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Pharmacological Overview of *Tinospora cordifolia*, an Ethnologically Important Plant of Bangladesh

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Abstract

Tinospora cordifolia (*Wild*) Hook, local name: Guduchi/Amrita; English: Indian Tinospora, Hindi: Giloya/Gulancha, belongs to the family of *Menispermaceae* and is found in abundance in Bangladesh, Myanmar, Sri Lanka, and China, the plant is a spreading and mounting shrub with a lot twisting branches. *T. cordifolia* is used in Ayurveda medicinal system and has numerous therapeutic properties. This article summarizes the chemical constituents and pharmacological properties found within the plant. The review will provide a scientific basis of its use in Ayurveda and is an informative database on an ethno-pharmacologically important medicinal plant for future researchers.

Keywords

Tinospora cordifolia, Ethnopharmacology, Chemical Constituents, Biological Activities

1. Introduction

Earlier in the twentieth century, phyto-medicine was one of the supreme medication systems since analgesics, antibiotics and other allopathic medications were not available everywhere. Gradually usage of allopathic system of medicine was augmented. Due to quicker therapeutic action of allopathic medicines, the popularity of phyto-medicines started to be declined. However, a significant population still uses phyto-medicines while only fewer adverse effects are exerted by them [1].

Tinospora cordifolia (Wild) Hook, local name: Guduchi/Amrita; English: Indian *Tinospora*, Hindi: Giloya/Gulancha, belongs to the family of *Menispermaceae* and is found in Bangladesh, Myanmar, Sri Lanka, and China [2] is a spreading and mounting shrub with a lot twisting branches. *T. cordifolia* is used in ayurveda medicinal system and has numerous therapeutic properties [3] [4]; these include usage in inflammation, rheumatism, anemia, urinary disorder, skin diseases, jaundice, diabetes, allergic condition, etc. [5] [6]. The root of *T. cordifolia* is a strong antiemetic and is also used in bowel obstruction. Few researchers also testified *T. cordifolia* is useful for remedy of chronic fever, increasing appetite and energy and relieving burning sensation. Guduchi is also in general used by local healers for the treatment of leprosy, helminthiasis, rheumatoid arthritis and to boost up immune system [7]. The plant bears some putative roles on digestive ailments like colitis, hyperacidity, abdominal pain, vomiting, worm infestation [8] [9]. A group of chemical constituents of this plant could be responsible for all these pharmacological activities. These include: glycosides, sesquiterpenoids, aliphatic compounds, polysaccharides, steroids, aliphatic compounds, phenolics and a combination of fatty acid residues within the stem, root and whole plant part [10].

2. Discussion

2.1. Pharmacognostic Description

T. cordifolia is an extensively spreading climbing shrub with several coiled branches. The stem of the plant is fleshy, filiform, and climbing in nature; bark is slightly gray [11]. Stem is in powdered form looks like brown to dark brown and has an unpleasant bitter flavor with characteristic odor [12]. The leafstalks of the leaves are long and heart-shaped, round and partially twisted. Lamina is ovate-shaped and deeply membranous [13]. Flowers are asexual; leaflet are divided or branched with yellowish green color [14]. Each fruit bears a single seed; seeds get matured usually during winter while flowers are in hot humid weather of summer days [15]. The plant has the elevated and thread-like root [16]; the seeds are bended shaped [17].

2.2. Chemical Constituents

T. cordifolia possesses numerous chemical constituents including polysaccharides, steroids, phenolics, aliphatic compounds, alkaloids and steroids; leaves are enriched with phosphorus, calcium and protein [18]. The chemical structure is elucidated through numeral spectroscopic analysis [19] [20] [21]. Some of the essential constituents are reported in **Table 1** whereas the structure of major active chemical constituent for *Tinospora cordifolia* has been depicted in **Figure 1**.

2.3. Pharmacological Activities

2.3.1. Antioxidant Activity

Mehra and his research group evaluated the antioxident activity by the method

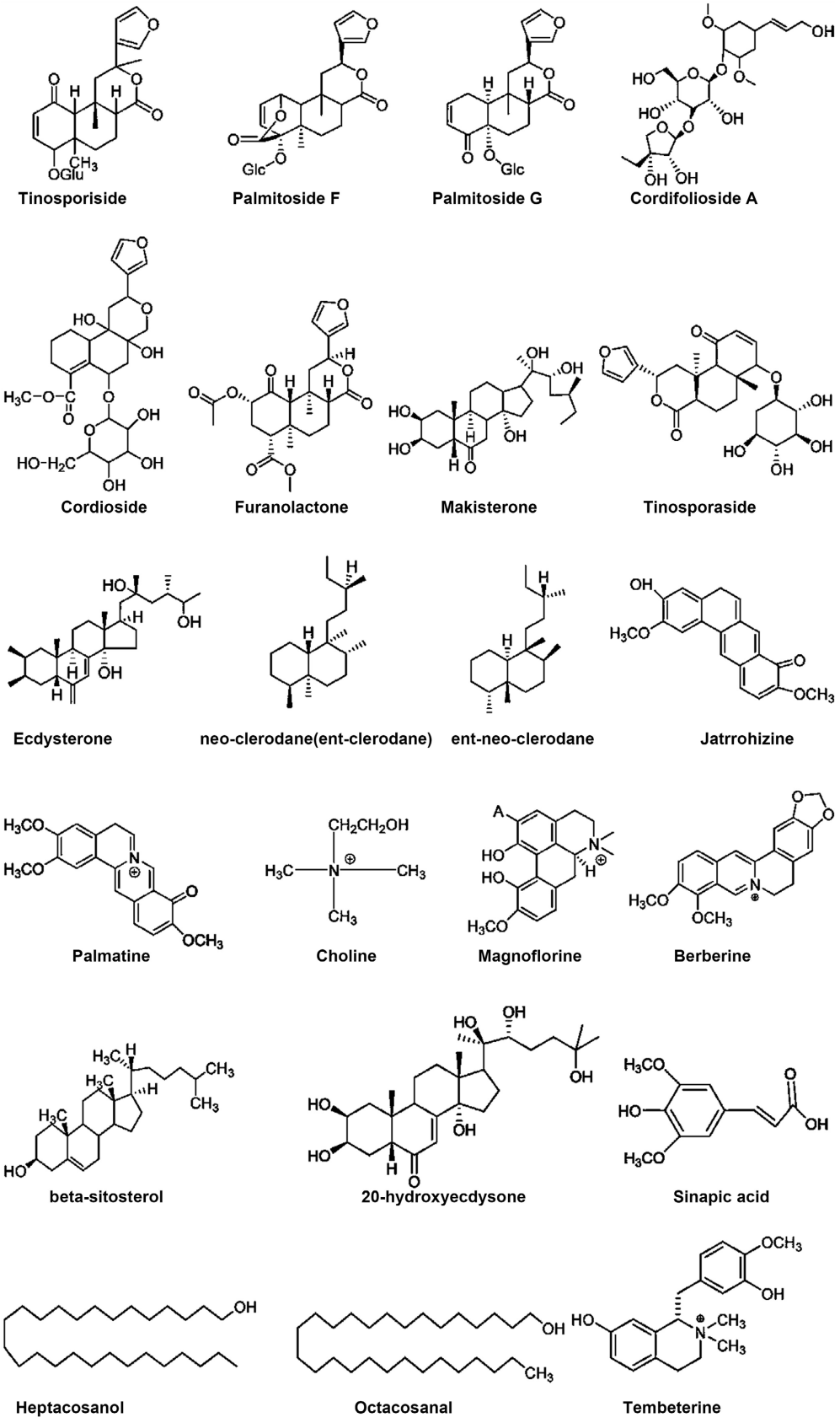

Figure 1. Structure of the major chemical constituents of *T. cordofolia*.

Table 1. Some of the essential chemical constituents of *T. cordifolia*.

Active Component(s)	Compound(s)	Reference(s)
Terpenoids	Tinosporide, Furanolactone diterpene, Furanolactone clerodane diterpene, furanoid diterpene, Tinosporaside, ecdysterone makisterone and several glucosides isolated as poly acetate, phenylpropene disaccharides cordifolioside A, B and C, cordifoliside D and E, Tinocordioside, cordioside, palmatosides C and F, Sesquiterpene glucoside tinocordifolioside, Sesquiterpene tinocordifolin.	[22]-[32]
Alkaloids	Tinosporine, (S), Magnoflorine, (S), Berberine, (S), Choline, (S), Jatrorrhizine, (S), 1,2-Substituted pyrrolidine(S), Alkaloids, viz. jatrorrhizine, palmatine, beberine, tembeterine, choline.	[33] [34] [35] [36] [37]
Lignans	3 (a, 4-dihydroxy-3-methoxybenzyl)-4-(4-hydroxy-3-methoxybenzyl), (S)	[38]
Steroids	Giloinsterol, (S), ß-Sitosterol, (S), 20a-Hydroxy ecdysone, (S).	[39] [40] [41] [42]
Others	Giloin, Tinosporan acetate, Tinosporal acetate, Tinosporidine, Heptacosanol, Octacosanol, sinapic acid, Tinosponone, two phytoecdysones, an immunologically active arabinogalactan.	[40] [43] [44] [45] [46]

of DPPH free radical scavenging. Total flavonol and phenolic content were also measured. They presented antioxidant activity at a significant level with the inhibitory concentration (IC_{50}) at 5 μg/ml as compared to standard drug ascorbic acid [47]. George *et al.* compared different extracts to understand their relative activity; ethanolic extract was reported to augment the level of lipid peroxidase in erythrocyte membrane and augment action of catalase and decrease glutathione peroxidase in alloxan-induced diabetic rats in comparison to polar and methanolic extracts. Methanolic leaf extract obtained from partitioning of ethyl acetate and butanol demonstrated antioxidant activity; extracts of methanol phosphomolybdenum and metal chelating activity were high followed by ethyl acetate, butanol, and water extract [48]. On quantirtative measurement, free radical species was also found decreased in diabetic rat and upregulated the antioxidant enzyme [49] [50] [51], Free radical scavenging activity for methanolic extract was higher compared to phenol extract [52]. The plant modifies the diverse enzymatic framework and keeps up with the oxidative burden by managing lipid peroxidation and glutathione level [53] [54]. Dried leaves of *T. cordifolia* were extracted with various solvents and yielded ethanolic extract with high antioxidant activity. The antioxidant activity of the ethanolic extract was linked to the total polyphenols extracted [55].

2.3.2. Antimicrobial Activity

The antimicrobial properties of the *T. cordifolia* when used with different sol-

vents have been reported [56]; *in-vitro* studies were performed, outcome showed activity against both gram positive and gram negative bacteria [57]. The plants exhibited activity against different pathogenic bacterial strains including *Salmonella paratyphi*, *Proteus vulgarisus*, *Salmonella typhi*, *Klebsiella pneumoniae*, *Shigella flexneri*, *Staphylococcus aureus* and *Serratia marcesenses* [58].

The acetone, ethyl alcohol and aqueous extract of *T cordifolia* inhibited the activity of certain pathogens in human urine [59]. Silver nanoparticles were also reported to have antibacterial activity against different bacterial strains [60]. Potent activity against fungi was observed including various fungi including *Aspergillus fumigatus*, *Aspergillus flavus*, and *Aspergilles nigar* [61]. The etholic extract made by exposing plates to varying concentrations for 48 hours and the zone of inhibition was measured while 0.2% chlorhexidine and dimethylformamide were used respectively as positive and negative controls for evaluation. The data were analyzed by means of analytical tests which demonstrated that 2% concentration of *T. cordifolia* led to the maximum antibacterial activity [62]. The antifungal activity with variable doses (10, 25, and 50 mg/kg) of TCAE (*Tinospora cordifolia* aqueous extract) was tested in vitro against different species of *Aspergillus*. The *in-vivo* activity was also evaluated in mice [63].

2.3.3. Antidiabetic Activity

The antidiabetic activity of the *T. cordifolia* stems is likely to be due to various compounds such as alkaloids, tannins, flavonoids, and saponins [64]. The crude extract obtained from the stem in dichloromethane, ethyl acetate, chloroform and hexane had been studied while the enzyme inhibited action on hypoglycemic diabetic animal and normal animals. The extract that is aqueous studied within the rats, with no addition of *T. cordifolia* extract upsurge in sugar by 21.3%, insulin by 51.5%, triglycerides by 54.12%, and glucose-insulin index by 59.8% [65]. Methew and his research group have actually reported *in-vivo* studies of different extracts to reveal association with diabetic patients. Different amounts (200 mg/kg and 400 mg/kg b.w.) of ethanolic plant of *T. cordifolia* leaves were prepared. The amounts had been administered orally for ten days and thirty days period in streptozotocin-diabetic albino rats. *T. cordifolia* revealed the antidiabetic activity on test animals; the efficacy was within the range of 50% - 70% in comparison to insulin [66]. Alkaloids obtained from plant *T. cordifolia* showed insulin-mediated activities due to the activity of insulin hormone [67]. *T. cordifolia* was included in the daily food diet up to diabetic-pregnant rats (streptozocin-induced diabetes) which revealed a defensive impact by decreasing the oxidative load therefore preventing the general incidence of disease-conditions [68]. *T. cordifolia* lowered the brain interposed lipid and blood glucose in diabetic rat model indicating its possible lipid-lowering and antidiabetic activity [69]. The root extricate of Guduchi appeared an antihyperglycemic impact within the alloxan-induced diabetic model demonstrated by diminishing its overabundance of glucose in urine [70]. Few natural preparations including Guduchi like Hyponidd, Dihar and Ilogen-Excel have been applied in diabetic rodent models and

the antidiabetic effect of *T. cordifolia* was noticed. The impact by Ilogen-Excel lowered extent of overabundance of systemic glucose level and improved the insulin efficiency by expanding its quantity in blood circulation Hyponidd was found to diminish the glucose-mediated hemoglobin count while maintaining oxidative load via diminishing reactive species. When "Dihar" was evaluated for one and a half months in a streptozotocin-induced animal model, it reduced urea and systemic creatinine level whereas elevating enzyme activity [71] [72] [73].

2.3.4. Anti-Anxiety Action

Sarma *et al.* found that a 100 mg/kg ethanolic extract of *T. cordifolia* has noteworthy anti-anxiety action in comparison to standard diazepam (2.5 mg/kg) [74]. Patients' I.Q. level demonstrated improved level as per clinical investigation. In Ayurveda preparation of *T. cordifolia* is used as a brain tonic and thought to work by improving mental abilities such as memory and recall [75].

2.3.5. Hypolipidemic Effect

In alloxan diabetic rats, Stanely *et al.* analyzed the hypolipidemic impact of an aqueous extract of the root on rats weighing 2.5 and 5.0 g/kg body weight on the sixth week, which brought about in diminished tissue cholesterol, diminished serum, phospholipids, and free fatty acid. The root extract at a dose of 5.0 g/kg of body weight had the most noteworthy hypolipidaemic impact. *T. cordifolia* root extract's capacity to lower serum or tissue lipid level in diabetic rats had never been investigated earlier [76].

2.3.6. Hepatic Disorder

Sharma *et al.* investigated the effects of *T. cordifolia* water extract (TCE) on hepatic and gastrointestinal toxicity, finding a substantial increase in the levels of gamma-glutamyl transferase, aspartate transaminase, alanine transaminase, triglyceride, cholesterol, HDL, and LDL in alcoholic samples though their level get down-regulated after TCE mediation, patients appeared the standardized liver capacity of *T. cordifolia* remain to diminish the signs [77].

2.3.7. Anti-Proliferative Potential

Ali *et al.* used response surface approach to investigate the anticancer efficacy of *T. cordifolia* extract in animal models. In a mouse skin cancer model generated by 7, 12-dimethylbenz(a)anthracene (DMBA), the extract showed antitumor activity [78]. Rahul *et al.* in dose-dependent manner prepared the extract at 200, 400, and 600 mg/kg dry weight and C57 BI mice were given a 50 percent methanolic extract of *T. cordifolia* for 30 days at a concentration of 750 mg/kg body weight. The tumor's size shortened the expected length of life [79].

2.3.8. Anti-HIV Potential

The root concentrate of *T. cordifolia* promotes the safe arrangement of HIV positive patients, according to Kalikae *et al. T. cordifolia* stem concentrate lessens eosinophil count, B lymphocyte incitement, macrophage incitement, hemoglobin level, and polymorphonuclear leucocytes [80] [81] and therefore could have

a significant anti-HIV potential.

2.3.9. Wound Healing Property

The wound healing profile of alcoholic extract of *T. cordifolia* and its outcome on the wound healing was found suppressed by dexamethasone, as evaluated by Shanbhag T. *et al.* The injury mending capability of the plant showed expanded elasticity of the extract of *T. cordifolia* which might be credited to the advancement of collagen combination. The concentrate of *T. cordifolia* didn't invert dexamethasone stifled injury recuperating [82].

2.3.10. Immunomodulating and Anticomplement Activities

Kapil *et al.* conducted a study on two pure isolates from *T. cordifolia*, syringin and cordiol and tracked down that these compounds hindered *in-vitro* resistant hemolysis of sheep erythrocytes by guinea pig serum. Hemolysis in immune system was declined because of hindrance of the C3-convertase of the traditional complement pathway. The mixtures of *T. cordifolia* ascend to significant expansions in IgG antibodies in the serum of guinea pig. Cordioside, cordiofolioside-A and cordiol actuated macrophase with expanding the time for incubation. Sharma *et al.* described various classes of dynamic mixtures revealing their immunomodulatory movement [4].

2.3.11. Use in Parkinson's Disease

Birla *et al.* detailed *T. cordifolia* concentrate is profoundly alluring against the parkinosonism. They noticed the counter inflammatory movement of watery concentrate in 1-methyl-4-phenyl-1, 2, 3, 6-tetra hydropyridine (MPTP)-intoxicated parkinsonian mouse model. The concentrate turned around the behavioral changes of the objective MPTP-inebriated mice and the outcome recommended that *T. cordifolia* ensured dopaminergic neurons by overturning neuroinflammation in the MPTP-instigated parkinsonism [83].

The plant showed different bioactivities because of assorted compound constituents present in it (**Table 2**). The organically dynamic compounds are available in various parts of the *T. Cordifolia* which clarifies why the people with different illnesses utilizing different parts of this phenomenal plant from the ancient time.

2.3.12. Anti-Osteoporotic Effect

T. cordifolia influence the differentiation in proliferation, mineralization of bone-like matrix on osteoblast model frameworks *in-vitro* and subsequently finds an expected application to combat osteoporosis, as claimed by Abiramasundari and his research group. Alcoholic concentrate of *T. cordifolia* has exhibited to animate the development of osteoblasts, expanding the separation of cells into the osteoblastic heredity and furthermore expanding the mineralization of bone-like grid [84]. Isolated ecdysteroids from the plant have been accounted for of protein anabolic and against osteoporotic impact in vertebrates. Beta-Ecdysone (Ecd) from *T. cordifolia* extricates have been accounted for to initiate a significant

Table 2. Concerned biological activities of different plant parts of *T. cordifolia*.

Dynamic component	Biological properties
Teroenoids	Stem: Infectious disease related to lower and upper respiratory tract [87], disease related to skin [5], properties to counter glucose deviation [88]
Alkaloids	Stem and plant root: Anti-proliferative potential [89], Antioxidant property [90].
Lignans	Plant root: Anti-neoplastic property [91], Antioxidant property [92]
Steroids	Arial part of stem: Anti-stress action [74]
Others	The entire part of plant: Rheumatoid joint pain, elevated cholesterol content, gout, diabetes, neuropharmacological and analgesic effects, cancer, anti-fever and radioprotective properties [92] [93] [94] [95]

expansion in the thickness of joint ligament, instigate the osteogenic separation in mouse mesenchymal Stem cells [85] and to get rid of osteoporosis in animal models [84]. 20-OH-β-Ecd secluded from *T. cordifolia* has been accounted for its role against osteoporotic impact [84] which suggests *T. cordifolia* could be used in management of osteoarthritis and osteoporosis [86].

3. Conclusion

The various compounds found in *T. cordifolia* have been discussed in this review. Some of these include antioxidant, antimicrobial, anti-HIV, analgesic, anti-fungal, antiproliferative and anti-epileptic. Its properties have been acknowledged as effective in treating various diseases. Isolating pure lead compounds from the plant part as well as from endophytic fungi isolated from different parts could pave a way in future to combat different pathological conditions. This review, therefore, can be used for further research investigations as well as a clinical purpose in the development of novel drugs.

Conflicts of Interest

Authors declare no conflict of interest.

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