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Tinospora cordifolia - An Overview

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[*1]M.R.N. Shaikh, [2]S.S. Khadabadi

[1,3]Royal College of Pharmaceutical Education and Research, Sayne Khurd, Malegaon.

[2]Government College of Pharmacy, Osmanpura, Aurangabad.

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ABSTRACT

Tinospora cordifolia (T. cordifolia) is widely used shrub in folk Ayurvedic systems of medicine. This review presents detailed survey of literature on phytochemical and medicinal properties of the plant. The chemicals reported from the plant belong to different classes such as alkaloid, diterpenoid lactones, glycosides, steroids, phenolics, aliphatic compounds, etc. The notable pharmacological properties include antidiabetic, antineoplastic, antioxidant, immunomodulation, antilipidemic, anti-allergic and many more activities which are yet to be explored.

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INTRODUCTION

T. cordifolia (Guduchi) is an Indian medicinal plant. It has been used in Ayurvedic preparations for the treatment of various ailments throughout the centuries. Ancient Hindu physicians prescribed it for gonorrhea. European medical men in India became interested in the tonic and diuretic properties of *T. cordifolia*. Today, the drug and a tincture prepared from it are having official recognition in the Indian Pharmacopoeia [1, 2, 3]. It has been used to treat general weakness, fever, dyspepsia, dysentery, gonorrhea, secondary syphilis, urinary tract diseases, impotency, gout, viral hepatitis, skin diseases, and anemia. In compound formulations, guduchi is used clinically to treat jaundice, rheumatoid arthritis and diabetes. The root is considered to be a strong emetic and is used for bowel obstruction [1, 3, 4].

Plant

Tinospora

Scientific Name(s): *Tinospora cordifolia* (Willd.) Miers. Family: Menispermaceae (moonseeds)

Common Name(s): Guduchi, Amrita (Sanskrit), Giloe, Gulancha (Bengali), Giloya (Hindi), Gado, Galo (Gujarati), Duyutige, Teppatige (Telugu), Heartleaf moonseed (English).

T. cordifolia is a glabrous, succulent, climbing shrub native to India. The plant is shown in Figure 1 (a). It is also found in Burma and Sri Lanka. It thrives easily in the tropical region, often attains a great height and climbs up the trunks of large neem trees. The bark is gray or creamy-white, deeply cleft spirally and longitudinally with the space between spotted with large rosette-like lenticels. The stem bark of the plant is shown in figure 1(a) and 1(b). The wood is white, soft, and porous, and the freshly cut surface quickly assumes a yellow tint when exposed to air. The branches bear smooth heart-shaped leaves, unisexual greenish flowers in summer and red berries in winter. Long thread-like aerial roots come up from the branches. The viscous sap is light yellow and has an odor and a nauseating bitter taste [1, 2].

Chemical constituents

A large number of compounds have been isolated from the aerial parts and roots of *Tinospora cordifolia*. In the early 1900s, giloin, gilenin and gilosterol as well as the bitter principles columbine, chasmanthium and pomeranian were identified in the plant. A wide variety of

sesquiterpenes and diterpenes have been isolated from the stems of the plant. The major isolated compounds include the norditerpene furan glycosides cordifolisides A, B and C [5]; the daucane-type sesquiterpenes, tinocordifolin and tinocordifolioside [6, 7]; the furanoid diterpene glucosides palmatosides C and F and amritosides [8, 9]; the clerodane diterpenoids cordioside, tinosponone and tinocordioside [10, 11]; tinosporaside, a novel 18-norclerodane diterpene glucoside [12] and tinocordiside, a cadinane sesquiterpene glycoside. In addition, syringin, cordiol, cordioside and the phenylpropene disaccharides cordifoliosides A and B were identified as the active principles with anticomplement and immunomodulatory activities [13]. The stems of the plant contain the alkaloid berberine. Cultures of the stem callus have the capability of synthesizing this compound [14, 15]. Ecdysterone, makisterone A and 20 beta hydroxyecdysone are phytoecdysones isolated from the aerial parts of the plant [16, 17]. Other constituents reported from *T. cordifolia* include a phenolic lignan, octacosanol, nonacosan-15-one, heptacosanol, beta-sitosterol [18-20], tinosporidine, cordifolia, cordifolia [21, 22], magnoflorine, tembetarine, syringine, syringine apiosylglycoside and a glucan polysaccaride [23-25].

The roots of *T. cordifolia* contain isocolumbin, palmatine, tetrahydropalmatine, magnoflorine and jatrorrhizine [26, 27]. A simplified classification of chemical constituents present in *T. cordifolia* is given in Table 1.

Clinical Overview

Uses of Tinospora

T. cordifolia is used in the Indian Ayurvedic system of medicine for the treatment of jaundice, diabetes and rheumatoid arthritis. It is also used as an immunostimulant. Limited studies have examined its antineoplastic, antioxidant, hepatoprotective, hypolipidemic and immunologic properties.

Tinospora Dosing

Few clinical trials are available to support dosing. In examining the efficacy of Tinospora in allergic rhinitis, 300 mg of an aqueous extract was given 3 times daily for 8 weeks [1, 2].

Contraindications

Contraindications have not been determined.

Pregnancy/Lactation

Information regarding safety and efficacy during pregnancy and lactation is lacking.

Tinospora Interactions

Not well documented.

Tinospora Adverse Reactions

Limited clinical studies reveal few adverse reactions.

Toxicology

Little is known about the toxicology of *T. cordifolia.*

Tinospora Uses and Pharmacology

Antineoplastic effects

Tinospora plant extracts made with water, ethanol/methanol or methylene chloride extracts have been evaluated for antineoplastic effects in various animal experiments.

A dose-dependent cytotoxic effect of Tinospora extract in HeLa-cultured cells comparable with doxorubicin has been reported.

Tumor mass reduction and increased survival time have been observed with administration of the extract in several experiments in mice with induced carcinomas [34, 35]. Tinospora extract showed a regulatory effect on serum cytokine with consequent angiogenesis inhibition in mice melanoma cells [36, 37].

Survival time was increased after irradiation, and body weight loss was decreased in mice pretreated with a single dose of Tinospora extract [38].

At low doses, an ethanol extract of Tinospora increased bone marrow cell counts, while higher doses resulted in decreased counts in mice with induced lymphoma [39, 40]. In similar experiments, Tinospora extracts restored thymus homeostasis, retarded tumor growth and prolonged survival times [41-44].

Clinical data

No clinical trials in cancer have been published.

Antidiabetic and hypolipidemic effects

Aqueous and ethanol extracts of *T. cordifolia* root administered to alloxan-induced diabetic rats caused a dose-dependent reduction in blood glucose levels, similar to glibenclamide and insulin. In similar experiments, serum and tissue cholesterol, phospholipid, and free fatty acid levels were reduced [45-49].

Clinical data

No clinical trials have been published to date.

Antioxidant effects

The antioxidant properties of *T. cordifolia* roots were studied by administering the aqueous extract to alloxan-induced diabetic rats. After 6 weeks, the levels of the plasma thiobarbituric acid-reactive substances ceruloplasmin and alpha-tocopherol were reduced, while the levels of glutathione and vitamin C were increased. The root extract at a dose of 5 g/kg was the most effective[46]. In other *in vitro* studies, guduchi extract inhibited lipid peroxidation and generation of superoxide and hydroxyl radicals [41, 50].

In experiments with rat hippocampal slices, extracts of *T. cordifolia* demonstrated antioxidant effects such as inhibition of nitric oxide synthase activity and direct nitric oxide-free radical scavenging [51, 52].

Clinical data

No clinical trials have been published to date.

Immunologic effects

T. cordifolia is widely used in the Indian Ayurvedic system of medicine as an immunostimulant [25]. Syringin, cordiol, cordioside, and cordifoliosides A and B are considered the active principles responsible for anticomplement and immunomodulatory activities [14, 28]. An arabinogalactan polysaccharide isolated from the dried stems of *T. cordifolia* showed polyclonal mitogenic activity against β-cells [3]. An aqueous extract of the

aerial parts of the plant containing an α-D-glucan was demonstrated to increase the activation of natural killer cells and exert a dose-dependent effect on the production of cytokines [25, 29].

Clinical data

An aqueous extract of *T. cordifolia* reduced allergic rhinitis, sneezing, nasal obstruction and pruritus in a randomized clinical trial over 8 weeks [30].

T. cordifolia was suggested to strengthen host defenses and improve the surgical outcome in patients with extrahepatic obstructive jaundice [31-33].

Other effects

Other reported properties of the plant include a decreased infarct size in rats [53] and hepatoprotection with a return to normal levels of ALT, AST, serum alkaline phosphatase and serum bilirubin in carbon tetrachloride-injured rats [54, 55].

Dosage

Few clinical trials are available to determine dosing. In examining the efficacy of Tinospora in allergic rhinitis, 300 mg of an aqueous extract was given 3 times a day for 8 weeks [30].

Pregnancy/Lactation

Information regarding safety and efficacy during pregnancy and lactation is lacking.

Interactions

In an experiment in mice, an extract of the aerial parts of *T. cordifolia* increased the activity of some CYP-450 enzymes [41].

Adverse Reactions

Few adverse reactions were reported in limited clinical trials [30].

Toxicology

There is little known about the toxicology of *T. cordifolia* in humans. No adverse reactions were noted when *T. cordifolia* stem extract was administered to rabbits up to the highest oral doses of 1.6 g/kg [34, 56] and in rats at doses of 1,000 mg/kg of the whole plant extract [53].

However, 40 % mortality resulted after mice were given 500 mg/kg body weight of an extract of the stems of Tinospora [39].

Figure 1 (a): *Tinospora cordifolia* plant.

Figure 1 (b): Stem bark of *Tinospora cordifolia*

Table 1: Classification of chemical constituents present in *Tinospora cordifolia* plant.

S.No.	Type of Chemicals	Active principles	Part in which present
1.	Alkaloids	Berberine, [56, 57, 74] Palmatine [56, 57] choline [56, 57] Tinosporine [56, 57] Palmatine [58]	Stem Root
2.	Glycosides	18-norclerodane glycoside [59] Furanoid diterpene glucoside [60, 61] Tinocordiside [62, 63] Tinocordifolioside [64, 65] Syringin [66, 67]	Stem
3.	Diterpenoid lactones	Furanolactone [68] Tinosporon [69] Columbin [70]	Whole plant
4.	Steroids	b – Sitosterol [71] g - Sitosterol	Aerial plant stem
5.	Sesquiterpenoid	Tinocordifolin [72]	Stem
6.	Aliphatic compound	Octacosanol [73] Heptacosanol [73]	Whole part
7.	Miscellaneous compounds	Tinosponidine [59] Cordifol [59] Cordifelone [59] Jatrorrhizine [74]	Root Whole plant (mostly)

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