

# Tinospora Cordifolia: A Comprehensive Review of its Botanical, Phytochemical, and Therapeutic Profile

Miss. Kalyani Arun Tambe, Miss. Nivedita Navnath Dhokane, Dr. Jyoti Wagh,  
Mr .Kunal Sanjay Rewale, Mr .Mangesh Yuvraj Pawar  
MES's College of Pharmacy, Sonai, India

**Abstract:** *Tinospora cordifolia* is a deciduous climbing shrub described as „the one who protects the body against diseases” belonging to family Menispermaceae known as Amrita (Guduchi). Guduchi (*Tinospora cordifolia*) is commonly known as rasayana plant and its rejuvenating property is well reported in Ayurvedic and other ancient literature. It is a fairly common plant of the dry deciduous forests growing over hedges and small trees. Various parts of the plant are being prescribed in Ayurveda and other systems of medicine as a monoherbal or polyherbal preparation. In India, various extracts of the plant are used as a remedy for many diseases and are included in various polyherbal preparations used for the treatment of diabetes, hepatitis, etc. Since each part of guduchi has some medicinal property, it is very much commercially exploitable. During the last few decades considerable progress has been achieved regarding its biological activity and medicinal applications. Hence, it can be chosen as a source for the development of industrial products for treatment of various diseases. We have put an effort to compile available literature on research work done for this plant mainly on its therapeutic utility till recent, from the early beginning. This review gives a bird view of the main biological activities, pharmacological actions and medicinal applications of guduchi extracts and also biological activities of few guduchi compounds isolated.[1].

**Keywords:** *Tinospora cordifolia*, Menispermaceae, Chemical constituents, Pharmacological activity

## I. INTRODUCTION

The genus *Tinospora* (Menispermaceae) possesses about 32 species of climbing shrubs that are distributed throughout tropical Africa, Madagascar, Australia and the Pacific Islands . Of these species, the most medicinally and commercially important is *T. cordifolia* (Willd.) Miers ex Hook. f. & Thoms. commonly known as Guduchi or Amrita, which is distributed throughout the Indian subcontinent and some The parts of China . The estimated annual consumption of *T. cordifolia* in the Indian System of Medicines is approximately 1,000 tonnes . *T. cordifolia* is categorized as ‘Rasayana’ in Ayurveda and is used as a tonic and vitalizer, and to treat diabetes, skin, heart diseases, jaundice, rheumatoid arthritis, allergies, leprosy, urinary disorders and dysenter. The whole plant is reported to possess hepatoprotective, antiulcer and antioxidant properties, whereas the stems showed hepatoprotective, antipyretic, cytotoxic, antidiabetic and immunomodulatory activity. Dried fruits are used to treat jaundice and rheumatism, whereas the leaves are used to treat diabetes , and the roots are employed for their powerful emetic, antistress, antioxidant, antiulcer, and hypoglycemic properties, as well as for the treatment of visceral obstructions. *T. cordifolia* is a rich source of alkaloids, furano diterpenoids, clerodane norditerpenoids, sesquiterpenoids, phenolics, lignans, sterols, aliphatic compounds, polysaccharides, essential oil and fatty acids. The alkaloids (e.g. berberine), bitter compounds (tinosporin, tinosporic acid and tinosporol) and lipids have been found to exhibit medicinal effects. In its pharmacological actions, *T. cordifolia* targets body organs, mainly kidney, liver and spleen. The reviews on *T. cordifolia* have been mostly in open access or non-SCI journals and dealt with different aspects like Ayurvedic preparation, botanical aspects with



morphology, growth constrains, genetic diversity and biological activity of crude extracts. In the present review, the pharmacological activities and mechanism of actions of the phytochemicals are used as a referral point after the review by Panchabhai et al. in 2008 on the therapeutic evidence of different extracts of *T. cordifolia*. [2]

### **HISTORY AND AYURVEDIC ASPECTS**

Ayurveda a 5,000-year-old system of medicine, names three elemental substance such as Kapha, Vata and Pitta rooted in Indian scriptures known as The Vedas. As per Ayurvedic text viz: Ashtang Hridaya and Sushrut, Charak and other treaties like Bhava Prakash and Dhanvantri Nighantu *T. cordifolia* named as : Amara, Amritvalli, Chinmarruha, Chinnodebha and Vatsadani etc, and most commonly recognised as Guduchi or Amrita. 11-15 In Sushurta Samhita, under Tikta-SakaVarga, it is traditionally claimed for the treatment of several diseases like Svasa (asthma), Maha Jvara (fever), Aruci (anorexia) and kustha (leprosy). 14 In context of Ashtang Hridaya and Charak Samhita, there is also a great evidence for the treatment of different diseases like Jvara (fever), Vat Rakta (gout) and Kamala (jaundice). 13,15 In Bhavya Prakash, it is considered as diuretic, astringent, bitter tonic and potential curative and aphrodisiac against jaundice, diabetes, chronic diarrhea, dysentery and skin infections. 16 In Dhanvantri Nighantu, it has been depicted for treatment of bleeding piles, curing itching, erysipelas and promoting longevity. 17 Additionally, guduchi has been shown as: Deepanam (kindles digestive fire), Laghu (light), Dhatukrit (builds the seven bodily t issues), Chakshushyam (good for the eyes), Bayasthaapankarakam (maintains youthfulness and longevity) and Medhayam (rejuvenating for the mind). Guduchi has been considered by European practitioners in India as a major source of medicament like tonic, diuretic and antiperiodic and further it was comprised in Bengal Pharmacopoeia of 1868. 19 According to Ayurvedic literature *T. cordifolia* is a major constituent of formulations used for the treatment of several disease such as dyspepsia, urinary related diseases debility and fever. Some of the imperative formulations prepared from *T. cordifolia* are: Guduchi taila, Sanjivani vati, Kanta-Kariavaleha, Guduchyadi churna, Chyavnaprasha, Guduchu ghrita, Guduchi satva, Brihat guduchi taila, Amrita guggulu, amritashtaka churna and many more. *T. cordifolia* is the mostly used herbs of Ayurvedic medicine that, has been widely used by folks and tribal as a remedial herb for the treatment of various diseases. *T. cordifolia* is highly valuable in Ayurveda for its numerous medicinal properties like rejuvenating, immune-boosting, anti-rheumatic and detoxifying properties. Medicinal properties of *T. cordifolia* is presently applied in modern medicine for treatment of cold and flu prevention, skin disorders, liver disorders, immune support, gout, arthritis and lately to overcome the adverse effects of chemotherapy. 18 So, now it is clear that *T. cordifolia* is most important medicinal herb considered by the ancient rishis in Vedic times with a great potential (medicinal qualities) of curing number of diseases. [3]

#### **Distribution:**

It is indigenous to areas of India, Myanmar, Sri Lanka, China, Thailand, Philippines, Indonesia, Malaysia, Borneo, Vietnam, Bangladesh, North Africa, West Africa, and South Africa 7-10. It typically grows in deciduous and dry forests at elevations up to 1000ft.

#### **o Origin and Habitat:**

*T. cordifolia* is a climbing shrub native to lower elevation in tropical areas of the Indian subcontinent and climbs numerous types of trees 11. It prefers wide range of soil, acid to alkaline and it needs moderate level of soil moisture.

#### **o The Family:**

*T. cordifolia* belongs to the family Menispermaceae which consists of about 70 genera and 450 species that are found in tropical lowland regions. They are generally climbing or twining, rarely shrubs. This family is a rich source of alkaloid and terpenes.

#### **o The Genus:**

The genus *Tinospora* Miers (Menispermaceae) has about 32 species distributed in tropical Africa, Madagascar, Asia to Australia and the Pacific Islands . In India, the genus is represented by four species; two species, *T. cordifolia* (Thunb.)



Miers and *T. sinensis* (Lour.) Merr., are known to occur in South India and other two *T. crispa* (L.) Hook. f. & Thomson and *T. glabra* (Burm.f.) Merr., are reported from Northeast India and the Andaman Islands.

**o The Species:**

*Tinospora cordifolia* (Thunb.) Miers

**o Synonyms:**

1. *Menispermum crispum* Linnaeus,
2. *Tinospora gibbericaulis* Handel-Mazzetti
3. *Tinospora mastersii* Diels
4. *Tinospora rumphii* Boerlage
5. *Tinospora thorelii* Gagnepain.

**o Vernacular Names:**

The common names are Gilo (Arabic); Amarlata (Assamese); Gadancha, Guluncha, Giloe (Bengali); K'uan chu Hsing (Chinese); Culancha (French); *Tinospora* (English); Gado, Galo, Gulo (Gujerati); Giloe, Gulbel, Gurcha (Hindi); Amrytu, Sittamrytu (Malayalam); Ambarvel, Giroli, Gulvel (Marathi), Garjo (Nepali); Gulancha (Oriya); Gulbel (Persian); Gilo (Punjabi, Kashmiri), Amrita, Guduchi, (Sanskrit); Gurjo (Sikkim); Amridavalli, Niraidarudian (Tamil); Guduchi, Iruluchi (Telugu) and Guruch (Urdu).

Kingdom: Plantae Subkingdom: Tracheobionta Division: Magnoliophyta Class: Magnoliopsida

Order: Ranales

Family: Menispermaceae Genus: *Tinospora* Species: *Cordifolia*

**o Botanical Description:**

*T. cordifolia* is a large extensively spreading glabrous, dioecious perennial deciduous climber, grows on wide range of hedges and trees. It is reported to bear distinct male and female flowers 21-23. Its stem, when fresh, have a green succulent bark covered by a thin brown bark and are studded with warty lenticels when dry, the stem shrinks and the bark separate from the wood. Branches are sending down slender pendulous fleshy roots, terete, striate, with tubercled, pale sometimes shining or glabrous bark.

Leaves membranous, 7-9 nerved, 5-10 cm, roundish, cordate or heart shaped (giving name *cordifolia* to the plant) with a 2.5- 7.0 cm petiole. The flower bloom in summer. Racemes is rather lax, 5.0 cm, elongating and often longer than leaves. The male flowers are small, yellow or green in colour, and occur in clusters in the axils of small subulate bracts. Sepals are 6, 3 outer very small, ovate-oblong, acute, the inner 3 larger, membranous, broadly elliptical, concave, yellow. Petals are 6, equal, broadly spatulate, each loosely embracing a stamen, claw cuneate, reflexed to apex, pistillode. Female flowers usually solitary, similar to male, but sepals green, margins not reflexed, staminode short, linear. Carpels 1-3, widely separated on the short fleshy gynophores, dorsally convexed, and scarlet. The fruit are the size and shape of a large pea and turn from green to red when ripe in winter and mucilaginous.[4]

Traditional uses of different parts of *T. cordifolia*:

*T. cordifolia* has been used as a constituent of several folk and Ayurvedic preparations in the form of juice, decoction, paste, powder and pill to treat general debility, fever, skin diseases, chronic diarrhea, jaundice, asthma and bone fracture, which were described in ancient texts like Rasayana, Sangrahi, Balya, Agnideepana, Tridoshamaka, Dahnashaka, Mehnashaka, Kasa-swasahara, Pandunashaka, Kamla-Kushta-Vataraktanashaka, Jwarhara, Krimihara, Prameha, Arshnashaka, and Kricch-Hridroga nashak. *T. cordifolia* as a blood purifier removes defective and damaged red blood cells from peripheral blood circulation by stimulating liver and spleen. The stem of *T. cordifolia* is approved by the Ayurvedic Pharmacopoeia of India as a medicine because of its high alkaloidal content. The starch from *T. cordifolia* (*Guduchi satva*) climbing on *Azadirachta indica* is very bitter, with more medicinal efficacy

o Leaves: 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.

o 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.



- o Bark: In North Gujrat (India), root and stem bark of the plant is used along with milk to treat cancer.
- o Fruits: These are used in the treatment of jaundice and rheumatism.
- o Roots: Roots are used as an emetic for visceral obstructions, leprosy, diarrhea and dysentery.



FIG: Morphology of different parts of *T. cordifolia* A. Stem, B. Leaf, C. Fruit, D. Inflorescence, E. Flower, F. Aerial Roots

#### Chemical constituents:

**Alkaloids:** Thirteen alkaloids of isoquinoline and aporphine skeletons, amine and amide were reported of which main alkaloids were protoberberine alkaloids berberine, palmatine, jatrorrhizine, magnoflorine and corydine .

**Terpenoids:** Thirty two diterpenoids and their glycosides of clerodane and norclerodane skeleton one monoterpenoids five sesquiterpenoids and one triterpenoid cyclo euphordenol were isolated from *T. cordifolia*. A bicyclic diterpenoid (C<sub>21</sub>H<sub>24</sub>O<sub>7</sub>) from the whole plant was tentatively identified as tinosporin .

**Phenolics:** Four phenyl propanoids , two flavonoids , three lignans and two benzenoid derivatives have been isolated from *T. cordifolia*.

**Steroids:** Four steroids along with  $\delta$ -sitosterol and 2,3,14,20,22,25-hexahydroxyl-5-cholest-7-en-6-one have reported .  
**Essential oil and aliphatic compounds:** The GC-MS profile of the hydrodistilled essential oil of fresh leaves showed the presence of alcohols (32.1%), phenols (16.6%), aldehydes (16.2%), fatty acids (15.7%), alkanes (8.3%), esters (3.2%), and terpenes (1.2%), along with

hydroquinone (16.6%), 2-hexenal (14.2%), palmitic acid (14.1%) and phytol (11.4%)[108]. GC-MS analysis of the hexane extract of stems identified methyl-9,12-octadecadienoate (23.2%), methyl 9-octadecenoate (19.7%), methyl hexadecanoate (16.3%) and methyl octadecanoate (5.5%) . Heptacosanol, octacosanol, nonacosan-15-one and cyclohexyl-11-heneicosanone identified from the stems and whole plant.

**Polysaccharide:** The polysaccharide of the stems of *T. cordifolia* was shown to be composed of glucose 98.0%, arabinose 0.5%, rhamnose 0.2%, xylose 0.8%, mannose 0.2% and galactose 0.3% units .

**Others:** Several compounds reported from *T. cordifolia* had no detailed chemical and biological study. Some of these are giloinsterol, a bitter glucoside giloin, a non-glucoside bitter substance giloinin, gilo-sterol, tinosporan acetate, tinosporic acid, tinosporal acetate, tinosporone and tinosporal .Tinosporidine, cordifolone, tinosporon, tinosporic acid



and tinosporol were isolated from different parts of *T. cordifolia*. Two bitter compounds, tinosporide and cordifolide, were isolated from the fresh stems of *T. cordifolia*. Three furanolactone diterpenoids, C<sub>20</sub>H<sub>20</sub>O<sub>6</sub>, C<sub>20</sub>H<sub>22</sub>O<sub>8</sub> and C<sub>26</sub>H<sub>34</sub>O<sub>11</sub>, were also reported from the stems, but with only physical properties listed. The structures of the compounds isolated from *T. cordifolia* are presented in Figure 1. The leaves of *T. cordifolia* are rich in protein (11.2%), calcium and phosphorus, and the stems contain an appreciable quantity of zinc.[2]

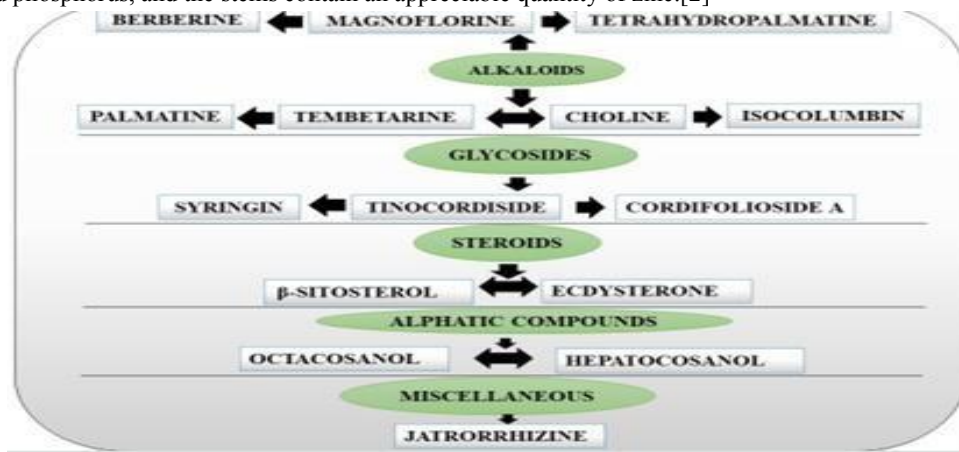


Fig: Phytoactive Constituents of *T. cordifolia*

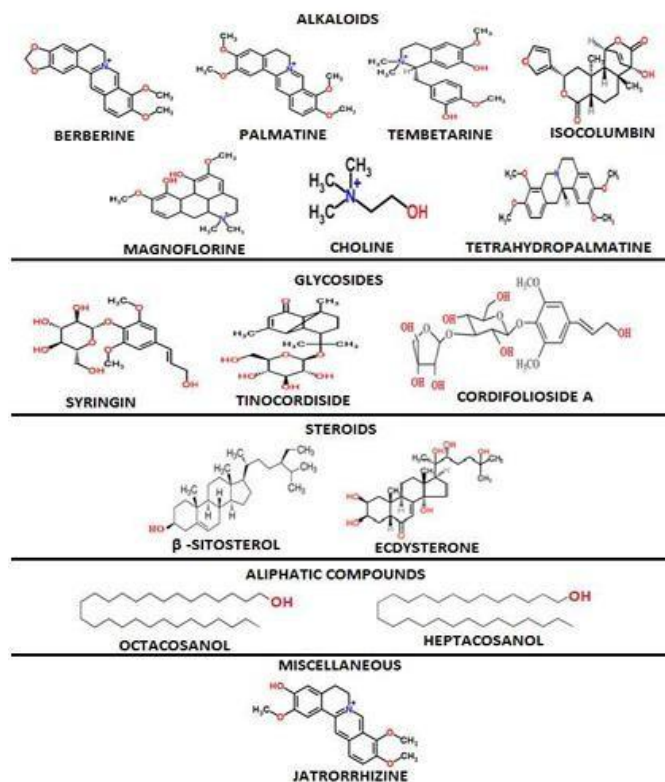


Fig.: Some phytoactive compounds from *Tinospora cordifolia* [5]



### **PHARMACOLOGICAL ASPECTS [TherapeuticActivitie]:**

The major biological activities of *Tinospora cordifolia* summarized in the following manner

#### **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, promoting insulin secretion by inhibiting gluconeogenesis and glycogenolysis. The anti-diabetic properties exhibited by this plant species are attributed due to the presence of alkaloids (Magnoflorine, Palmetine, Jatrorrhizine), tannins, cardiac glycosides, 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-prandial cose level and shows potential activities against Diabetes mellitus disease. The root extract of this plant has also been reported to have anti-diabetic properties which decrease the level of glycosylated haemoglobin, hydroperoxidase and vitamin E [9].

#### **Immunomodulatory Activities:**

*T. cordifolia* is 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 [46]. 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.

#### **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. Further alkaloids such as choline, tinosporine, isocolumbin, palmetine, tetrahydropalmitine and magnoflorine from *T. cordifolia* showed protection against aflatoxin induced nephrotoxicity. Furthermore *T. cordifolia* shows protective effect by lowering the concentration of thiobarbituric acid reactive substance (TBARS) and enhancing the glutathione (GSH), ascorbic acid, protein and the activities of antioxidant enzymes viz., superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase, glutathione S-transferase (GST) and glutathione reductase (GR) in kidney. However, leaf and stem extract of *T. cordifolia* has 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 [49-50] [10-11]

#### **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, level of hemoglobin and polymorphonuclear leucocytes [51-52]. [12-13]

#### **Anti-Cancer Activities:**

*T. cordifolia* shows anti-cancer activity, this activity is mostly shown in animal models. Root extract of *T. cordifolia* has 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 [54]. [14]



**Anti-Microbial Activities:**

Methanolic extract of *T. cordifolia* has been reported against microbial infection. Anti bacterial activity of *T. cordifolia* extract has been bio assayed against *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Proteus vulgaris*, *Salmonella typhi*, *Shigella flexneri*, *Salmonella paratyphi*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Enterobacter aeruginosa*, *Enterobacter aerogene*. Further, *T. cordifolia* extract has been reported against bacterial growth and improved phagocytic and intracellular bacterial capacities of neutrophils in mice [58] [15].

**Anti-Oxidant Activities:**

Methanolic extract of stem of *T. cordifolia* has been reported to anti-oxidant activity, by increasing the erythrocytes membrane lipid peroxide and catalase activity. It also decreases the activity of SOD, GPx in alloxan induced diabetic rats. Extract of *T. cordifolia* has been reported its free radical scavenging properties. Leaf extract of *T. cordifolia* reported to have an alpha-glucosidase inhibitor, characterized as saponarin was found to be also significant anti oxidant and hydroxyl radical scavenging activity. Due to the presence of alkaloids it shows protection against aflatoxin-induced nephrotoxicity. *T. cordifolia* aqueous extract has a radio protective activity, enhancing the survival of mice against a sub-lethal dose of gamma radiation [6]

**Anti-arthritic, anti-osteoporotic effects:**

Single or synergistic formulations of *Tinospora cordifolia* with *Zingiber officinale* has been used in rheumatoid arthritis treatment in traditional medicine *Tinospora cordifolia* have been reported to affect the proliferation, differentiation and mineralization of bone like matrix on osteoblast model systems in vitro and hence finds potential application as an anti-osteoporotic agent. Alcoholic extract of *Tinospora cordifolia* have been shown to stimulate the growth of osteoblasts, increasing the differentiation of cells into osteoblastic lineage and also increasing the mineralization of bone like matrix. Ecdysteroids isolated from the plant have been reported of protein anabolic and anti-osteoporotic effects in mammals. Beta-Ecdysone (Ecd) from *Tinospora cordifolia* extracts have been reported to induce a significant increase in the thickness of joint cartilage, induce the osteogenic differentiation in mouse mesenchymal stem cells and to relieve osteoporosis in osteoporotic animal models. Further 20-OH- $\beta$ -Ecd isolated from *Tinospora cordifolia* has been reported of its anti-osteoporotic effects thus highlighting the role of *Tinospora cordifolia* in the treatment of osteoporosis and osteoarthritis.[64]

**Anti-arthritic activity**

The polyphenols present in *Tinospora cordifolia* extract(TCE) were identified through HPLC analysis. TCE significantly reduced the levels of pro-inflammatory mediators (IL-6, TNF  $\alpha$ , PGE2, and NO) in LPS-stimulated RAW 264.7 cells. Additionally, the elevated expression of COX-2 and iNOS that occurred after LPS stimulation was also diminished by TCE. Moreover, TCE affected the upstream kinases of the JAK/STAT pathway, which is a vital inflammatory pathway. The expression of VEGF, an important angiogenic factor and inflammatory mediator, was also lowered after pre-treatment with TCE. The anti-arthritic properties of TCE (150 mg/kg) were assessed in the CIA model as well. Histopathological results indicated that oral administration of TCE effectively alleviated clinical symptoms of arthritis, including paw edema, erythema, and hyperplasia. In vivo findings corroborated the in vitro results, showing a significant decrease in serum levels of pro inflammatory cytokines and mediators (IL-6, TNF  $\alpha$ , IL-17, NO, and PGE2). Furthermore, the phosphorylation of STAT3 and the expression of VEGF were also reduced following TCE treatment[54].

**Anti –allergic activity**

The anti-allergic properties of an aqueous extract of the stem of *Tinospora Cordifolia* was evaluated on histamine induced bronchospasm in guineapigs, capillary permeability in mice and mast cell disruption in rats. The aqueous extract of *Tinospora cordifolia* demonstrated an average protection rate of 95fl.09 against 5% histamine aerosol-



induced broncho-constriction in guinea pigs. This result was comparable to the average protection rate of 78.46 provided by pheniramine maleate, the standard antihistamine medication. Additionally, *Tinospora cordifolia* exhibited a notable protective effect on mast cells in rats. It resulted in a 22.8%±2.23 disruption of mast cells, in contrast to 85.5%±8.17 observed in the control group. Finally, the aqueous extract significantly reduced capillary permeability in mice. The extract significantly decreased the bronchospasm induced by 5% histamine aerosol, decreased capillary permeability and reduced the number of disrupted mast cells in the above experimental animals respectively. *Tinospora cordifolia* significantly reduced all allergic rhinitis symptoms while also being well-tolerated. The anti-allergic and bronchodilator properties of an aqueous extract of the stem were tested on histamine-induced.

#### **Anti-inflammatory activity**

The anti-inflammatory properties of an aqueous extract of the stem of *Tinospora Cordifolia* was evaluated on Carrageen an induced paw edema rats. Animals were divided in three groups, having six animals in each. Group A received test drug, Group B received market sample at a dose of 50 mg/kg orally, while Group C (control group) received tap water. Reduction in edema was observed in Group A and B at 3 h interval by 33.06% and 11.71% respectively. Group A showed significant effects ( $P < 0.05$ ) in comparison to control group. These experimental results have shown anti-inflammatory activity of Guduchi Ghana<sup>56</sup>. The anti-inflammatory activity of *Tinospora cordifolia* is due to the presence of flavanoids, alkaloids and phenols which decrease the production of inflammatory mediators like IL 6, Cox, and bradykinins<sup>[8]</sup>.

#### **Hepato-protective activity**

*Tinospora Cordifolia* extract also deleted the immunosuppressive effect of CCl<sub>4</sub>, since a significant increment in the functional capacities of rat peritoneal macrophages (PM phi) was observed following *Tinospora Cordifolia* treatment<sup>58</sup>. *Tinospora Cordifolia* extract is a potent hepato protective agent. It is assumed that this hepato protective effect of *Tinospora Cordifolia* may be due to several reasons such as antioxidant and/or free radical scavenger property and ability to induce hepatic regeneration.

#### **Anti-fungal activity**

Methanolic leaves and stem extracts of *Tinospora cordifolia* has higher antifungal activity in comparison to ethanolic leaves and stem extracts against test fungal species in the form of inhibition zone<sup>60</sup>. Leaves of *T.cordifolia* are rich in protein and fairly rich in Ca and P. Anti-fungal chemical constituents such as giloin, columbin, chasmanthin, palmatin, isocolumbin, tembetarine, cordioside, palmatin, tinosporin, tinosporic acid have been isolated from different parts of *Tinosporacordifolia*<sup>61</sup>.

#### **Neuro protective activity**

*Tinospora cordifolia* extract in STZ induced neurotoxicity and evaluating mechanisms responsible for attenuating neuropathic pain. Leaf extract significantly relieved thermal hyperalgesia and allodynia by increasing the antioxidant enzyme levels, decreasing the lipid peroxidation and by increasing the Nerve growth factor (NGF) expression in diabetic rat sciatic nerves<sup>62</sup>. *Tinospora cordifolia* ethanol extract (TCEE) exhibited significant neuroprotection by increasing the dopamine levels ( $1.96 \pm 0.20$  and  $2.45 \pm 0.40$  ng/mg of protein) and complex I activity ( $77.14 \pm 0.89$  and  $78.50 \pm 0.96$  nmol/min/mg of protein) at 200 and 400 mg/kg respectively when compared with negative control group. Iron asymmetry ratio was also significantly attenuated by TCEE at 200 ( $1.57 \pm 0.18$ ) and 400 mg/kg ( $1.11 \pm 0.15$ ) when compared with negative control group. Neuroprotection by TCEE was further supported by reduced oxidative stress and restored locomotor activity in treatment groups. The increased levels of dopamine by the treatment of TCEE might be due to decreased metabolism of dopamine or due to increased biosynthesis of dopamine by the dopaminergic neurons present in SN. The increased dopamine levels by TCEE is further supported by the anti-stress and anti-depression activity of *Tinospora cordifolia* root extract in which dopamine levels were normalized after treatment<sup>63</sup>.



### Anti-stress activity

The serum glucose, lipid like triglyceride, cholesterol, cholesterol parameters like anxiety, and psychological depression were significantly increases in patients with chronic mental stress. However following treatment with *Tinospora cordifolia* associated with practice of yoga significantly reduced various stress induced psychological and biochemical parameters ( $P < 0.001$ )<sup>64</sup>. In Ayurveda *Tinospora cordifolia* (Willd.) Miers, has been used for its Rasayana, Deepana, Jwaranashana, TridoshaSha maka properties. It is an immunomodulator, useful in stress. It is found to be safe on hematological and biochemical organ function tests and has muscle strengthening, lipid lowering action in healthy individuals. It has been shown that the immune system can function as a neuroendocrine organ since it can synthesize not only hormones and neuropeptides but also cytokines that have an impact on the neuroendocrine system. *Tinospora cordifolia* improved physical performance and suppressed over activation of the sympathetic nervous system showing its adaptogenic property [7]

### ACTIVE COMPOUNDS AND THERAPEUTIC ACTIVITY OF *Tinospora cordifolia*[7]

CLASS	CHEMICAL CONSTITUENTS	USES	PLANT PARTS
Alkaloids	Berberine, CholinePalmatin, Tinosporine, Magnoflorine, Tembetarine, and Isocolumbin, Aporphine alkaloids, Jatrorrhizine, Tetrahydropalmatine	Antiviral infection, Neurological, Immunomodulatory, Antidiabetes, Anticancer	Stem & root
Steroids	20 $\delta$ -Hydroxyecdysone, $\delta$ sitosterol, $\beta$ -sitosterol, Giloinsterol Ecdysterone Makisterone A	Inhibits TNF $\alpha$ , IL-1 $\beta$ , IL-6 and COX2. inflammatory arthritis, IgA neuropathy	Shoot
Glycosides	Tinocordiside, Tinocordifolioside, Cordioside, 18-norclerodane glucoside, Cordifolioside Syringin, Syringinapiosyll glycosides, Furanoid diterpene Glucoside, Palmatosides, Cordifolioside A, B, C, D and E, Pregnane glycoside	Anticancer activities Treats neurological disorders like ALS, Parkinsons, Dementia	Stem
Diterpenoid lactones	Furanolactone Tinosporides, Tinosporon, Columbin, Clerodane derivatives, Jateorine	Anti-inflammatory, microbial, anti-viral, Anti hypertensive, Vasorelaxant Induce apoptosis in leukemia by activating caspase-3 and bax, inhibits bcl- 2	Whole plant
Sesquiterpenoid	Tinocordifolin	Antiseptic	Stem
Aliphatic compounds	Heptacosanol, Nonacosan-15-one dichloromethane Octacosanol,	Anti-inflammatory, Protection against 6-hydroxy dopamine induced parkinsonism's in rats	Whole plant
Miscellaneous compound	3, ( $\alpha$ ,4-di hydroxyl-3-methoxybenzyl)-4-(4-Compounds hydroxyl-3-methoxy-benzyl)-tetrahydrofuran, Giloinin, Tinosporic acid, Tinosporidine, Cordifellone, Jatrorrhizine, Ntrans	Protease inhibitors for HIV and drug-resistant HIV.	Whole plant & Root



	feruloyltyramineas diacetate		
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Tab: Phytochemical constituents and their Pharmacological activity of *Tinospora cordifolia*[7]

Name of Market Product	Biological Roles
Tinospora Cordifolia Pellets	A number of diseases
Guduchi	The immune system and the body's resistance to infections
Brave Heart Capsule	It lowers the lipid levels especially cholesterol and LDL cholesterol in body, diuretic
Rebuild	Anti- stress and anti- oxidant
Cirrholiv capsules	Hepatoprotective

Tab: Pharmaceutical products of *T. cordifolia* and their biological roles

## II. CONCLUSION

*T. cordifolia* being a resourceful plant constitute innumerable biologically active compounds that have been reported to have a therapeutic potential. There are reports in pharmacological and clinical studies which validate the curative and remedial role of this plant to combat different ailments. The different bioactive compounds including alkaloids, steroids, glycosides, sesquiterpenoids etc found to have potential application especially as immunomodulator and antioxidant agent. 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. Overall, this review gives information about the classical anti-toxin, antidiabetic, anticancer, immunomodulatory, antioxidant, antimicrobial activity of *T. cordifolia* and can be used for further research investigations in development of novel drug.

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