpenoid lactones (e.g., columbin), and sesquiterpenoids.

## CONCLUSION

*Tinospora cordifolia* holds considerable promise as a multi-purpose medicinal herb due to its broad spectrum of pharmacological effects and low toxicity profile. While its historical and cultural significance in traditional medicine is well-established, modern validation through systematic scientific inquiry remains essential. Strengthening the evidence base with controlled clinical trials, phytochemical standardization, and

molecular-level research will enable safe and effective integration of *T. cordifolia* into modern therapeutic frameworks.

## ACKNOWLEDGEMENT

The authors extend their appreciation to the authorities of ITM University for providing the necessary support and resources.

## ABBREVIATIONS

**IL-6:** Interleukin-6; **TNF- $\alpha$ :** Tumor Necrosis Factor-alpha; **COX-2:** Cyclooxygenase-2; **NF- $\kappa$ B:** Nuclear Factor kappa-light-chain-enhancer of activated B cells; **MAPK:** Mitogen-Activated Protein Kinase; **GLUT:** Glucose Transporter; **AMPK:** AMP-Activated Protein Kinase; **SGOT:** Serum Glutamic-Oxaloacetic Transaminase; **SGPT:** Serum Glutamic-Pyruvic Transaminase; **ALP:** Alkaline Phosphatase; **ROS:** Reactive Oxygen Species; **SOD:** Superoxide Dismutase; **GPx:** Glutathione Peroxidase; **GSH:** Glutathione; **DPPH:** 2,2-Diphenyl-1-picrylhydrazyl; **TBARS:** Thiobarbituric Acid Reactive Substances; **MDA:** Malondialdehyde; **PPAR $\alpha$ :** Peroxisome Proliferator-Activated Receptor Alpha; **iNOS:** Inducible Nitric Oxide Synthase.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of Interest.

## FUNDING

This study did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

## AUTHOR CONTRIBUTION

RK conceptualized and designed the study. RK, MKB, SS, AK, SA, and AR contributed to the literature review, data compilation, and manuscript drafting. RK and PK supervised the overall process and provided critical revisions. All authors were involved in reviewing scientific literature, preparing Figures and Tables, and refining the manuscript content. RK finalized the manuscript and approved it for submission and publication.

## SUMMARY

The paper provides an in-depth analysis of *Tinospora cordifolia*'s phytochemistry and pharmacological properties. It begins by establishing the plant's Ayurvedic and ethnomedicinal relevance, especially as a Rasayana (rejuvenative herb). The core sections detail the major bioactive compounds such as tinosporin, cordifoliosides, and berberine, followed by their associated biological activities. These include immune enhancement, anti-diabetic effects, liver protection, and activity against microbial infections. The discussion also addresses the increased attention *T. cordifolia* received during the COVID-19 pandemic, underlining both its therapeutic promise and the gaps in

empirical validation. Overall, the review emphasizes the need for clinical trials, pharmacokinetic studies, and standardized extracts to facilitate its incorporation into evidence-based healthcare systems.

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**Cite this article:** Kothari R, Bajhaiya MK, Soni S, Kumar A, Ali S, Rajput A, *et al.* Phytochemical and Pharmacological Properties of *Tinospora cordifolia* (Giloy). *Pharmacog Res.* 2025;17(4):1171-82.