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A COMPREHENSIVE REVIEW ON TINOSPORA CORDIFOLIA

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ABSTRACT

Tinospora cordifolia commonly known as "Gulvel" is known for its vast application in the treatment of various diseases in the traditional ayurvedic literature. The plant also possesses various pharmacological activity including its use as antihyperglycemic, anti-inflammatory, Antiarthmetic and osteoporotic, enhance cognition, antidiarrheal and immunomodulatory effects. Tinospora cordifolia contains phytochemicals constituent such as alkaloids, diterpenoids lactones, glycosides, steroids, sesquiterpenoids, phenolics, aliphatic compounds and polysaccharide. T. cordifolia considered as an important herbal drug of Indian System of Medicinces (ISM). The herb is known for its therapeutic efficacy and used in treatment of dyspepsia, diabetes, fever, urinary problems, jaundice, chronic diarrhea, cardiac disease, dysentery, helmenthiasis, skin diseases, leprosy and many more diseases. Present review highlights the classical antitoxin, anti-diabetic, anticancer, immunomodulatory, antioxidant, antimicrobial, hepatoprotective activity of Guduchi and their validation through existing literature. The plant is reported to contain alkaloids, glycosides, steroids and terpenoids. The current study is under-taken to explore and establish the phytochemistry and pharmacological activity of T. cordifolia.

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INTRODUCTION

Tinospora cordifolia commonly named as "Guduchi" in Sanskrit belonging to family menispermaceae. A variety of active components derived from the plant like alkaloids, steroids, diterpenoids lactones, aliphatic and glycosides has been isolated from the different part of plant body including root, stem and whole plant. [2] Tinsopora cordifolia is an important drug of Indian systems of medicine and used in medicines since times immemorial. The drug is well known Indian bitter and prescribed in fevers, diabetes, dyspepsia, jaundice, urinary problems, skin diseases and chronic diarrhoea and dysentery. It has been also indicated useful in the treatment of heart disease, leprosy, and helmenthiasis. The medicinal properties of Tinospora cordifolia is presently applied in modern medicine and use to overcome the adverse effect of chemotherapy. [9] The starch obtained from the stem is highly nutritive and digestive and used in many diseases. [15] Tinospora cordifolia is a well know medicinalplant in traditional medicinal system and recent scientific studies have emphasized the possible use of Tinospora cordifolia in modern medicine. The present review aims to document the medicinal properties of Tinospora cordifolia and its potential prospects for the further scientific investigation for the development of effective therapeutic compounds [12] In India, medical plants are widely used by all sections of people either directly as folk remedies or in different indigenous medicinal plants and their therapeutic values. [3]

Vernacular Name: [6]

Latin : Tinospora cordifolia (wild) Hook.F. & Thomson

English : Indian Tinospora, Gulancha

Sanskriant : Guduchi, Amrita, Tantrika, Madhuparni.

Hindi : Giloya, Guduchi
Bengali : Gulancha
Telugu : Thippateega
Tamil : Shindilakodi
Marathi : Gulwel
Gujarathi : Galo
Kannada : Amrita balli

Taxonomic Classification: [4]

Kingdom : Plantae-Plants;

Subkingdom : Tracheophyta-Vascular Plants; Super-division : Spermatophyta-seed bearing plants;

Division: Mangnoliopsia-DicotiledonsClass: Magnoliopsia-DicotiledonsSubclass: Polypetalae –Petals are free;

Order : Ranunculales
Family : Menispermaceae
Tribe : Tinosporeaceace
Genus : Tinospora
Species : Cordifolia

Growth Requirement:

Guduchi is growing in a variety of soil. The plant is very rigid and it can be grown in almost all weather but prefers warm weather. Planting is usually done during rainy season (July to August). [4] As it is climber so it requires support for its growth. Fast growing species such as Neem, Jatropha and Moringa have been planted to provide support for growth. Tinospora cordifolia growing with Neem is called as Neem Giloy has chemical composition as similar as neem as well as giloy and show better therapeutic properties. [8]

Distribution:

It grows as a climber on small trees and shurbs, both species are distributed almost throughout the India. [5] The plant is distributed throughout the tropical and subtropical regions of India. It is indigenous to areas of India, Sri Lanka, China, Myanmar, Thailand, Philippines', Indonesia, Malaysia, Vietnam, Bangladesh and South Africa. [4]

Phytochemistry:

T.cordifolia mainly consists of alkaloids, glycosides, steroids, aliphatic compound, and essential oil, mixture of fatty acid, calcium, phosphorous, protein and polysaccharide. [1] The pharmacological activities of these phytochemicals comprise health benefits which help to preventing from diseases and cure the diseases. [10].



Active compounds of T. cordifolia.

Botanical Description:

Different parts exhibits different types of morphology which are described below.

Leaves:

Leaves of this plant are membranous, simple, alternate, with long petiole approximately 15cm which is round, pulvinate, heart shaped, twisted partially and half way round.[4] Powdered leaves and their decoction are reported to treat gout, ulcers, jaundice, fever, and wounds, and to control blood glucose, along with cow's milk.[11]



Fig 1: Leaves on Tinospora Cordifolia.

Stem:

The extract of stems alone and with honey is useful as a tonic in jaundice, skin diseases and fever; stem starch (satva) is used as a tonic. A combination of root and stem is prescribed as an antidote to snake bite and scorpion sting. [11]



Fig 2: Stem of Tinospora cordifolia.

Fruits:

Fruits are fleshy and single seeded which are aggregates of one to three. These are used in the treatment of jaundice and rheumatism. [11]



Fig 3: Fruits of Tinospora Cordifolia.

Bark:

In north Gujarat, root and stem bark of the plant is used along with milk to treat cancer.[11].



Fig 4: Bark of Tinospora cordifolia.

Roots:

Roots are aerial, thread like, long filiform, squairsh, which arise from the mature branches or cut bits of stems grow downward and by continiously lengthening sometimes reach the ground.[4] Roots are used as an emetic for visceral obstructions, leprosy, diarrhea and dysentery. [11] Starch is present throughout the parenchyma of the aerial root. [4]



Fig 5: Root of T. cordifolia.

Flowers:

Flowers are small unisexual which are greenish yellow in color. Sepals are six in two series of three each. Outer ones are smaller than the inner sepals. Petals are also six, smaller than sepals, free and membranous. Flowering is seen during summer. [4].



Fig 6: Flowers of T. cordifolia.

Seeds:

Seeds are white, bean shaped and curved. Embryo also turned into curve shape automatically. Hence, the endocarps have different ornamented with important taxonomic characters.[14].



Fig 7: Seeds of T. cordifolia.

Active Components and Biological Activities of Tinospora cordifolia:

Stem and root part of T. cordifolia contain alkaloids as active constituents. These are tembetarine, choline, magnoflorine, berberine, tinosporin, isocolumbin, palmetine, jatrorrhizine, aporphine alkaloids, tetrahydropalmatine which showed anti-cancer, anti-diabetes, anti-viral, anti-inflammatory, anti-psychiatric and immunomodulatory action. Further, whole plant of T. cordifolia contain furanolactone, diterpenoid Lactones, Cleodrane derivatives, columbin tinosporides, tinosporin, jateorine. They showed biological actions such as Vasorelaxant, anti-inflammatory, anti-microbial, anti-hypertensive and anti-viral. Shoot part of T. cordifolia contains Steroids. They are effective in glucocorticoid induced osteoporosis in early inflammatory arthritis. Stem part of T. cordifolia contain Glycosides. Their active constituents are 18-norcleodrane glucoside, Tinocordifolioside, Cordioside, cordifolioside A, B, C, D and E, Furanoid diterpine glucoside, Syringin, pregnane glycoside Syringing-apiosylglycoside, palmatosides. They showed immunomodulation in Parkinson's disease, dementia, motor and cognitive disorder, neurological disorders like ALS. They inhibit NF-k Band to show anti-cancer properties. Whole plant of T. cordifolia contain aliphatic compounds. The active constituents are Octacosanol, Nanocosan15-one dichloromethane, Heptacosanol. They showed anti- nociceptive and anti-inflammatory activity. They also inhibit TNF-α from binding to the DNA and provide protection against 6-hydroxydopamine induced Parkinsonism in rats. Stem part of T. cordifolia contain Sesquiterpenoids and Tinocordifolin which exhibits an antiseptic activity.[1]

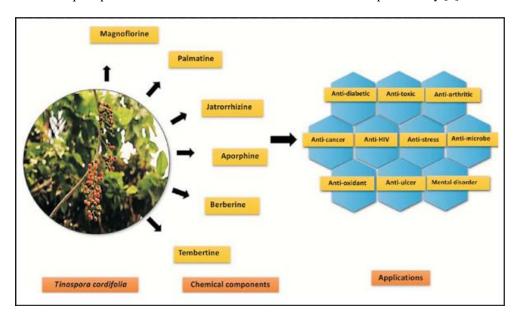


Fig: Phytoactive Constituents and Application of Tinospora cordifolia.

Natural products present in different parts of Tinospora cordifolia and their biological activities. [8].

Active Component	Compound	Plant part	Biological Activity (In Human being)
Alkaloids	Berberine, Choline, Tembetarine, Magnoflorine,	Stem,	Anti-viral infections, Anticancer, anti-diabetes,
	Tinosporin, Palmetine, Isocolumbin, Aporphine	Roots	inflammation, Neurological,
7 .	alkaloids, Jatrorrhizine, Tetrahydropalmatine,	****	immunomodulatory, psychiatric condition
Dieterpenoids	Furanolactone, Clerodane derivatives [(5R,10R)-	Whole	Vasorelaxant: relaxes norepinephrine induced
Lactones	4R-8Rdihydroxy-2S-3R:15,16- diepoxy-cleroda-13	Plant	contractions, inhibits Ca++ influx, anti-
	(16), 14-dieno-17,12S:18,1Sdilactone], Tinosporon,		inflammatory, anti-microbial, antihypertensive,
	Tinosporides, Jateorine, Columbin		anti-viral. Induce apoptosis in leukemia by activating caspase-3 and bax, inhibits bcl-2.
Glycosides	18-norclerodane glucoside, Furanoid diterpene	Stem	reats neurological
Grycosides	glucoside, Tinocordiside, Tinocordifolioside,	Stelli	disorders like ALS,
	Cordioside, Cordifolioside Syringin,		Parkinsons, Dementia,
	Syringinapiosylglycoside, Pregnane glycoside,		motor and cognitive
	Palmatosides, Cordifolioside A, B, C, D and E		deficits and neuron loss in
	rumatosides, cordiforioside 11, B, C, B and E		spine and hypothalamus,
			Immunomodulation,
			Inhibits NF-kBand act as
			nitric oxide scavenger to
			Show anticancer activities.
			Treats neurological disorders like ALS,
			Parkinsons, Dementia, motor and cognitive
			deficits and neuron loss in spine and
			hypothalamus, Immunomodulation, Inhibits NF-
			kBand act as nitric oxide scavenger to show anticancer activities.
Steroids	β–sitosterol, δ-sitosterol, 20 β-hydroxyecdysone,		IgA neuropathy, glucocorticoid induced
	Ecdysterone, Makisterone A, Giloinsterol	Shoots	osteoporosis in early inflammatory arthritis,
			induce cell cycle arrest in G2/M phase and
			apoptosis through c-Myc suppression. Inhibits TNF α , IL-1 β , IL-6 and COX-2.
Sesquiterpenoids	Tinocordifolin	Stem	Antiseptic
Aliphatic	Octacosanol, Heptacosanol Nonacosan-15-one	Whole	Anti-nociceptive and Anti-inflammatory.
compound	dichloromethane	plant	Protection against 6-hydroxydopamine induced
			parkinsonisms in rats. Down regulates VEGF
			and inhibits TFN-alpha from binding to the
			DNA

Medicinal Properties of Tinospora Cordifolia

A myriad of biologically active compounds have been isolated from different parts of the plant body. These compounds have been reported to have different biological roles in disease conditions.

1. Anti-Diabetic Activities:

The stem of this plant is generally used to cure diabetes by regulating level of blood glucose. It has been reported to act as anti-diabetic drug through explanatory oxidative stress, promotinginsulin secretion by inhibiting gluconeogenes is and glycogenolysis. The anti-diabetic properties exhibited by this plant species are attributed due to the presence of alkaloids, tannins, cardiacglycosides, flavonoids, saponins, steroids etc. The crude extract of stem in ethyl acetate, dichloromethane, chloroform and hexane inhibits the enzymes like salivary, amylase and glucosidase resulting increase in post-prandia glucose level and shows potential activities against Diabetes mellitus disease.[8]

2. Immunomodulatory Activities:

The immunomodulatory activity of T. Cordifolia is due to the synergistic effects of compounds including Chemistry and pharmacology of Tinospora cordifolia. T. cordifoliais well known for its immunomodulatory response. This property has been well documented by scientists. A large variety of compounds which are responsible for immunomodulatory and cytotoxic effects are 11-hydroxymuskatone, N-methyle-2 pyrrolidone, N-formylannonain, cordifolioside A, magnoflorine, tinocordioside and syringin.[5] These natural compounds have been reported to improve the phagocytic activity of macrophages, enhancement in nitric acid production by stimulation of splenocyte, and production of reactive oxygen species (ROS) in human neutrophil cells.[8]

3. Anti-toxic Activities:

Aqueous extract of this plant has already been reported to show scavenge activity due to the presence of antioxidant against free radicals generated during aflatoxicosis. Furtheralkaloids such as choline, tinosporine, isocolumbin, palmetine, tetrahydropalmatine andmagnoflorine from T.cordifoliashowed protection against aflatoxin induced nephrotoxicity. However, leaf and stem extract of T. cordifoliahas been reported to show hepatoprotective effect in male albino mice against lead nitrate induced toxicity. Similarly, oral dose of plant extract prohibited the lead nitrate induced liver damage.[8]

4. Anti-HIV Activities:

Root extract of this plant has been shown a decrease in the regular resistance against HIV. This anti HIV effect was exposed by reduction in eosinophil count, stimulation of B lymphocytes, macrophages and level of hemoglobin and polymorphonuclear leucocytes. [8]

5. Anti- Cancer Activities:

T. cordifoliashows anti-cancer activity, this activity is mostly shown in animal models. Root extract of T. cordifoliahas been shown radio protective role due to extensively increase in body weight, tissue weight, tubular diameter. Dichloromethane extracts of TC shows cytotoxic effects owing to lipid peroxidation and release of LDH and decline in GST. In pre-irradiating mice, root extract has widely affected radiation, induced rise in lipid peroxidation and resulted in the decline of GSH in testes. Most of the synthetic chemotherapeutic agents laid toxic side effects on the living organisms. The effect of Giloy has been reported better than doxorubicin treatment. [8]

6. Anti-Microbial Activities:

Methanolic extract of T. cordifolia has been reported against microbial infection. Antibacterial activity of T. cordifolia extract has been bio assayed against Escherichia coli, Staphylococcus aureus, Klebsiella pneumonia, Proteus vulgaris, Salmonella typhi, Shigella Flexner, Salmonella paratyphi, Salmonella typhimurium, Pseudomonas aeruginosa, Enterobacter aeruginosa, Enterobacter aerugene. Further, T. cordifolia extract has been reported against bacterial growth and improved phagocytic and intracellular bacterial capacities of neutrophilsin mice. [8]

7. Activity in SARS-CoV-2 (Covid-19):

A molecular docking and molecular dynamics (MD) stimulation study on the Ayurvedic medicinal plant such as ashwagandha, tulsi, and Guduchi against COVID-19. This study discovered six possible inhibitors against SARSCoV-2 main protease, Tinocordiside, which comes from Guduchi. ADMET profile prediction showed that the phytochemicals from these plants were safe and possessed drug-like properties with no toxicity. Guduchi can inhibit COVID-19 by modifying the chemical structures and employing computational geometry optimization and molecule docking method.[16]

8. Anti-inflammatory Activity:

The anti-inflammatory activity by the invitro method in acute and sub-acute models of inflammation. According to the researcher, Guduchi induced odema arthritis and human arthritis. The dried leaves of Guduchi produced an anti-inflammatory effect that was more effective and useful than acetylsalicylic acid and effective in joint inflammation. Guduchi shows a significant anti-inflammatory effect in both acute and sub-acute models of inflammation. [16]

9. Anti- tuberculosis:

The ether extract of the stem distillate of the aerial part of Guduchi had inhibited the invitro growth of Mycobacterium tuberculosis. Its ethanolic extract has exhibited significant antipyretic activity in experimental rats. 'Septilin' syrup, a compound preparation containing Guduchi (7.82% in 5 ml of syrup) has been found to elicit a good clinical response in children suffering from upper respiratory tract infection and chronic otitis media. [16]

10. Wound Healing:

The alcoholic extract of Guduchi effect on dexamethasone suppressed healing. Excision, Incision, and dead space of the wound models were employed to investigate the wound healing potential of the plant; increased tensile strength extract of Guduchi may be attributed to the promotion of collagen synthesis. This extract did not reverse dexamethasone suppressed wound healing. [16]

11. Anti-malaria Activity:

The hyper-reactive malarious splenomegaly (HMS) is thought to be the result of immunological dysfunction due to recurrent episodes of malaria. HMS is treated by chloroquine (CQ)/pyrimethamine prophylaxis/ proguanil by invivo and in-vitro models. The aqueous extract of Guduchi and chloroquine in treating three cases of hyper-reactive malarious splenomegaly (HMS) was studied. The plant extract (500 mg/kg b.w.) added to chloroquine (CQ) base (300 mg/kg b.w.) was administered weekly, and the results showed regression of spleen by 37-50% after six weeks and 45- 69% after six months. Likewise Decrease in IgM and an increase in Hb were observed. Their finding required a large-scale trial to confirm the beneficial effect of Guduchi extract in combination with chloroquine. [16]

12.Anti-allergic activity:

In a clinical study, 100% relief was reported from sneezing in 83% of the patients on treatment with T. cordifolia. Thus Tinospora cordifolia significantly decreased all symptoms of allergic rhinitis and was well tolerated. [13]

13. Hypoglycemic activity:

Oral administration of the water extract of Tinospora cordifolia root caused a significant reduction in blood glucose, brain lipid level, hepatic glucose-6-phosphatase, serum acid phosphatase, alkaline and lactate dehydrogenase and increase in body weight, total haemoglobin and hepatic hexokinase in alloxanized diabetic rats.[13]

14. Cardioprotective activity:

A dose-dependent reduction in infarct size and in serum and heart lipid peroxide levels was observed with prior treatment with Tinospora cordifolia in ischemia-reperfusion-induced myocardial infarction in rats. [13]

15. Hepatoprotective:

The hepatoprotective action of T. cordifolia was reported in one of the experiment in which goats treated with Tinospora cordifolia have shown significant clinical and hemato-biochemical improvement in CCl4 induced hepatopathy. Extract of T. cordifolia has also exhibited in vitro inactivating property against Hepatitis B and E surface antigen in 48-72 Hours. [13]

16.Anti-ulcer activity:

Treatment with a formulation containing Tinospora cordifolia has been shown to reduce ulcer index total acidity, with an increase in the pH of gastric fluid in pylorus-ligated rats and in the ethanol-induced gastric mucosal injury in rats. [13]

17. Anti leprotic activity:

Tinospora cordifolia is used for its anti-leprotic properties, along with wide use of various types of skin disorders and has been shown to exert anti-leprotic activity in a combination formulation. [13]

18. Diuretic Activity:

In a scientific study on rats and human volunteers, Tinospora cordifolia was found to have diuretic effects. It was also found effective in modulation of morphology and some gluconeogenic enzymes activity in diabetic rat kidney. [13]

19. Antibacterial Activity:

Aqueous ethanol and chloroform extracts of T. cordifolia were evaluated for their antimicrobial activity against some gram-positive and gram-negative bacteria. [13]

Marketed products of T. cordifolia and their Biological role

Name of Marketed product	Biological Roles		
Tinospora Cordifolia Pellets [8]	A number of diseases		
Giloy Juice	Fever, Rheumatism, Gout, Jaundice, Anemia, Urinary disorder, Immunodeficiency		
Giloy Powder	It can Boost Immunity,		
	It can improve Metabolism,		
	It may regulate blood glucose level		
Tulsi Cinnamon Giloy	Stress Relieving & Immunity Enhancing		
Guduchi Ayurveda Anti-smoking Herbal tea	Helps Suppress Smoking Craving,		
	Helps Quit Smoking Habit		
Carifit	Platelet Booster,		
	Immuno-modulator,		
	Dengue fever,		
	Acute Microbial Infection		
Cirrholiv-ds syrup[8]	Hepatoprotective		
Mussaffen[8]	Blood purifier and anti-allergic		
MadhuMehari[8]	Cure by urinary problems, maintain blood sugar, fatigue		
Tonplex[8]	Increase immunity		
Rebuild[8]	Anti-stress and anti-oxidant		



1. Tinospora Cordifolia Pellets.



2. Giloy Juice.



3. Giloy Powder.



4. Anti- smoking Tea.

Future Prospects:

Tinospora cordifolia is one of the most versatile rejuvenating herbs, it promotes longevity hence called Vayastha. It is extremely useful in strengthening the immunity of body and keeping the functions of various organs of the body in harmony. It is one of the important medicinal plants used in veterinary folk medicine/Ayurvedic system of medicine for the treatment of diverse diseases and recommended for improving the immune system by means of body resistance. Its therapeutic strength lies in its rejuvenating and strengthening properties while also detoxifying and cleansing the whole system, specifically via liver. It has always attained significant medical importance, since the time of ancient samhitas to the present day, which in a way itself substantiates its therapeutic utility. Extensive research efforts have been directed to study different aspects of T. cordifolia ranging from experimental to clinical studies and from phytochemistry to bio efficacy for most of its properties with encouraging results. However, further research is required on this species to develop the conservation strategies and improvement programmes with the utilization of modern biotechnological tools. [17]Substantial work has been done on the isolation and purification of active components of T.cordifolia which are mainly responsible for the treatment of various diseases along with their validation. Being a therapeutic agent, it provides immense health beneficial properties to the consumers. However, the crude form of this medicinal plant is unpleasant and bitter in taste, therefore, further research domain should mainly focus on the Tinospora cordifolia incorporated product and its diversification.[18] During past 2-3 decades, some molecular markers have been utilized to characterize the germplasm of T.cordifolia however, concerted efforts need to be directed to assess the genetic diversity available in this plant and select markers linked to desirable traits, so that elite lines can be conserved. In addition, genetic analysis may also be used as a powerful tool for the authentication of the botanical identity of the herbal materials. [17]

CONCLUSION

The present review focuses on the botanical description and medicinal importance of the Tinospora Cordifolia. The different bioactive compounds including alkaloids, steroids, glycosides, Sesquiterpenoids etc. found to have potential application in many diseases. The various studies that have been conducted on T. cordifolia reveals that it is an excellent drug and does not have any adverse or toxic effects till now. This review gives information about the classical Anti-diabetic, Immunomodulatory, Anti-toxic, Anti- HIV, Anti-cancer, Anti-microbial, SARS-CoV-2(Covid-19), Anti-inflammatory, Anti-tuberculosis, Wound Healing, Anti-malaria, Anti-allergic, Hypoglycemic, Cardioprotective, Hepatoprotective, Anti-ulcer, Anti-leprotic and Diuretic activity of T. cordifolia and can be used for further research investigations in development of novel drug.

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