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**Original Research Article**

# Ethanobotany, Phytochemistry and Pharmacology of *Tinospora cordifolia*

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**ABSTRACT**
Herbal medicinal plants are the major source of various bioactive molecules which have enormous medicinal properties and no or less side effects compared to allopathic system of medicine. Usage of medicinal and health plants have over grown in pharmaceutical health care industry due to their low cost, affectivity in the management of critical diseases and abundant availability to a large populations of developing countries. *Tinospora cordifolia* commonly called Giloy have immense potential for the treatment of numerous ailments in ancient Ayurvedic medicines. Recently during COVID 19 pandemic this plant is of great interest to medical practitioners due to its antipyretic, antimalarial, antidiabetic, antioxidants, antistress, anti-inflammatory and anticancer properties. Its use in folklore medicine for the management of fever, malaria, jaundice, diabetes, inflammations, gout, and maintaining overall health is well established. This plant is rich source of various secondary metabolites such as flavonoid, saponins, glycosides, alkaloids, phenolics, lignans; validating its role in various herbal drugs and formulations. This review gives an insight of various pharmacological and phytochemicals actions of *Tinospora cordifolia* along with its immense potential in several traditional system of medicine.

## 1. Introduction

With the emergence of human establishments plants have been widely used in various traditional and folklore medicines. Natural products are the source of multiple interests of researchers as an alternative to synthetic drugs for promoting defense mechanism and having healing Properties. World Health Organization is promoting research development in the areas of traditional medicine not only for the dealing of various deadly infections which are on the rise and posing serious challenges in 21$^{st}$ century, but also for restoring the balance of human health by a more holistic approach. A majority of populations in third world countries still depend on herbal products as prime medication system as they are economical and have better harmony with human body than allopathic system of medicine [1].

*Tinospora cordifolia* (Miers) belonging to family Manispermaceae is a climbing shrub native to tropical area of Srilanka, China, India, Mayanmar, Bangladesh, Malaysia, Indonesia and South Africa. In Hindi it is called as Giloy/Guduchi referring to its reinvigorate properties. In Ayurvedic system of medicine this plant is mentioned as "Rasayan" which enhances body endurance against infections, helps it to cope up with stress and promote longevity [2]. A versatile herb Giloy is beneficial for Jaundice, diabetes, skin diseases, eye disorders, gout, leprosy, rheumatism and anaemia. It is a powerful medicine for combating fever, expelling toxins from the body, boosting immune system, improving memory, increasing stamina and revitalizing the body [3, 4]. The whole plant has medicinal properties but most important part mentioned in Ayurvedic Pharmacopia is stem because of higher alkaloid content. Traditional Giloy Satva is the starch; obtained from Giloy plant growing on neem tree is more effective as it also incorporates the medicinal value of neem [5, 6]. These pharmacological and healing capabilities are due to presence of diverse range of chemical compounds like alkaloids, glycosides, flavonoids, diterpenoid lactones, steroids, aliphatic compounds, essential oils and polysaccharides extracted from different portions of *T. cordifolia* [7]. This paper intends to give an overview of pharmacological potential of *T. cordifolia* and the presence of various photochemicals making it a magical herb for the treatment of numerous human ailments.

## 2. Botanical description

*T. cordifolia* is a perennial, deciduous glabrous climbing plant having a large number of extremely spreading branches that twin around the nearby objects. It thrives fine in a varied variety of soil ranging from acidic to alkaline with adequate drainage and it grows best from stem cuttings. Aerial roots are long filiform, membranous when young and leathery when aged, arising from branches and grow downward sometimes touching the ground. Stem is slander, twisted, succulent, climbing in nature and growing to great heights. Bark is grey to creamy white and exfoliates on drying [8, 9]. The name *cordifolia* comes from heart shaped leaves which are simple alternate, exstipulate, ovate, petiolate, deeply cordate and swollen at base with multicostate reticulate venation [10]. Flowers bloom in summer is small, yellow or greenish yellow, unisexual in terminal or auxiliary racemes, appearing when the plant is leafless. Male flowers are born in clusters while female flowers are solitary. Sepal are 6, in two whorls of 3, outer 3

small, ovate; acute while inner 3 are large membranous, elliptical and yellow in colour. Petals are 6, yellow coloured closely embracing six stamens. Female flowers have 1-3 carpels on short gynophores similar to male flowers but with green sepals [11]. Fruits appear in winter in aggregates of 1-3 druplets having sub-terminally style scars on thick stalks and are orange, red or scarlet. Seeds are white, bean shaped, curved and endocarp is ornamented [12, 13].

## 3. Ethano medicinal uses

In different tribal and folk medicine *T. cordifolia* has been specified as a potent therapeutic plant [2, 14, 15]. All the parts of plant in the form of juice decoction, maceration infusion or powder are well documented in ethano botanical surveys for the treatment of general infection jaundice, ulcers, leprosy, calming body heat, general disability, asthma, bites of venomous snakes and improving digestion [16, 17]. Paste of guduchi along with seeds of *Piper nigrum* (Kali mirch) is used by females of Rajasthan to cure leucorrhoea. Juice of roots is used for eye disorders while juice of leaves is used for pain in ears in certain parts of India. In Karnataka (Davanagere district) Giloy decoction is given to treat acidity, indigestion and to cure leucorrhoea [18]. Some of the traditional uses of different regions *T. Cordifolia* are summarized in Table 1.

(a) (b) (c)

**Figure 1:** *Tinospora cordifolia:* (a) stem, (b) leaves, and (c) fruits.

**Table 1:** Ethanomedicinal uses of different parts of *T. Cordifolia*

| | |
|---|---|
| Leaves | Decoction of leaves for treatment of gout, ulcers, jaundice, fever and for lowering blood glucose. Paste of leaves is applied for dressing of wounds. |
| Stem | Stem starch is used for cure of fever, jaundice, chronic diarrhea, asthma, body cooling, skin infections, against intestinal worms, improving digestion and maintenance of good health.<br>Stem juice is useful for diabetes, leucorrhea & splenomegaly.<br>Decoction of stem used in washing eye sores & syphilitic sores |
| Stem + root | Used as an antidote to venomous strike bite & scorpion sting along with other drugs. |
| Bark | Have antiallergic, antileprotic, anticancer and antispasmodic properties. |
| Root | Root decoction is used for dysentery, visual obstruction, leprosy & diarrhoea. |
| Over all plant | Skin disease, boost immune system, bone frcture, bronchitis, promotes longevity |
| Fruit | With ghee and honey for treatment of jaundice & rheumatism. |

**Source:** Choudhary *et al.,* [2]; Neha *et al.,* [19]; Bharath *et al.,* [20]; Thakur *et al.,* [21].

## 4. Photochemical constituents

A wide range of secondary metabolites, have been obtained from different parts of *T. cordifolia* belongs to different phytochemical classes such as alkaloids, glycosides, steroids, terpenoids, aliphatic compounds and polysaccharides [22]. Its stem contains high fibre, sufficient protein, ample carbohydrates and low fat. Different minerals such as potassium, chromium, iron, zinc, copper along with other micronutrients have been reported making it a nutritious herb [23]. Putative active compound isolated from *T. cordifolia* are berberine, tinosporine, tinosporaside, clerodane furono diterpene glucoside (amritoside A, B, C, D), palmatine, tembertarine, isocolumbin, magniflorine, cordifol, jatrorrhizine, cordioside, tinucordioside and β- sitosterol [24, 25] (Table 2).

**Table 2:** Phytochemical constituents present in different parts of *T. cordifolia*

| Phytochemical class | Compound | Parts | References |
|---|---|---|---|
| Alkaloids | Berberin, choline, tembetarine, palmetin, magnoflorine, Jatorrhizine, isoculmbin, aporphine, tetra-hydropalmatine, corydine, Salsolinol, tyramine, paprazine, columbamine | Stem, Root | [26] |
| Glycosides | Tinocordiside, tinocordifolioside, Cordioside, norclerodane glucoside, furanoid diterpene glucoside, syringin, pregnane glycoside, palmatosides, cordifolioside A, cordiofolioside B, cordiofolioside C, cordiofolioside D, cordiofolioside E, Palmatosides C, Palmatosides F, Syringin - apiosyl glycoside | Stem | [27] |
| Steroids | β-sitosterol, δ-sitosteral, 20β hydroxy ecdysone, Ecdysterone, Makisterone A, Giloinsterol | Aerial part, stem bark | [28, 29] |
| Terpenoids | Furanolactone clerodane diterpene Tinosporide, furanolactone diterpene, furanoid diterpene, tinocrispol A, borapetol A, borapetol B, rumphiol E, Jateorine, Columbin, tinosporin | Whole Plant | [30, 31] |
| Miscellaneous Compounds | Giloin, Heptacosanol, giloinin Octacosanol, sinapic acid, tinosporic acid, Tinosporan acetate, Tinosporal acetate, tinosporone, tinosporal, arabinogalactan | Whole Plant | [26-31] |

**Table 3:** Pharmacological activities of *Tinospora cordifolia*

| Pharmacological activity | Disease name and Biological role | Application part | *In vivo /In vitro* | Reference |
|---|---|---|---|---|
| Antiosteoporotic effect | Osteoporosis and Osteoarthritis | Giloy extract | ovariectomized rats<br>In Silico | [32, 33] |
| Antimicrobial activity | *E. faecalis, E. Coli, K. pneumoniae* and *P. acnes*<br>*E. coli, Bacillus subtilis, Aspergillus niger and Candida* sp.<br>Subclinical mastitis<br>*S. typhi, E. coli, P. aeruginosa*, and *S. aureus*<br>*Candida albicans* | *T. cordifolia* Satva (TCS) and *T. cordifolia* Ghana (TCG)<br>Giloy stem extract<br>Giloy and neem extract<br>Guduchi satva (GS) and Guduchi Ghana (GG)<br>Aqueous extract | *In vitro* | [34 – 37] |
| Antioxidant activity | DPPH radical scavenging activity<br>DPPH, superoxide radical scavenging activity, total reducing powder, total antioxidant activity and lipid peroxidation inhibitory activity | Stem metanolic extract<br>Giloy leaf extract in different solvent | *In vitro* | [38, 39] |
| Antiviral activity | SARS-CoV-2 | Giloy extract<br>Aqueous extract of Giloy Ghanvati<br>Bioactive Compounds | In silico<br>Humanized Zebrafish Model<br>Docking and molecular dynamic( in silico) | [40-42] |
| Immunomodulation activity | Increasing antibody titer, neutrophil activity<br>Increased phagocytic activity of human neutrophils.<br>Increase in platelet count | Giloy leaf extract.<br>Stem extract in ethyl acetate, hot water extract and water<br>hydro alcoholic leaf extract | On finfish<br>Albino rats<br>Albino wistar rats | [32, 43, 44] |
| Anti-inflammatory activity | Anti-inflammatory and antipyretic activity<br>Inhibit the production of TNF-α, IL-1β | stem aqueous extract<br>Aqueous extract | Albino wistar rats<br>Albino wistar rats | [45, 46] |
| Neurodegeneration activity | Neurodegeneration<br>Parkinson's disease | Giloy leaf aqueous extract<br>Aqueous extract | *Drosophila melanogaster*<br>Mice | [47, 48] |
| Anti-toxic activity | Nephrotoxicity<br>Lead toxicity | Ethanolic extract of root<br>Leaves aqueous extract | Swiss albino male mice<br>Male albino mice | [49, 50] |
| Anti-diabetic activity | Diabetes mellitus | Stem part<br>Alkaloid fraction (AFTC) | Albino rats<br>*In vitro* and *in vivo*(rat) | [51, 52] |

## 5. Pharmacological activities

Pharmacological importance of *Tinospora cordifolia has* been established by several researchers. They highlighted its role as antimicrobial, antiviral, anti-diabetic, anticancer, antioxidant, immunomodulating, anti-inflammatory, antiosteoporotic cardioprotective, radioprotective, cytoprotective, and antitoxic agent [32] (Table 3).

### 5.1 Antiosteoporotic effects

Sarkar *et al.,* [21] reported the role of *T. cordifolia* in bone maintenance through molecular docking on RANKL/OPG gene. They concluded that out of 41 compounds found by ethanol extraction method some of them are more active constituents like berberine, palmatine, cordifolioside A, tinosporinone, ecdysterone, isocolumbin and tinocordifolin. Ecdysone (Ecd) ingredient found in giloy extract was investigated in ovariectomized rats by Kapur *et al*. [33]. Their studies showed significant increase in the thickness of joint cartilage, thickness in epiphyseal growth and trabecular bone. It has been concluded from their report that Ecdysone containing plants including giloy can be used in the treatment of osteoporosis and osteoarthritis.

### 5.2 Antimicrobial activity

*T. cordifolia* showed antibacterial, antifungal activity in various extracts. Javed *et al.* [34] study on two form of giloy *i.e. T. cordifolia* Satva (TCS) and *T. Cordifolia* Ghana (TCG) on different kind of bacterial strain as *Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae* and *Propionibacterium acnes*, found that TCS can have more antimicrobial potential as compared to TCG at low concentration. Giloy powder at various concentrations has been used against Streptococcus *mutans* (MTCC 890) by Agarwal *et al.* [53] and found that at two percent concentration it showed highest antimicrobial activity against this microbe and suggested to be used as mouthwash to prevent plaque formation. Prasad and Chauhan *et al.* [35] studied the effect of various concentration (50 to 200 mg/ml) of root and stem extract (methanolic and ethanolic) of giloy plant on pathogenic microorganism viz *E. coli, Bacillus subtilis, Aspergillus niger and Candida* sp. and found that antimicrobial activity is increased with increase in extract concentration. Stem metanolic extract shows highest antimicrobial activity.

Solanki *et al.,* [36] studied the antimicrobial activity of giloy stem on microorganisms isolated from milk of cattle suffering from subclinical mastitis. It has been concluded that extract can be used in the treatment of subclinical mastitis in combination with *Azadirachta indica.* Sharma and Prajapati [37] studied the antimicrobial activity of Guduchi satva (GS) and Guduchi Ghana (GG) against microbial strain such as *Salmonella typhi, Escherichia coli, Pseudomonas aeruginosa*, and *Staphylococcus aureus a*nd compared it with Ampicillin. Both GS and GG showed better results than ampicillin, GS was more effective in inhibiting *E. coli* while GG showed more promising results for *S. aureus*. The total bacterial count found was 20 cfu/g and 30 cfu/g in GG and GS respectively. Result shows that GG to be effective against yeast and mold up to 100% but in GS they are under permissible limit i.e., 10 cfu/g. It has been concluded by researcher that both satva and ghana have great antimicrobial activity against microorganisms. Phytochemical investigation showing various functional group, alkaloid, tannins, phenols, starch, sterols and glycosides present in GS and GG confirm its antimicrobial activity. *Candida albicans* infected mice were treated with AETC dose (50 to 100 mg/kg) and fluconazole dose (50 mg/kg) showing 40% to 60% survival in AETC treatment and only 20 % survival rate in fluconazole treatment. Fungal load was less in kidney in 100 mg/kg treated AETC mice.

### 5.3 Antioxidant activity

Khan *et al.,* [38] in his study on methanolic and ethanolic extracts of stem extracts of *T. cordifolia* found that its methanolic extract has higher tannin, phenolic and flavonoid content, exhibited higher total antioxidant activity and be able to scavange DPPH radical at lower IC50 value (9.36 ± 0.01 mg/ml) Specific bioactive molecules like ellagic acid, gallic acid, quercetin, rutin hydrate, caffeic acid, syringic acid, vanillic acid, myricetin, p-coumaric acid, trans-cinnamic acid, hydroquinone, kaempferol, (+)– catechin hydrate reported in both the extracts enables it as source of neutraceutical and functional food development capable of reducing the onset of degenerative diseases.

Premanath and Lakshmidev [39] studied the antioxidant activity of giloy leaves in hexane, chloroform, methanol, ethanol and aqueous extract using *in vitro* models as DPPH radical scavenging activity, total reducing powder, total antioxidant activity, superoxide radical scavenging activity and lipid peroxidation inhibitory activity. Active antioxidant compounds of ethanol extract show better activity as compared to other extracts. Ethanolic extract showed greatest DPPH radical scavenging activity (EC 50: 0.5 mg/ml) and highest flavonoid (0.52 ± 0.02 mg/g) and phenol content (5.1 ± 0.25 mg/g) was also reported.

### 5.4 Antiviral activity

Chowdhury [40] has done in silico study of *Tinospora cordifolia* phytoconstituents against SARS-CoV-2 (COVID-19) using molecular dynamics approach and found that chemical constituents of giloy e.g. berberine. β-sitosterol, coline, tetrahydropalmatine can be able to regulate 3CLpro protein's function by its inhibition and help in control of viral replication. Balkrishna, 2021 study on Giloy Ghanvati (GG) aqueous extract in the treatment of SARS-CoV-2 spike protein on Humanized Zebrafish Model found that GG treatment effective in pro-inflammatory cell infiltration in swim bladder, tubule damage and necrosis in the kidney. Higher body temperature raised due to introduction of SARS-CoV-2 spike protein was reversed using GG treatment. The mortality rate has been completely reversed by higher dose i.e. 142 µg/kg/day but at lower concentration which is 6 and 28 µg/kg/day only rescue the mortality up to 89% for 10 days only. It was concluded by author that morphological, cytological and behavioural changes observed were reversed to normal level using GG treatment.

Murugesan *et al.* [42] studied docking and molecular dynamic and found that bioactive compound as amritoside, apigenin-6-C-glucosy l7-O-glucoside, pectolinarin and astragalin has binding affinities towards COVID-19 (corona virus disease – 2019) Mpro. CoV-2 main protease (COVID-19$M^{pro}$) is an enzyme that has a role in viral replication and transcription. In silico study on these bioactive compounds

shows their inhibitory effect on COVID-19M$^{pro}$ by non-covalently binding with catalyticresidues C145 and H41.

### 5.5 Anti-neurodegenerative activity

Singh and Himalian [47] studied the effect of leaf aqueous extract of giloy on neurodegeneration in wild type *Drosophila melanogaste*r (Oregon R+). They treated *D. melanogaster* with paraquat (PQ) for 24 and 48 hours and their neuro-degeneration was examined by locomotors and memory assay. It was found that co treatment of Drosophila alongwith PQ and *T. cordifolia* show significant amelioration which is due the presence of phenolic and free scavenging content that help in reducing neuro-degeneration. Birla *et al.,* [48] reported the effect of *T. cordifolia* aqueous extract in the treatment of Parkinson's disease. They found that *T. cordifolia* extract showed anti-inflammatory activity in 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP) intoxicated Parkinsonian mouse model. The extract is able to reverse the behavioural and biochemical abnormality induced by MPTP intoxicated mice. It has been suggested that it can be used to protect dopaminergic neuron by suppressing the neuro-inflammation in parkinsonian mouse model.

### 5.6 Immunomodulating activity

Giloy has been used in old ayruveda extensively because it help in boosting immune system and provide protection. Sudhakaran *et al.,* [43] reported the immunostimulatory effect of giloy leaf extract on finfish. The leaf extract supplementation either in ethanol or petroleum ether result in increasing the antibody titer, neutrophil activity which make the animal resistance to disease. Sharma *et al.,* [50] study the immunomodulatory activity of *T. cordifolia* stem extract in ethyl acetate, hot water extract and water fraction. They found that among several active compound cordifolioside A and syringin shows this kind of activity by increasing the phagocytic activity of human neutrophils. Sarkar *et al.* [32] done comparative study of hydro alcoholic extract of *T. cordifolia* leaf and prednisolone on the albino wistar rats in which thrombocytopenia was used by toxin cyclophosphamide and Chloramphenicol. They found that increase in platelets count in rat supplemented with prednisolone, low dose of giloy and high dose of giloy was 1246583, 903014 and 997078 respectively. Their study shows significant increase in the platelets count of thrombocytopenia rats when supplemented with high dose of giloy extract.

### 5.7 Anti-inflammatory activity

Sumanlata *et al.,* [45] studied the anti-inflammatory and antipyretic activity of *T. cordifolia* stem aqueous extract in dose (1.25 g/kg, 2.5 g/kg and 5 gm/kg) on carrageenan and histamine induced rat paw edema and Brewer's yeast induced pyrexia model in albino rats as comparable to that of standard drugs diclofenac sodium and paracetamol. Anti-inflmmatory and anti-pyreticactivity is due to inhibition of COXcyclooxygenase (COX), an lipoxygenase (LOX) enzymes.

Ghatpande *et al.* [46] found antiinflammatory properties of giloy on wistar rats having inflammation associated anemia (AI) along with reduced liver and spleen iron store, high inflammatory biomarkers and hepcidin expression induced by repeated injection of HKBA (heat-killed *Brucella abortus*). TC treated animal showed improved body weight, preservation of liver and spleen size within limits and protected liver and spleen from inflammation induced cellular damage. TC extract exhibited anti-inflammatory by lowering expression of TNF- α and Cox-2 genes and inhibiting expression of HAMP and TLR-4 gene. Extract of TC also inhibit the production of TNF-α, IL-1β (inflammatory cytokines). Studies conclude that anti inflammatory activities are due to chemical tinosporaside present in TC extract.

### 5.8 Anti-toxic activity

Gupta and Sharma [49] studied the *T. cordifolia* provide protection against aflatoxin induced nephrotoxicity which is due to the presence of chemical like palmatine, tinosporin, magnoflorine, isocolumbin and terahydopalmatine alkaloid found in ethanolic extract of root. Swiss albino male mice was given orally with crystalline aflatoxin B1(AFB1) from *Aspergillus falvus* (2 µg/30 g b.wt, orally) alone or in combination with *T. Cordifolia* (50, 100, 200 mg/kg) daily for 25 days. *T. cordifolia* help in lowering down the concentration of the thiobarbituric acid reactive substances and increase the level of SOD (superoxide dismutase), catalase (CAT), GST (glutathione-s-transferase), GSH (reduced glutathione), ascorbic acid, protein and activities of antioxidant enzymes.

Sharma *et al.* [44] observed the effect of *T. cordifolia* stem and leaves aqueous extract on lead toxicity on male albino mice. It was found that there was a significant increase in haemoglobin (Hb) and packed cell volume (PCV) in giloy (400 mg/kg body weight per day for 30 days) treated animals. So giloy can help in reducing the effect of lead on animal to some extent.

### 5.9 Antidiabetic activity

Chougale *et al.* [51] studied the antidiabetic activity of giloy plants extract on albino rats. Extract of *T. cordifolia* in ethyl acetate, chloroform, hexane and dichloromethane (DCM) were studied on animal model and found that DCM extract is more effective in 100% inhibition of alpha glucosidase in non-competitive manner. Extract was also inhibiting the salivary amylase and pancreatic amylase about 75% and 83% respectively which then help in reduction in increase of postprandial glucose level. Giloy plant thus can be used for the treatment of diabetes mellitus. Patel and Mishra [52] studied *in vitro* and *in vivo* effect of chemical from *T. cordifolia* like isoquinoline alkaloid rich fraction, palmatien, magnoflorine and jatrorrhizine on insulin releasing and insulin mimicking effect. Insulin releasing effect was studied on rat pancreatic β-cell line, RINm5F. Result showed that TC have antihyperglycemic activity by decreased gluconeogenesis in rat hepatocytes and increased the secretion of insulin *in vitro* study. During in vivo study it decreases the fasting serum glucose and help in decreasing blood glucose level when orally given to animals.

## 6. Conclusions

In ayurveda, traditional medicinal plants have been used for the treatment of various diseases. *T. cordifolia* commonly known as giloy has found to contain lots of active compound that play their diverse role in the treatment of various diseases. Their role as antimicrobial activity, anti-inflammatory, anti ostporotic, anti toxin, antioxidant, and immunomodulating activities were confirmed by various studies in vitro and in vivo. As their stem, root and leaf extract or powder shows its

better pharmacological activity as compared with standard drugs. Giloy has been used in dengue fever and COVID-19 patients to increase the platelets and white blood cell as it considered as an immunity boosting plant. In future use of *T. cordifolia* for the development of drugs in critical disease treatment where current medicine have restricted potential is beyond doubt.

## Authors' contributions

The author read and approved the final manuscript.

## Conflicts of interest

The author declares no conflict of interest.

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## Data availability

No new data were created.

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