

Review Article

***Tinospora cordifolia* Chemical Constituents and Medicinal Properties: A Review**

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Abstract: Since the beginning of human civilization, medicinal plants have been used by mankind for its therapeutic value. Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources. Traditional medicine has remained as the most affordable and easily accessible source of treatment in the primary healthcare system of resource poor communities in India. A huge interest always exists in exploring nutraceuticals from plant materials to replace synthetic drugs in order to overcome their adverse effects and also for economic reasons. *Tinospora cordifolia* is a widely used shrub in folk and Ayurvedic systems of medicine all over India. Though almost all of its parts are used in traditional systems of medicines, leaves stem and roots are the most important parts which are used medicinally. *Tinospora cordifolia* is a versatile resource for all forms of life. It belongs to family Menispermaceae. It contains many different chemicals that affect the body. The present review aims to summarize the information concerning the chemical constituents and medicinal aspects of the *Tinospora cordifolia* plant.

Keywords: Medicinal plants, *Tinospora cordifolia*, pharmacology, Herbal drugs.

INTRODUCTION

The World Health Organization reported that 80% of the world population relies chiefly on traditional medicines involving the use of plant extracts or their active constituents. India with its mega-biodiversity and knowledge of rich ancient traditional systems of medicine (Ayurveda, Siddha, Unani, Amchi and local health traditions) provide a strong base for the utilization of a large number of plants in general healthcare and alleviation of common ailments of the people [1]. *Tinospora cordifolia* is one of the non-controversial and extensively used herbs in Ayurvedic medicine. It belongs to family Menispermaceae. It is a glabrous, succulent, woody climbing shrub native to India. It is also found in Burma and Sri Lanka. It thrives well in the tropical region, often attains a great height, and climbs up the trunks of large trees. The stem is gray or creamy white, deeply cleft spirally and longitudinally, with the space between spotted with large rosette-like lenticels. The wood is white, soft, and porous, and the freshly cut surface quickly assumes a yellow tint when exposed to air. Leaves are simple, alternate, exstipulate, long petiolate, chordate in shape showing multicoated reticulate venation. Long thread-like aerial roots come up from the branches. Flowers are small and Unisexual. Male flowers are in clusters female flower are solitary. Six sepals arranged in two whorls of three each. Six petals arranged in two whorls, they are obovate and membranous. Aggregate fruit is red, fleshy, with many drupelets on thick stalk with sub

terminal style scars, scarlet coloured [2]. *Tinospora cordifolia* is known by different name in various different languages in India viz, Tippa-teega (Telugu), Shindilakodi (Tamil), Amruthu, Chittamruthu (Malayalam), Amrutha balli (Kannada), Rasakinda (Sinhala), gurucha (Hindi), garo (Gujarati), Amritavalli (Sanskrit), Guduchi (Marathi), Guluchi (Oriya) [3].

Tinospora 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 starch obtained from the stem is highly nutritive and digestive and used in many diseases [4].

Tinospora cordifolia is a well known medicinal plant 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.

Chemical Constituents

Tinospora cordifolia belong to different classes of constituents such as alkaloids, diterpenoid

lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides etc. Structures of some phytoactive compounds from *Tinospora cordifolia* are illustrate in figure 1.

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 insulin-induced 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 methanol extracts 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 dose-dependent 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 in MCF-7 cells, T1 treatment significantly suppressed the proliferation, migration and invasion of MCF-7 cells 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, N-formylannonain, 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 TNF- α 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 haemopoietic 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 N-nitrosodiethylamine (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 ($IC_{50} = 25 \pm 0.3 \mu\text{g/mL}$). 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 marcescens* (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 multidrug-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 $\mu\text{g/ml}$) and *Bacillus subtilis* (200 $\mu\text{g/ml}$). The compound also showed activity against fungi; the lowest minimum inhibitory concentration values were seen against *Trichophyton simii* (31.25 $\mu\text{g/ml}$), *Trichophyton rubrum* 57 (62.5 $\mu\text{g/ml}$), *Trichophyton rubrum* 296 (62.5 $\mu\text{g/ml}$) [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 carbapenemase-producing *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 could

reduce the toxicities of L-DOPA therapy for Parkinson's disease [37]. *Tinospora cordifolia* alkaloids such as choline, tinosporine, isocolumbin, palmetine, tetrahydropalmetine 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 Interferon- γ and IL-2 and 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].

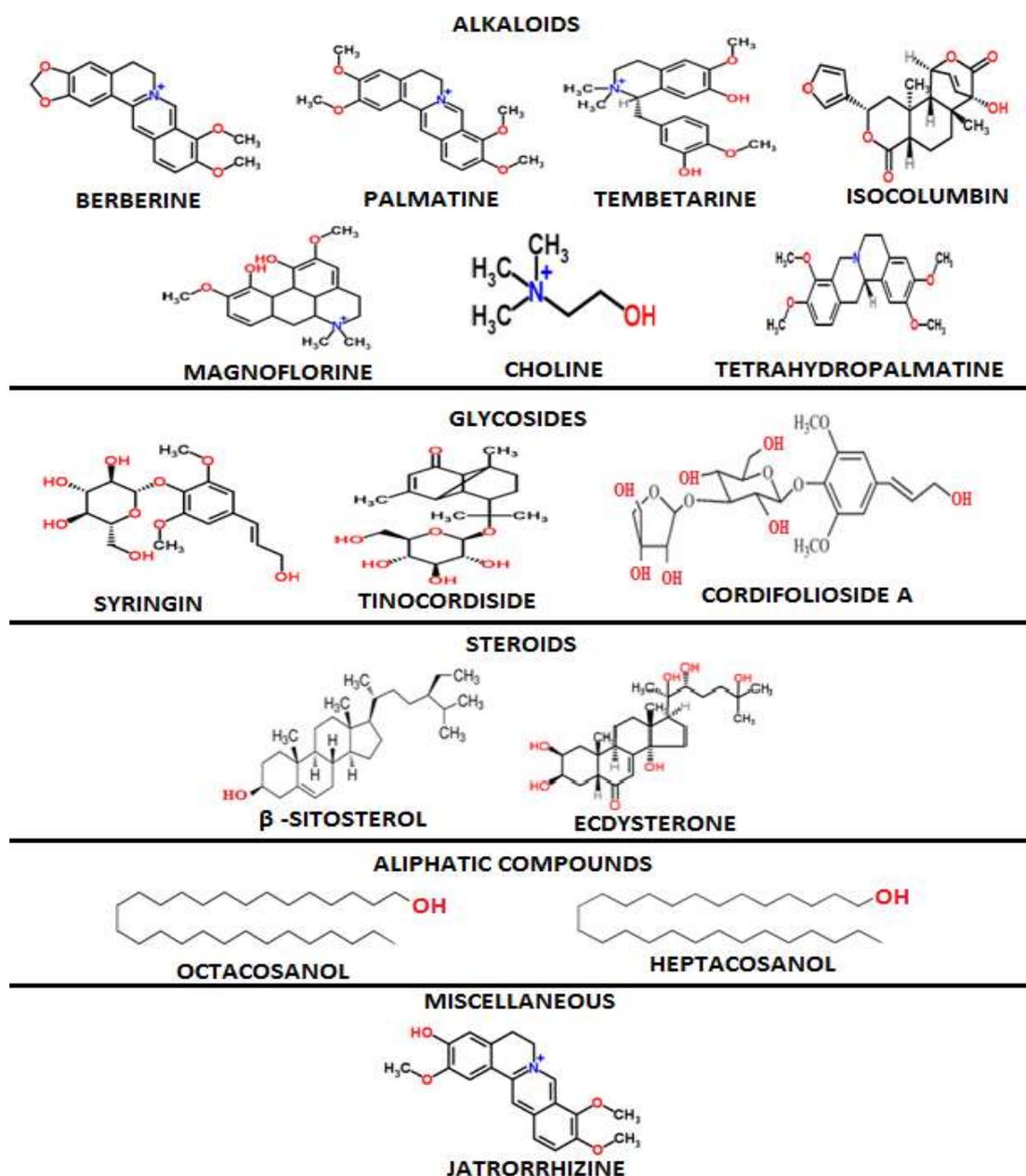


Fig. 1: Some phytoactive compounds from *Tinospora cordifolia*.

CONCLUSION

Tinospora cordifolia, the versatile medicinal plant is the unique source of various types of compounds having diverse chemical structure. Very little work has been done on the biological activity and plausible medicinal applications of these compounds and hence extensive investigation is needed to exploit their therapeutic utility to combat diseases. A drug-development programme should be undertaken to develop modern drugs with the compounds isolated from *Tinospora cordifolia*. Present review spotlights the classical antidiabetic, anticancer, immunomodulatory, antioxidant, antimicrobial, antitoxic claims of *Tinospora cordifolia* and their validation by contemporary researches. For the last few years, there has been an increasing trend and awareness in medicinal plants research. Quite a significant amount of research has already been carried out during the past few decades in exploring the chemistry of different parts of *Tinospora cordifolia*. While *Tinospora cordifolia* has been used successfully in Ayurvedic medicine for centuries, an extensive research and development work should be undertaken on *Tinospora cordifolia* and its products for their better economic and therapeutic utilization. This review can be used for further research as well as clinical purpose.

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