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Tinospora Cordifolia: Medicinal Plant: A Review

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ABSTRACT

Wild Tinospora cordifolia Guduchi/Amrita, native name; English: Indian Tinospora, also known as Giloya/Gulancha in Hindi, belongs to the Menispermaceae family and is abundant in Bangladesh, Myanmar, Sri Lanka, and China. The plant is a spreading and climbing shrub with many twisting branches. T. cordifolia is utilised in Ayurvedic medicine and has a variety of therapeutic characteristics. This page summarises the plant's chemical ingredients and pharmacological characteristics. The review will offer future researchers with a scientific basis for its usage in Ayurveda as well as an instructive database on an ethno-pharmacologically valuable medicinal plant.

Key Words: Tinospora cordifolia, Ethnopharmacology, Chemical Constituents, Biological Activities.



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INTRODUCTION

Tinospora cordifolia in the wild Guduchi/Amrita, native name; English: Indian Tinospora, also known as Giloya/Gulancha in Hindi, is a Menispermaceae family member that is common in Bangladesh, Myanmar, Sri Lanka, and China. The plant is a climbing and spreading shrub with several twisted branches. T. cordifolia is used in Ayurvedic medicine and has several medicinal properties. This page highlights the chemical components and pharmacological properties of the plant. The review will provide future scholars with a scientific foundation for its use in Ayurveda, as well as a useful database on an ethno-pharmacologically beneficial medicinal plant. Medicinal plants are those plants which exhibit medicinal and therapeutic properties in the form of biologically active compounds in the form of secondary metabolites and these metabolites are found either incorporated in the plant parts like leaves or flowers, seed or bark or sometimes found in the form of exopolysaccharides, resins and gums. The recent discovery has pointed that the rhizosphere surrounding the plant roots have therapeutic properties that can be used and exploited by the mankind for his betterment. The medicinal plants have always been the hub and center for cultural and medicinal prosperity in various cultures and of all the cultures, the central and south Asian cultures and spirituality has been deeply rooted and supported by medicinal plants and their products. Various sages and ancient physicians like Susruta, who wrote the "Susruta Samhita" which praises the various medicinal and therapeutic properties of many plants. The ayurvedic scriptures depicts the transfer of the medicinal knowledge from godly sources to sages and thereby passed to human society via physicians in written form and orally transmitted knowledge from gurus(teachers) to their pupils. The practices usually uses well designed concentrations of substances like minerals, metals along with the herbal compounds in set manner for protective and curative effects.1

The scientific bodies have always been inquisitive and amazed by the medicinal plants for their beyond scientific explanation behavior and have always tried to replicate their effects in the laboratory conditions. Like seen, they have not been able to infuse and bind the ocean similar effects of the medicinal plants in the synthetic and semi–synthetic form. So the other concept of clubbing this age old medicinal form in the advanced technology methods is now widely followed. This method requires the well informed knowledge of the nature and working of the medicinal plants in their native and in combinational form. The know–hows and the in–depth working principles are important to justify the substantial medicinal and therapeutic value that has been tagged to the plants.2–4

Out of the many medicinal plants that have been seen throughout the globe, they have geographically found in strong numbers and multiple varieties in the tropical and sub-tropical regions of the Earth. Out of these regions, the Asian and African continents have the most quantity of medicinal plants and the extent of the medicinal properties that these medicinal plants bear are of very high extent. This is evidently seen in the dominant presence of medicinal plants and their compounds in the daily life and cultural practices of the respective places. India has always been known for her rich cultural and spiritual practices and the extent of the effect that the medicinal plants have on the culture, history and in the lives of the people dwelling in India is clearly visible. So the well-known and in-depth knowledge of both the medicinal

plants and their interactions with the advanced technology and how these in native and in combined form react with the biological system and bring about the desired medicinal and therapeutic properties.

Tinospora cordifolia is a medicinal plant whose status in the field of natural medicine and Ayurvedic is of the highest order. Vernacularly speaking, Tinospora cordifolia is known "Guduchi" whose origin is rooted to Sanskrit; and is known as "Amruthaballi" in Kannada and is an important drug of the Indian System of Medicine (ISM). T. cordifolia is an esteemed medicinal plant whose uses and application with reference to human benefits have been praised to indescribable heights in various ayurvedic and Vedic scriptures and the practices. The medicinal plant of interest in this paper, Tinospora cordifolia, a climber plant of great medicinal property which is widely and popularly used in the ayurvedic and local forms of medicine is studied in the phytochemical and different components that exhibit the properties that have been celebrated and upheld in the age old traditions and medicinal practices.



Fig;1; Tinospora cordifolia

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.

Anti-Diabetic Activity

Pharmacological studies have proven in vivo antidiabetic potential of various extracts of T. cordifolia. It has been reported to mediate its Antidiabetic potential through myriad of biologically active phytoconstituents isolated from different parts of plant, including alkaloids, tannins, cardiac glycosides, flavanoids, saponins and steroids [5]. These compounds have been reported to encompass different target activities in diabetic conditions, thus enabling the potential application in experimental and clinical research. Kannadhasan R and Venkataraman S study reported that 30 days treatment of Sedimental extract of Tinospora cordifolia (SETc) (1000mg/kg/p.o) on diabetic subjects was proven for its efficacy and clearly establishes the antidiabetic activity with antiobese body built [6]. The Ethanolic extract of *Tinospora* cordifolia leaves in different dosages (200 and 400 mg/kg b.w.) administered orally for 10 days and 30 days in streptozotocin diabetic albino rats. It is clearly showed that TC has significant antidiabetic activity in diabetic animals and has an efficacy of 50% to 70% compared to insulin [7]. Borapetoside C isolated from Tinospora crispa (5 mg/kg, i.p.) attenuated the elevated plasma glucose in diabetic mice, increased glucose utilization, delayed the development of insulin resistance and then enhanced insulin sensitivity. The activation of insulininduced IR-Akt-GLUT2 expression in liver and the enhancement of insulin sensitivity may have contributed to the hypoglycemic action of borapetoside C [8]. The isoquinoline alkaloid rich fraction from stem, including, palmatine, jatrorrhizine, and magnoflorine have been reported for insulin-mimicking and insulin releasing effect both in vitro and in vivo [9]. In Ehrlich ascites tumor cells model, water, ethanol and methanolextracts of the herb showed glucose uptake-stimulatory activity [10]. The protective effects of Tinospora cordifolia root extract were reported in presence of higher levels of anti-oxidant molecules and enzymes. Tinospora cordifolia root extract has been shown to significantly counterbalance the diabetes-associated oxidative stress in the maternal liver by lowering the levels of malondialdehyde and reactive oxygen species and the increased levels of glutathione and total thiols[11]. Oral treatment of Tinospora cordifolia (100 and 200 mg/kg body weight) for 14 days mediates its Antidiabetic potential through mitigating oxidative stress, promoting insulin secretion and also by inhibiting gluconeogenesis and glycogenolysis [12].

Anti-Cancer Activity

Tinospora cordifolia shows anti-cancer activity, this activity is mostly shown in animal models.

The extraction of alkaloid palmatine from *Tinospora cordifolia* by using response surface methodology (RSM) clearly indicate the anticancer potential in 7,12-dimethylbenz(a)anthracene DMBA induced skin cancer model in mice [13]. A single application of *Tinospora cordifolia* extract at a dose of 200, 400 and 600 mg/kg dry weight, 24 hrs prior the i.p. administration of cyclophosphamide (at the 50 mg/kg), significantly prevented the micronucleus formation in bone marrow of mice, in a dose dependent manner. C57 Bl mice when received 50% methanolic extract of *Tinospora cordifolia* at a dose 750 mg/kg body weight for 30 days showed increase in life span and tumor size was significantly

reduced as compared to control [14]. Mishra R et al study investigated the anti-brain cancer potential of 50% ethanolic extract of *Tinospora cordifolia* (TCE) using C6 glioma cells. TCE significantly reduced cell proliferation in dosedependent manner and induced differentiation in C6 glioma cells [15]. Manju Bala et al study evaluated eight secondary metabolites from *Tinospora cordifolia* against four different human cancer cell lines, KB (human oral squamous carcinoma), CHOK-1 (hamster ovary), HT-29 (human colon cancer) and SiHa (human cervical cancer) and murine primary cells respectively. All extracts and fractions were active against KB and CHOK-1 cells whereas among the pure molecules palmatine was found to be active against KB and HT-29; tinocordiside against KB and CHOK-1; yangambin against KB cells [16]. Two molecules from hexane and methanol fractions (T1 and T2) from the plant *Tinospora cordifolia* show that inMCF-7 cells, T1 treatment significantly suppressed the proliferation, migration and invasion of MCF-7cells when compared to that of T2. Epithelial—mesenchymal transition related genes, Twist and Snail, were downregulated by T1 with increased transcription of E-cadherin [17].

Immunomodulatory Activity

Tinospora cordifolia is well known for its immunomodulatory response. Active compounds 11-hydroxymustakone, N-methyl-2-pyrrolidone, Nformylannonain, cordifolioside A, magnoflorine, tinocordiside and syringin has been reported to have potential immunomodulatory and cytotoxic effects [18]. Vaibhav Aher et al study confirms the immunomodulatory activity of Tinospora cordifolia ethanolic extract (100 mg/Kg/p.o.) stem through altering the concentration of antioxidant enzymes, increasing T and B cells and antibody which play an important role in immunity, enhancing the concentration of melatonin in pineal gland and increasing the level of cytokines like IL-2, IL-10 and TNFα which plays an important role in immunity [19]. Aqueous Tinospora extracts has been also reported to influence the cytokine production, mitogenicity, stimulation and activation of immune effector cells [20]. Polymorphonuclear leucocytes (PMN) cells are an important component of the host defence system. Extracts of *Tinospora cordifolia* were able to stimulate the PMN cells for phagocytosis of added Candida cells through an in vitro slide method of phagocytosis [21]. Orally administration of T cordifolia alcoholic extract (100 mg/kg, p. o) was found distinct increase in foot pad thickness and also significant increase in the WBC counts and bone marrow cells significantly indicating stimulatory effect on haeomopoetic system, it shows potent immunomodulatory action [22]. Bharti Umretia et al study Results suggest that Guduchi Ghana (concentrated form of aqueous extract of Guduchi) prepared by classically was found to possess significant immunostimulatory action on immune system [23]. A randomized, controlled, parallel, pilot clinical study demonstrate effect of the formulated Tinospora lotion for Interleukin-1, Interleukin-6 and Interleukin-8 using blood serum samples. Down regulation of Interleukin 1, 6, and 8 levels in scabies infestation inhibits hyperkeratosis and infiltration of inflammatory cells into scabietic lesion. The modulation effect of the Tinospora lotion on interleukin levels reinforces its anti-scabies activity [24].

Anti-Oxidant Activity

The *Tinospora cordifolia* has potential application in food systems as an antioxidant and probably in biological systems as a nutraceutical. Methanolic, ethanolic and water extracts of *Tinospora cordifolia* showed significant antioxidant potential compared to other solvents and also possess metal chelation and reducing power activity [25]. V Sivakumar et al study Results suggest that *Tinospora cordifolia* stem methanol extracts administered orally increased the erythrocytes membrane lipid peroxide and catalase activity. It also decreased the activities of superoxide dismutase, glutathione peroxidase in alloxan-induced diabetic rats [26]. *Tinospora cordifolia* has the ability to scavenge free radicals generated during aflatoxicosis. *Tinospora cordifolia* showed protection against aflatoxin-induced nephrotoxicity due to the presence of alkaloids such as a choline, tinosporin, isocolumbin, palmatine, tetrahydropalmatine, and magnoflorine [27]. Neha Upadhyay et al study results suggest that *Tinospora cordifolia* bark ethanol extracts showed the highest free radical scavenging activity compared to the methanol extracts and also ethanol extracts had the highest phenolic content [28]. The administration of Ethanolic extract of *Tinospora cordifolia* (EETC) in Nnitrosodiethylamine (DEN) induced liver cancer in male Wister albino rats reverted the lipid peroxidation (LPO) levels, enzymic and nonenzymic antioxidants to near normal [29]. Essential oil isolated from leaf of *Tinospora cordifolia* (Willd.) was shown strong 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging

activity (IC50= 25±0.3 µg/mL). It also showed dose dependent reducing power activity [30]. The leaves of *Tinospora cordifolia* was extracted with methanol and partitioned in water with ethyl acetate and butanol At 250 mg/ml concentration, the antioxidant activity of the free radical scavenging activities of the extracts assayed through DPPH, reducing power, phosphomolybdenum and metal chelating activity were found to be highest with methanol, followed by ethyl acetate, butanol and water extract. The antioxidant activity of BHT was higher than the extracts at each concentration points [31].

Anti-Microbial Activity

The anti-bacterial activity of *Tinospora cordifolia* extracts has been assayed against *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Salmonella typhi*, *Shigella flexneri*, *Salmonella paratyphi*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Enterobacter aerogene*, and *Serratia marcesenses* (Gram-positive bacteria) [32]. Aqueous, ethanol and acetone extracts of leaves and stem of *Tinospora cordifolia* Hook. F. Thoms showed maximum inhibitory activity against on clinical isolates of urinary pathogens Klebsiella pneumoniae and Pseudomonas aeruginosa [33]. Silver Nanoparticles synthesized from stem of *Tinospora cordifolia* possess very good antibacterial activity against multi drug resistant strains of Pseudomonas aeruginosa isolated from burn patients [34]. The

active compound [(5R,10R)-4R, 8R-Dihydroxy-2S, 3R:15, 16-diepoxycleroda-13(16), 17, 12S, 18, 1S-dilactone] was isolated from ethanol extract of *Tinospora cordifolia* stem showed activity against bacteria and fungi. The lowest MIC values were observed against Enterococcus faecalis (125 μ g/ml) and Bacillus subtilis (200 μ g/ml). The compound also showed activity against fungi; the lowest minimum inhibitory concentration values were seen against Trichophyton simii (31.25 μ g/ml), Trichophyton rubrum 57 (62.5 μ g/ml), Trichophyton rubrum 296 (62.5 μ g/ml) [35]. Francesca Bonvicinia et al study results indicate that constituents from *Tinospora cordifolia* exhibited a higher inhibitory activity against reference microbial strains and clinical isolates of methicillin-resistant Staphylococcus aureus (MRSA) and carbapenemaseproducing Klebsiella pneumoniae [36]. Constituents from *Tinospora cordifolia* may be a potential source of new therapeutic strategies for infectious diseases.

Anti-Toxic Activity

The gold standard drug for the treatment of Parkinson's disease is L-DOPA, but various studies have proved that the treatment with L-DOPA leads to the death of surviving dopaminergic neurons in the CNS. The coadministration of *Tinospora cordifolia* crude powder protected the dopaminergic neurons when compared with Sham operated control group. The treatment with *Tinospora cordifolia* crude powder couldreduce the toxicities of L-DOPA therapy for Parkinson's disease [37]. *Tinospora cordifolia* alkaloids such as choline, tinosporine, isocolumbin, palmetine, tetrahydropalmatine and magnoflorine showed protection against aflatoxin induced nephrotoxicity. *Tinospora cordifolia* extracts have been reported to scavenge free radicals generated during aflatoxicosis. It exhibited protective effects by lowering thiobarbituric acid reactive substances (TBARS) levels and enhancing the GSH, ascorbic acid, protein, and the activities of anti-oxidant enzymes viz., SOD, CAT, GPx, Glutathione S-transferase (GST) and glutathione reductase (GR) in kidney [38]. Cyclophosphamide an anti-cancer drug has been reported to reduce the glutathione content in both bladder and liver and lowered levels of cytokines Inerferon-γ and IL-2 an increased levels of pro-inflammatory cytokine TNF-α. This effect could be reversed on *Tinospora cordifolia* treatment indicating the role of *Tinospora cordifolia* in overcoming Cyclophosphamide induced toxicities in cancer treatment [39]. 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 [40].

CONCLUSION

This review has covered the numerous chemicals found in T. cordifolia. Antioxidant, antibacterial, anti-HIV, analgesic, anti-fungal, anti proliferative, and anti-epileptic properties are among them. Its characteristics have been proven to be useful in the treatment of a variety of disorders. Isolating pure lead compounds from plant components as well as endophytic fungi isolated from various parts could pave the way for future treatments of many pathological disorders. As a result, this study can be used for further research as well as therapeutic purposes in the creation of novel medications.

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