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Review Article

THE MULTI-ACTIVITY HERBACEOUS VINE - *TINOSPORA CORDIFOLIA*

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ABSTRACT

Tinospora cordifolia (Willd.) Miers ex Hook. F. and Thoms is a large deciduous, climbing shrub found throughout India, especially in the tropical parts ascending to an altitude of 300 m and also in certain parts of China (Anonymous). It belongs to the family Menispermaceae. It is known as heart-leaved Moonseed plant in English, Guduchi in Sanskrit, and Giloy in Hindi. It is known for its immense application in the treatment of various diseases in the traditional ayurvedic literature. *T. cordifolia*, also named as "heavenly elixir," is used in various ayurvedic decoctions as panacea to treat several body ailments. (Mishra R,) Its root stems, and leaves are used in Ayurvedic medicine. *T. cordifolia* is used for diabetes, high cholesterol, allergic rhinitis (hay fever), upset stomach, gout, lymphoma and other cancers, rheumatoid arthritis, hepatitis, peptic ulcer disease, fever, gonorrhea, syphilis, and to boost the immune system (WebMD).

Keywords: *Tinospora cordifolia*, Heavenly elixir, Guduchi, Tippa-Teega, Tinosporic acid.

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INTRODUCTION

Tinospora cordifolia, commonly called as "GUDUCHI," Amrta, and Cinnodbhava in Sanskrit; Gllow in Punjabi; Tippa-Teega in Telugu; Shindilakodi in Tamil; Amruthu and Chittamruthu in Malayalam; Amruthaballi in Kannada; Bândaul pich in Khmer; Rasakinda in Sinhala; Boraphét in Thai; Guduchi and Gulvel in Marathi; Gurch and Guluncha in Urdu; Ningthou khongli in Manipuri; Theisawntlung in Mizo; Gulancha in Bengali; Guluchi in Odia; Gujro in Nepali; Galac and Garo in Gujarati; Geloy, Guruc and Gurcha in Hindi; Amritvel in Konkani; Hogunilot in Assamese; and Gurjo in Sikkhim, belongs to the family Memispermaceace. It is genetically large, diverse climbing shrub with flowers of greenish-yellow color and the flowering season expands over summer and winter. It is indigenous to topical areas of India, Myanmar, Sri Lanka. It is used in the treatment of various diseases and infections such as diabetes, high cholesterol, allergic rhinitis, Gout, upset stomach, lymphoma, and some cancers also.

MORPHOLOGICAL CHARACTERISTICS

Tinospora is a glabrous twiner. Its older stems are up to 2 cm diameter and have a corky bark. Stems and branches are with white vertical lenticels. Bark is gray-brown or creamy white, warty and paper-thin, and peels off easily. Leaves are ovate, acute, and long petiolate, with multicoated reticulate venation [1]. It has thread-like aerial roots. When roots are young , they are membranous and become more or less leathery with age.

This herb contains unisexual flowers - clustered male flowers and solitary female flowers. Fruits are drupe shaped that turn red on ripening. Flowers grow during summer and fruits during winter.

CULTIVATION AND COLLECTION

Tinospora is distributed toward topical regions of India that are located 1200 m above sea level from Kumaon to Assam. In India, it is easily available in Bihar, West Bengal, Kerala, and Karnataka. It commonly grows in deciduous and dries a forest which grows over hedges and small tree [2].

This herb prefers growing in large variety of soils but prefers red soil or medium black soil [3]. The soil should be well drained with sufficient organic matter and moisture as required. It can be propagated by seeds and vegetable cutting, but viability of seeds is very less and seeds germination is major problems related with clonal propagation. The plant is very rigid and can be grown in subtropical and tropical climate but mainly in warm and rainy climate. It does not tolerate high rainfall and waterlogged conditions.

As *Tinospora* is a climber, it requires support for its growth (fast-growing species such as neem, jatropa, and moringa). For example, *T. cordifolia* growing with neem (*Azadirachta indica*) is called as NEEM GILOY.

CHEMICAL CONSTITUENTS

Columbin, tinosporaside, jatrorhizine, palmatine, berberine, tembeterine, tinocordifolioside, phenylpropene disaccharides, choline, tinosporic acid, tinosporal, tinosporon, tinosporine, sitosterol (beta form), tinocordiside, magniflorine are the therapeutically active chemical constituents present in Tinospora (Wikipedia).

PLANT PROFILE

Family	**Menispermaceae**
Ayurvedic name	Amrita, Guduchi
Unani name	Giloe
Hindi name	Giloe, Gurcha
Trade name	Giloe
Parts used	Stem, root (whole plant sometimes)

TAXONOMIC CLASSIFICATION

Kingdom	**Plantae**
Subkingdom	Tracheophyta-Vascular plants
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Polypetalae
Series	Thalamiflorae
Order	Ranales
Family	Menispermaceae
Tribe	Tinosporeae
Genus	Tinospora
Species	Cordifolia

MEDICINAL PROPERTIES

T. cordifolia is used in ayurveda as an antiperiodic, antispasmodic, anti-inflammatory, antipyretic, antiarthritic, antipyretic, antiallergic and antidiabetic, antiasthmatic, and anticancer herb (Wikipedia).

Pharmacological activities

Immunomodulatory property

Vaibhav *et al*. reported that studies have found that there was distinct increase in footpad thickness after treatment with *T. cordifolia* alcoholic extract which indicates immunomodulatory effect of *T. cordifolia*, and there was enhancement in the bone marrow cellularity as well as α-esterase activity in the rats groups treated with alcoholic extracts of *T*. *cordifolia* which evidently show that these drugs have immunomodulatory activity. Studies revealed that the alcoholic extracts of *T. cordifolia* obtained from the dried ripe fruits possess good immunomodulatory activity. In order to explore the cellular changes and other pharmacological changes in male wister rat the research is under progress [4].

Chemical constituents responsible for this activity are cordifolioside A, tinocordiside, and syrigin.

Antidiabetic activity

T. cordifolia is an effective antihyperglycemic drug that can be used in the treatment of diabetes mellitus. Several experiments were conducted to prove the antidiabetic activity in TC. Attempts were made to investigate the antidiabetic activity in TC.

Stem extracts both aqueous and alcoholic in different doses (200 and 400 mg/kg b.w.) in streptozotocin-diabetic albino rats. The drug was given orally for 10 days and 30 days in different group of animals and the results were observed. The study clearly showed that TC has significant ($p<0.05$) antidiabetic activity in diabetic animals and has an efficacy of 40–80% compared to insulin. TC administration in diabetic animals did not cause any increase in serum insulin levels or regeneration of pancreatic β-cells but caused increased hepatic glycogen synthase and decreased glycogen phosphorylase activity. It was shown that the antidiabetic activity of TC is not through the insulin secretion by pancreatic beta-cells, but it may be due to the increased entry of glucose into the peripheral tissues and organs like the liver. The study strongly suggested that TC may not act like sulfonylureas, but like other oral antihyperglycemic drugs and indicated that treatment with TC may be an alternative to some of the present available drugs, which have some adverse effects [5].

Chemical constituents responsible for this activity are berberine, choline, tembetarine, palamtine, and jatrorrhizine.

Antitoxic activity

Tinospora scavenges the free radicals produced during aflatoxicosis. Some of the toxins present in *Tinospora* showed aflatoxin-induced nephrotoxicity. Oral administration of plant extracts (stem and leaf) prevented the occurrence of lead nitrate-induced liver damage, this antitoxic activity reported by the Saha *et al*. [6].

Anti-HIV activity

Root extract of *Tinospora* shows anti-HIV effect by indicating reduction in eosinophil count, stimulation in B-lymphocytes, macrophages, hemoglobin levels, and polymorphonuclear leukocytes. [7]. Ethyl acetate extract shows 85% of HIV-1 RT inhibition activity at a concentration of 20 mg/ml [8].

Antimicrobial activity

T. cordifolia shows antibacterial activity mainly its methanolic extract. Ethanolic activity has significant antibacterial activity against *Escherichia coli*, *Proteus vulgaris*, *Enterobacter faecalis*, *Salmonella typhi*, *Staphylococcus aureus*, and *Serratia maracescens* [9]. Chemical constituents responsible for this activity are furanolactone, tinosporon, jateorine, and columbin.

The methanolic extract of this plant was found to have antimicrobial activity against *Bacillus subtilis* (MTCC8), *E. coli* (MTCC1), *S. aureus* (MTCC98), and *S. typhi* (MTCC737) and is sensitive to different microorganisms; thus, this plant could be utilized as a natural source of antimicrobial drugs [10].

Anticancer activity

Dichloromethane extracts of TC show cytotoxic effects due to lipid peroxidation and release of lactate dehydrogenase and decline in glutathione-S-transferase (GST) [11]. Ethanolic extract of TC has been shown to induce apoptosis in breast cancer cells but not necrosis. This extract of *Tinospora* has less cytotoxic effect over non-cancerous cells. *Tinospora* shows activity against breast, colon, lung, skin, prostate, oral, cervical cancer, and lymphoma. Aqueous and ethanol extracts are used for this activity estimation.

Chemical constituents responsible for this activity are magnoflorine, palmatine, tinocordiside, and cordifolioside A.

Antioxidant activity

Stem of TC increases erythrocytes membrane lipid peroxide (LPO) and catalase (CAT) activity and decreases the activity in alloxan-induced rats. Ethanol stem extract has 56% free radical scavenging activity. Stem of TC has the highest phenol content which is responsible for highest 1,1-diphenyl-2-picrylhydrazyl radical scavenging activity [12]. Alpha-glucosidase inhibitor present in the leaf extract of Tinofolia also has both radical scavenging and antioxidant activity. Whole plant or ethanol extract is used to estimate this activity.

Chemical constituents responsible for this activity are (-)epicatechin, tinosporin, isocolumbin, and palmatine.

Antiulcer activity

Antiulcer activity of *Tinospora* was estimated in albino rats using pylorus ligation-induced ulcer. *T. cordifolia* extract has shown significant ($p<0.01$) reduction in gastric volume, total acidity, and ulcer index as compared to control and also significant ($p<0.01$) reduction in ulcer index seen among *T. cordifolia* extract treated rats of aspirin and ethanol-induced models. The antiulcer activity was further confirmed by histopathological examination of rat stomach [13]. Whole plant or ethanol and aqueous extracts are used to identify this activity.

Anticlastogenicity activity

Anticlastogenic potential of the ethanolic extract of *T. cordifolia* stem against arsenic-induced genotoxicity was evaluated in 25 animals which are divided into five groups and each group contains five animals and bone marrow cells were collected in Hank's Balanced Salt Solution and smeared on a slide followed by double staining (Giemsa and Harris hematoxylin). High index of micronucleus frequency was observed in the Groups 2 and 3 in contrast to Group 1 (control) while micronucleus frequency dramatically reduced in 4 and 5 groups. Investigation has shown that the test plant stem extract may have antimutagenic or anticlastogenic property so it is noteworthy in the preventive aspects of chemical carcinogenesis and several types of disorders caused by genetic damages due to arsenic toxicity and *T. cordifolia* may be used as a preventive herbal drug against chemical or arsenic toxicity [14].

Neuroprotective activity

The experiment conducted shows that *T. cordifolia* ethanolic extract on 6-hydroxy dopamine-induced Parkinson's disease by protecting dopaminergic neurons and reducing iron accumulation. Aerial parts or ethanolic extracts are used to estimate this activity.

Antidiarrheal activity

Whole plant and ethanol or aqueous extracts are used for the estimation of antidiarrheal activity. The *in vivo* activity of extracts was assessed using castor oil (induces diarrhea by inducing nitric oxide, stimulating prostaglandin synthesis, and increasing peristalsis) and magnesium sulfate (prevents reabsorption of water and promotes cholecystokinin release from duodenal mucosa) induced diarrhea by means of evaluating onset of diarrhea, frequency if wet and total stools, weight of wet stool, and total weight of stools [15].

Analgesic, anti-inflammatory, and antipyretic activity
Whole plant or ethanol extract is used for analgesic activity. It was assessed by hot plate and abdominal writing method in albino rats [16].

Stem or aqueous extract is used for anti-inflammatory activity. It was exhibited significantly in the carrageenan-induced inflammation test (paw edema model in rats). Chemical constituents responsible for this activity are furanolactone, tinosporin, tinosporide, jateorine, columbin, and clerodane derivatives.

Formulation guduchi ghrita is used to estimate antipyretic activity. Experiment was conducted in albino rats against yeast-induced pyrexia.

Aphrodiasic activity
Aqueous and hydroalcoholic extracts were used to estimate the activity. This activity was studied on male Wistar albino rats. The study gives the mount frequency, mount latency, intromission frequency, intromission latency, anogenital sniffing, and genital grooming [17].

Chemical constituents responsible for this activity are berberine, palmatine, tembatarine, magnoflorine, tinosporin, and isocolumbin.

Antidyslipidemic activity
The part used for estimation is stem extract. Alloxan-induced diabetic male adult rats of Charles Foster strain were used to carry out the experiment. Chemical constituent responsible for this activity is Berberine [18].

Gastroprotective activity
Whole plant is used to estimate this activity. Epoxyclerodane diterpene isolated from *T. cordifolia* Miers (Guduchi) on indomethacin has induced gastric ulcer in rats as *extracellular* domain exerts its antiulcer activity by reinforcement of defensive elements and diminishing the offensive elements. Epoxyclerodane diterpene is the chemical constituent responsible [19].

NOOTROPIC EFFECT

Whole plant or ethanol extract is used to estimate the nootropic effect of *Tinospora*. The nootropic property of n-butanolic fraction (TBF) of the ethanolic extract of *T. cordifolia* stem which contains saponin was evaluated by Amnesic rats using radial arm maze task performance and Barnes maze test. The result showed decreased in AchE concentration which indicates the involvement of cholinergic system in nootropic activity of TBF [20].

Cardioprotective activity
Whole plant or alcoholic extract of the herb is used here. The effect of *Tinospora* was dose dependent; as the dose was increased, the extract showed the increased effect as reflected by progressive decrease in plasma calcium and sodium levels and increase in potassium levels at higher doses when compared to that of verapamil. Hence, *cordifolia* is used for the treatment of atrial and ventricular fibrillation, flutter, and ventricular tachyarrhythmias [21]. Chemical constituents are furanolactone, tinosporin, tinosporide, jateorine, columbin, and clerodane derivatives.

Radioprotective and cytoprotective activity
Stems or ethanolic extracts of *Tinospora cordifolia* are used for the experimentation. The stem extract contains cordiofolioside-A which is a primary active constituent (terpenoid) of TBF of *T. cordifolia* against 4 Gy-γ radiation in mice and **c**yclophosphamide-induced genotoxicity [22].

Root extract of *T. cordifolia* (TCE) used for evaluating the possible radioactive potential against 2.5 Gy gamma radiation in adult Swiss albino mice. Mice were divided into four groups. Each group was administered differently with double distilled water and exposed to 2.5 Gy gamma radiation, and biochemical alterations were noted in the blood of mice at various post-irradiation intervals. Results have shown that there is considerable decrease in the level of total proteins, glutathione (GSH), CAT, and superoxide dismutase activity along with significant increase in cholesterol, lipid peroxidation due to irradiation of mice. There is enhanced activity of various antioxidant enzymes and reduction of the radiation-induced variations in total proteins, cholesterol, and LPO levels in the blood serum in TCE before irradiation. The investigation indicated that *T. cordifolia* root extract reduces the bioeffects of gamma radiation in mammals [23].

Antifeedant activity
Whole plant or chloroform extract of *Tinospora* is used for the estimation of antifeedant activity. *Tinospora* is a potent source of natural antifeedant and activities against selected important agricultural lepidopteran field pest *Spodoptera litura*, *Helicoverpa armigera*, *Earias vittella*, and *Plutella xylostella*. Least antifeedant activity was shown by hexane extract and significant activity by methanolic extract [24]. Chemical constituents responsible for the activity are tincordin, tinosporide, columbin, and 8-hydroxy columbin.

Ameliorative activity
Root or ethanol extract is used for the estimation of activity. *T. cordifolia* was found to show protective effect by lowering down the content of thiobarbituric acid reactive substances and enhancing the reduced GSH, ascorbic acid, protein, and the activities of antioxidant enzymes such as superoxide dismutase, CAT, GSH peroxidase, GST, and glutathione reductase in kidney. Protection against aflatoxin-induced nephrotoxicity is due to the presence of chemical constituents such as a choline, tinosporin, isocolumbin, palmatine, tetrahydropalmatine, and magnoflorine (alkaloids) in Tinospora cordifolia extract [25].

Hepatoprotective activity
Whole plant or aqueous extracts are used for the estimation of the activity while experimentation. Ethanolic extract of all the parts of *Tinospora* showed hepatoprotective effect by reduction in serum enzymes alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and total bilirubin accompanied by pet ether and aqueous extracts.

Some of the alkaloids and terpenoids such as magnoflorin, tinosporin, isocolumbin, palmatine, and tetrahydropalmatine present in the herb are responsible for hepatoprotective activity [26].

Antipsychotic activity
Aqueous and ethanol extracts are used here. Amphetamine challenged mice model has to be used for experimentation. *Tinospora* is an active central nervous system stimulant and helps in various neurological activities. Berberine, choline, tembetarine, magnoflorine, tinosporin, palmetine, isocolumbin, aporphine alkaloids, jatrorrhizine, and tetrahydropalmatine are the alkaloids responsible for the activity [27].

The other pharmacological activities of *T. cordifolia* include antidepressant (Swiss albino mice were used and activity was evaluated using tail suspension test and forced swim test), antisteoporotic (female Sprague-Dawley rats), antifertility (male rats), antiasthmatic (mice were sensitized with intraperitoneal ovalbumin followed by intranasal ovalbumin *in vivo* asthma model), diabetic neuropathy (streptozotocin-induced Wistar albino diabetic rats and *in vitro* aldose reductase inhibition assay and *in vivo* results were analyzed with Mann–Whitney test), and allergic rhinitis (double-blind placebo controlled trial) [1].

NATURAL BINDER

Mucilage was extracted from the fresh stems of *T. cordifolia* which was characterized for physicochemical parameters. Using 2%, 4%, 6%, 8%, and 10% concentration of mucilage of *T. cardifolia* as natural binder, diclofenac sodium tablets (f1-f6) were prepared by dry granulation method. The results show that all the pre- and post-compression parameters of the formulated tabled were in compliance with pharmacopoeial limits and the drug release mechanism from

formulation f1-f6 was found to be polymer disentanglement and erosion. Experimental findings revealed that *T. cordifolia* mucilage can be used as release retardant agent in the formulation of sustained release dosage forms [28].

INTERACTIONS

1. Usage of *Tinospora* along with diabetic medicines may lead to decline in the blood sugar level.
2. Taking *Tinospora* along with drugs that decrease the immune system may decrease the effectiveness of the medication.

CONCLUSION

T. cordifolia is an Indian ayurvedic medicine which is a plant having diverse roles. It has several chemical constituents such as steroids, lactones, terpenoids, alkaloids, flavonoids, and glycosides. It shows different pharmacological activities and better significant activity when compared to that of standard drugs. Based on this information, further research work can be explored, and *T. cordifolia* can be used for the treatment of various diseases and infections. This review is useful to study the *T. cordifolia* activities in a simple manner and it is helpful to further research work planning.

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AUTHORS' CONTRIBUTIONS

All authors had equally contributed to the recitation of the article.

CONFLICTS OF INTEREST

The authors have declared no conflicts of interest.

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