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TINOSPORA CORDIFOLIA: A PHYTOPHARMACOLOGICAL REVIEW

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Key words:

Tinospora cordifolia, Ayurvedic medicine, immunmodulatory, anti-allergic, health products

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ABSTRACT: Plants have been one of the important sources of medicines since the beginning of human civilization. There is a growing demand for plant based medicines, health products, pharmaceuticals, food supplements, cosmetics etc. A review of chemical constituents present in various parts of *Tinospora cordifolia* and their pharmacological actions is given in the present article. *Tinospora cordifolia*, is a commonly used shrub in Ayurvedic medicine. Although the review articles on this plant are already published, this review article is presented to comply all the updated information on its phytochemical and pharmacological activities, which were performed by widely different methods. The notable medicinal properties are anti-diabetic, anti-spasmodic, anti-malarial, anti-inflammatory, anti-arthritic, anti-oxidant, anti-allergic, anti-stress, anti-leprotic, hepatoprotective, immunmodulatory & anti-neoplastic activities.

INTRODUCTION: Herbal medicines represents one of the most important fields of traditional medicine all over the world. To promote the use of herbal medicine & to determine their potential as a source for new drugs, it is essential to study medicinal plants which have folklore reputation in a more intensified way [1]. Human beings have used plants for medicinal purposes for centuries. Traditional forms of medicine have existed and still exist in many countries of the world including countries in the Indian sub-continent like India, Pakistan and Bangladesh [2]. The writings indicate that therapeutic use of plants is as old as 4000–5000 B.C. and Chinese were the first to use the natural herbal preparations as medicines [3].

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Plants are one of the most important sources of medicines. Today the large number of drugs derived from plants, like morphine from *Papaver somniferum*, Aswagandha from *Withania somnifera*, Ephedrine from *Ephedra vulgaris*, Atropine from *Atropa belladonna*, Reserpine from *Rauwolfia serpentina* etc. The medicinal plants are rich in secondary metabolites (which are potential sources of drugs) and essential oils of therapeutic importance. The important advantages claimed for therapeutic uses of medicinal plants in various ailments are their safety besides being economical, effective and their easy availability [4, 5]. Because of these advantages the medicinal plants have been widely used by the traditional medical practitioners in their day to day practice.

The future of higher plants as sources of medicinal agents for use in investigation, prevention, and treatment of diseases is also very promising. Natural products have provided us some of the

important life-saving drugs used in the armamentarium of modern medicine. However, among the estimated 250,000-400,000 plant species, only 6% have been studied for biological activity, and 15% have been investigated phytochemically. This shows a need for planned activity guided phyto-pharmacological evaluation of herbal drugs [6]. This article intends to provide an overview of the chemical constituents present in various parts of *Tinospora cordifolia* and their pharmacological actions.

Tinospora cordifolia Family: Menispermaceae is one of the most widely used shrub from the ancient medicinal history of Ayurveda as a medicine. *Tinospora cordifolia* is commonly known as Guduchi, Amrita (Sanskrit), Giloe, Gulancha (Bengali), Giloya (Hindi), Galo (Gujrati), Teppatige (Telagu), Heartleaf moonseed (Hindi) [7]. It is large deciduous climbing shrub found throughout India, and also in Sri Lanka, Bangladesh, China [8].

Morphology of Plant:

Tinospora cordifolia is a glabrous, succulent, woody climbing shrub native to India. It thrives well in the tropical region, often attains a great height and climbs up the trunk of large trees. The stem is gray and 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 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 flowers are solitary. Six sepals arranged in two whorls, they are obovate and membranous. Aggregate fruit is red, fleshy with many drupelets on thick stalk with subterminal style scars, scarlet coloured [9, 10].

FIG.1: *TINOSPORA CORDIFOLIA*

History & Traditional uses:

The Ayurvedic drug Guduchi or Amrita is mentioned in various texts of Ayurvedic system of medicine viz: Charak, Sushrut & Ashtang Hridaya and other treaties like Bhava Prakash & Dhanvantri Nighantu under other various names viz: Amara, Amritvalli, Chinmarrhuha, Chinnodebha & Vatsadani etc, [11-15]. In Sushurta Samhita, it is mentioned under Tikta- Saka Varga & claimed to be useful in treating kustha (leprosy), Maha Jvara (fever), Svasa (asthma) and Aruci (anorexia) [14]. In other treaties like Charak Samhita & Ashtang Hridaya, it has been indicated in diseases like Kamala (jaundice), Javara (fever) & Vat Rakta (gout) [13, 15]. In Bhavya Prakash, it is considered as bitter tonic, astringent, diuretic and potential aphrodisiac & curative against skin infections, jaundice, diabetes, chronic diarrhea & dysentery[16].

In Dhanvantri Nighantu, its medicinal properties are mentioned for cure of bleeding piles, promoting longevity, curing itching and erysipelas [17]. It is reported to be a potent vegetable tonic. It is a traditional belief among Ayurvedic practitioners that Guduchi Satva obtained from Guduchi plant growing on Neem tree (*Azadirachta indica*) is more bitter & more efficacious and is said to incorporate the medicinal virtue of neem also [18].

The drug caught the attention of European practitioners in India as a specific tonic, antiperiodic and for its diuretic properties & it was included in Bengal Pharmacopoeia of 1868 [19]. *Tinospora cordifolia* is mentioned in Ayurvedic literature as a constituent of several formulations used in debility, dyspepsia, fever & urinary diseases. Some of the important formulations are: Guduchyadi churna, Guduchi taila, Sanjavani vati, Kanta-Kari avaleha, Chyavnaprasha, Guduchi satva, Guduchu ghrita, Amrita guggulu, Brihat guduchi taila, amritashtaka churna etc.

Uses In Folk And Tribal Medicine:

- The tribals Baiga, living in the interior areas of Naugarh and Chakia Block of Varanasi district, Uttar Pradesh make the paste of stem of the Guduchi (T. cordifolia) and the roots of Bhatkatiaya (Solanum surattense). The pills are prepared and used in the treatment of fever for three days [20].
- The tribals of Mumbai and its neighbouring areas and the fishermen along the sea coast use *T. cordifolia* as drug in the treatment of fever, jaundice, chronic diarrhoea and dysentery [21].
- The tribals of Khedbrahma region of North Gujarat use the plant in their day-to-day life as food or medicine. They use powdered root and stem bark of T. cordifolia with milk for the treatment of cancer; decoction of root is used for the cure of dysentery and diarrhoea and decoction of old stems is preferred in the treatment of periodic fever [22].
- Decoction of stem is administered orally by the people of Jammu (J & K) and Bigwada (Rajasthan) for the treatment of fever [23].
- The inhabitants of Bhuvneshwar (Orissa) use the warm juice of root of T. cordifolia orally for the treatment of fever [21].
- Juice or decoction of leaves is administered orally with honey in fever by the local people of Patiyala (Punjab) [21].
- The Muslim tribals of Rajouri, Jammu (Tawi) comprising Gujjar and Backwals used the plant in bone fracture [24].
- In Dahanu forest division of Maharashtra, tribal races, viz. Agaris, Bhils, Dhodias, Dublas, Khakaris, Rimoshis, Thakurs, Vardaris, Vagharis and Varlis use the stem decoction with cold or hot water (about 3-4 gm) in morning in an empty stomach as a tonic in general debility [25].
- Shirt of child is dyed in juice of Guduchi and worn in balashosha (emaciation in children) by the inhabitants of Banka (Bihar) [23].
- Paste or juice of Amrita (T. cordifolia) leaves and Sarsapa beeja churna (seed powder of *Brassica campestris*) is applied locally in case of Daha (Burning sensation) [23].
- Powder of *Terminalia chebula* (Haritaki), *Tinospora cordifolia* (Amrita) and *Trachyspermum ammi* (Ajwain) in equal quantity is administered orally, once daily early morning with salt for the treatment of Kasa (cough). Decoction of these drugs is also to be taken in dose of 50 ml for the treatment of Kasa (cough) by the people of Dhurala (Haryana) [23].
- Two drops of leaf juice of allied species of Guduchi is dropped in the ear for the

treatment of Karna Shula (pain in ear) by the local people of Patiyala (Punjab) [23].

- Paste of Guduchi (*T. cordifolia*) and 5 seeds of Krishna marich (*Piper nigrum*) is administered orally once daily in morning in rakta pradar (leucorrhoea) by the local women of Arjunpura (Rajasthan) [23].
- The inhabitants of Badala (U.P.) take the juice of stem orally with honey for the treatment of swasa (Asthma) [23].
- Decoction of stem is administered orally in case of twak-roga (skin disease) by the people of Dehrabara Kolaras, Sivpuri District of M.P.[23].

Phytochemistry:

The plant mainly contains alkaloids, glycosides, steroids, sesquiterpenoids, aliphatic compounds, essential oils, mixture of fatty acids and polysaccchrides. The alkaloids include berberine, bitter gilonin, non-glycoside gilonin gilosterol [26].

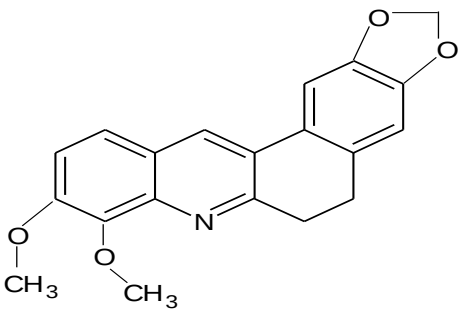
The major phytoconstituent in *Tinospora cordifolia* include tinosporine, tinosporide, tinosporaside, cordifolide, cordifol, heptacosanol, clerodane furano diterpene, diterpenoid furano lactone, tinosporidine, columbin, b-sitosterol. Berberine, palmatine, tembertarine, magniflorine, choline and tinosporin are reported from the stem of the plant [27, 28].

A rearranged cadinane sesquiterpene named tinocordiside, consisting of tricyclic skeleton with a cyclobutane ring, has been isolated from the aqueous fraction of *T. Cordifolia* [29].

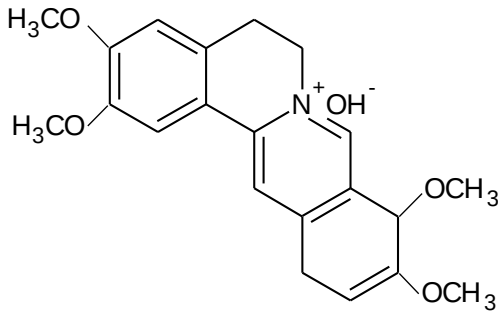
The new clerodane furano diterpene 2 with the molecular formula $C_{20}H_{20}O_8$, has been isolated from the stems of the plant [30].

A new daucane type sesquiterpene, tinocordifolin, has been isolated from the stem of *Tinospora cordifolia*. The new sesquiterpene has been named as tinocordifolin together with tinocordifolioside, N-trans-feruloyl tyramine [31].

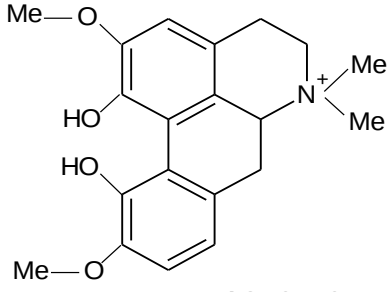
Phytochemical investigation of the methanol extract of *Tinospora cordifolia* aerial parts led to the isolation of four new and seven known compounds. The structure of the new aporphine alkaloids, N-formylasimilobine 2-O-β-D-glucopyranosyl –(1-2)-β-D-glucopyranoside (tinoscorside A) and N-acetylasimilobine 2-O- β-D- glucopyranosyl –(1-2)-β-D-glucopyranoside (tinoscorside B), a new clerodane diterpene, tinoscorside C and a new phenylpropanoid , sinapyl 14-O- β-D-apiofuranosyl-(1-6)-O- β-D-glucopyranoside (tinoscorside D) [32].



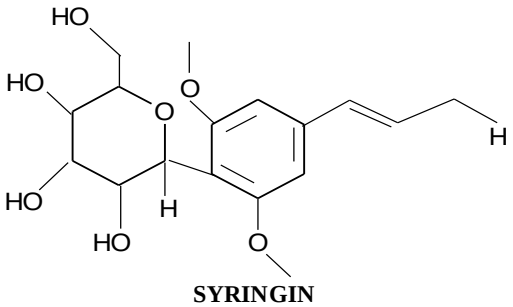
BERBERINE



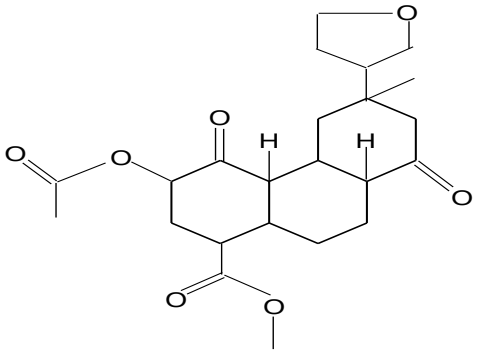
PALMATINE



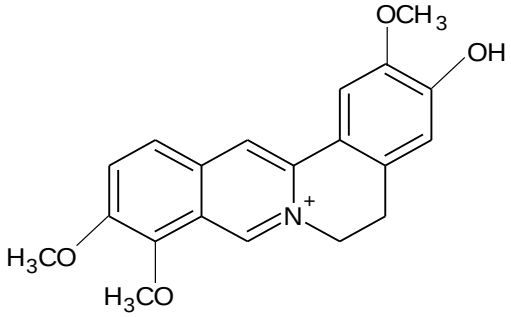
MAGNOFLORINE



SYRINGIN



FURANOLACTONE



JATRORRHIZINE

FIG.2: CHEMICAL CONSTITUENTS ISOLATED FROM *TINOSPORA CORDIFOLIA*

Medicinal Properties:

Tinospora cordifolia is widely used medicinal plant in Ayurvedic system for its general tonic, antiperiodic, anti-spasmodic, anti-inflammatory, antipyretic, anti-arthritic, anti-lepritic, anti-allergic and anti-diabetic properties [33].

The plant is used to improve the immune system and the body resistance against infections. The root of this plant is known for its anti-stress and anti-malarial activities. The stem is bitter, stomachic, diuretic, stimulates bile secretions, allays thirst, enriches the blood and cures jaundice. The extract of the stem is useful in skin problems. The root and stem of *Tinospora cordifolia* is prescribed in combination with other drugs as an antidote to snakebite and scorpion. [33] The plant is also used in the treatment of wounds, pneumonia, asthma and cough. *Tinospora cordifolia* has anti-cancer, immune stimulating, nerve cell protecting, anti-diabetic, cholesterol-lowering and liver-protective actions. *Tinospora cordifolia* is also responsible for decreasing the tissue damage caused by radiation, the side effects of some forms of chemotherapy and speeding healing of diabetic foot ulcers [34].

TABLE 1: PHARMACOLOGICAL ACTIVITIES REPORTED FROM *TINOSPORA CORDIFOLIA*

Sr. No	Activity	Part/Extract	Animal Model/Cell Lines
1.	Neuroprotective effect	Aerial parts/Ethanol extract	6-hydroxy dopamine lesion rat models of Parkinson's disease.[35]
2.	Antiulcer activity	Whole plant/ Ethanol & aqueous extracts	Albino rats using pylorus ligation induced ulcer.[36]
3.	Antidiarrhoel activity	Whole plant/Ethanol & aqueous extract	Castor oil &Magnesium sulphate induced diarrhea in Albino rats.[37]
4.	Analgesic activity	Whole plant/Ethanol extract	Hot plate & abdominal writhing method in albino rats.[38]
5.	Aphrodisiac property	Aqueous & hydroalcoholic extract	Adult Albino rats of wistar strain.[39]
6.	Immunomodulatory activity	Whole plant/Aqueous extract	Swiss male albino mice.[40]
7.	Antidyslipidemic activity	Stem Extract	Alloxan induced diabetic male adult rats of Charles Foster strain.[41]
8.	Antioxidant activity	Whole plant/Ethanol extract	n-nitrosodiethylamine induced liver cancer in male wistar albino rats.[42]
9.	Anti-inflammatory activity	Stem/Aqueous extract	Carrageenan induced paw edema model in rats.[43]
10.	Gastroprotective activity	Whole plant	Indomethacin induced gastric ulcer in rats.[44]
11.	Nootropic effect	Whole plant/Ethanol extract	Amnesic rats using radial arm maze task performance & barnes maze test.[45]
12.	Radioprotective & cytoprotective activity	Stem/Ethanol extract	4 Gy-γ radiation in albino mice & cyclophosphamide induced genotoxicity.[46]
13.	Antifeedant activity	Whole plant/ Chloroform extract	Microorganism used: Earias vitella, Plutella xylostella, Spodoptera litura.[47]
14.	Ameliorative effect	Root/Ethanol extract	Male Swiss albino mice exposed to aflatoxin B1.[48]
15.	Cardioprotective effect	Whole plant/ Alcohol extract	Calcium chloride administrated by intravenous infusion to produce arrhythmia in rats.[48]
16.	Hepatoprotective activity	Whole plant/ Aq. extract	Bile duct ligation induced jaundice in rats.[50]
17.	Hypoglycemic activity	Stem/ Aq. extract	Insulin released effect was detected in vitro using rat pancreatic β-cell lines.[51]

18.	Antipsychotic activity	Aqueous & ethanol extract	Amphetamine challenged mice model.[52]
19.	Antidepressant activity	Pet.ether extract	Swiss albino mice & activity was evaluated using tail suspension test & forced swim test.[53]
20.	Antiosteoporotic activity	Stem/ethanol extract	Female Sprague-Dawley rats.[54]
21.	Antineoplastic activity	Aerial parts/DCM extract	Mice transplanted with Ehrlich ascites carcinoma.[55]
22.	Antifertility effect	Stem/Methanol extract	Male rats.[56]
23.	Antiasthamatic activity	Stem/hydroalcoholic extract	Mice were sensitized with intraperitoneal ovalbumin followed by intranasal ovalbumin in vivo asthma model.[57]
24.	Antitumor activity	Aqueous alcoholic extract	C6 glioma cells were used, extract reduced the cell proliferation in dose dependant manner.[58]
25.	Diabetic neuropathy	Stem/aqueous extract	Streptozotocin induced wistar albino diabetic rats & in vitro aldose reductase inhibition assay & in vivo results were analysed with Mann whitney Test.[59]
26.	Hepatocellular carcinoma	Aerial parts/ Ether extract	Diethyl nitrosamine induced hepatocellular carcinoma in male wistar rats.[60]
27.	Antimalarial activity	Stem/ Ethanolic extract	Microorganism used Plasmodium berghei on white swiss mice models.[60]
28.	Antibacterial activity	Stem/ Aqueous & ethanolic Extract	Microorganisms used: E.*coli, P.vulgaris, E.faecalis, S.typhi, S.aureus, S.marcesenses*.[62]
29.	Anticancer activity	Aqueous & ethanolic extract	IMR 32 human neuroblastoma cell lines as a model system.[63]
30.	Antipyretic activity	Formulation guduchi ghrita	Albino rats against yeast induced pyrexia.[64]
31.	Allergic rhinitis	Aq.extract	Double blind placebo controlled trial.[65]

TABLE 2: CHEMICAL CONSTITUENTS RESPONSIBLE FOR THE BIOACTIVITY: [7, 34, 66, 67]

Sr. N	Activity	Chemical constituent	Class
1.	Neuroprotective effect	Berberine, choline, Tembetarine, Tinosporin, Palmitine, Jatrorrhizine	Alkaloids
2.	Aphrodisiac property	Berberine, Palmatine, Tembatarine, Magnoflorine, Tinosporin, Isocolumbin	Alkaloids
3.	Immunomodulatory activity	Cordifolioside A, Tinocordiside, Syrigin	Glycosides
4.	Antidyslipidemic activity	Berberine	Alkaloids
5.	Antioxidant activity	(-)Epicatechin, Tinosporin, Isocolumbin, Palmatine,	Alkaloid, Diterpenoid lactone
6.	Anti-inflammatory activity	Furanolactone, Tinosporin, Tinosporide, Jateorine, Columbin, Clerodane derivatives	Diterpenoid lactones
7.	Gastroprotective activity	Epoxyclerodane diterpene	Terpenoids
8.	Radioprotective & cytoprotective activity	Cordifolioside A	Terpenoid
9.	Antifeedant activity	Tincordin, Tinosporide, Columbin, 8-hydroxy columbin	Terpenoid, Diterpenoid lactone
10.	Ameliorative effect	Tinosporin, Isocolumbin, Palmatine, Magnoflorin, Tetrahydropalmatine	Alkaloids, Terpenoids
11.	Cardioprotective effect	Furanolactone, Tinosporin, Tinosporide, Jateorine, Columbin, Clerodane derivatives	Alkaloids, Terpenoids
12.	Hepatoprotective activity	Magnoflorin, Tinosporin, Isocolumbin, Palmatine, Tetrahydropalmatine	Alkaloids, Terpenoids
13.	Antipsychotic activity	Berberine, Choline,Tembetarine, Magnoflorine, Tinosporin, Palmetine, Isocolumbin, Aporphine alkaloids, Jatrorrhizine, Tetrahydropalmatine	Alkaloids
14.	Antidepressant activity	Tinosporin, berberine, Jatrorrhizine	Alkaloids
15.	Anticancer activity	Magnoflorine, palmatine, Tinocordiside, Cordifolioside A	Alkaloids, Terpenoids
16.	Antiarthritic activity	B- sitosterol, Makisterone A, Giloinsterol	Steroids
17.	Antidiabetic activity	Berberine, choline, Tembetarine, Palamtine, Jatrorrhizine	Alkaloids
18.	Antimicrobial activity	Furanolactone, Tinosporon, Jateorine, Columbin	Diterpenoid lactones

CONCLUSION: There has been an increase in demand for the phytopharmaceuticals all over the world because of the fact that the allopathic drugs have more side effects. This forms a good basis for the selection of plant for further phytochemical and pharmacological investigation.

The pharmacological and clinical studies reported in the present review confirm the therapeutic value of *Tinospora cordifolia.* Presence of chemical compounds indicates that the plant could serve as "lead" for development of novel agents for disorders in the coming years. In this regard, further studies need to be carried out to explore *Tinospora cordifolia* for its potential in preventing and treating diseases. So, the present review gives a direction for future investigators to carry out

research on the plant so that they could get some medicinally important drugs.

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