Research article Available online www.ijsrr.org ISSN: 2279–0543

International Journal of Scientific Research and Reviews

Enumerations on Ethnobotanical, Phytochemical and Pharmacological Aspects of Guduchi (*Tinospora Cordifolia* (Willd.)Miers Ex Hook. F. And Thoms)

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ABSTRACT

Guduchi (*Tinospora cordifolia* (Willd.)Miers ex Hook. F. and Thoms) is a semi-perennial, glabrous, succulent climber grown universally as wild or cultivated in warmer areas. It contains commercially important grey-brown, rough, thin stem bark which used in various drugs. The plant climbs on other plants with fleshy thread like aerial roots. The dry stem is odourless but freshly cut stem has very bitter taste. It produced bioactive compound or secondary metabolites *viz.* columbin (tinosporin), chasmanthin, palmarin, cordioside, tinoside and cordifoliside-A. Stem contains several phenylpropanoids (syringin, cordifolioside-A, cordifolioside-B, cordiol and sinapic acid). Pharmacologically it has bioactive isoquinoline alkaloids (berberine, jatorrhizine, magnoflorine, tembetarine, N-formylanonaine, N-formylnornuciferine), lignans (a phenolic lignan), carbohydrates (an arabinogalactan polysaccharide) and aliphatic compounds.

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INTRODUCTION

In recent trends of research various parts of medicinal plants are used universally due to their natural origin and lesser side effect. Guduchi or Tinospora [*Tinospora cordifolia* (Willd.)Miers ex Hook. F. and Thoms] (Syn. *Menispermum crispum* L., *T. gibbericaulis* Handel-Mazzetti, *T. mastersii* Diels, *T. rumphii* Boerlage and *T. thorelii* Gagnepain) is a glabrous, deciduous climber of family Menispermaceae. This family have about 70 genera and 450 species found in tropical lowland regions and most of them are generally climber or twiner but rarely shrubs[1-3]. The family is medicinally important due to rich source of alkaloid and terpenes[4]. It is listed amongst 29 highly prioritized medicinal plants of agro climatic zone 8 (Rajasthan, U.P. and M.P.) by National Medicinal Plant Board, India due to the presence of immense medicinal properties[5].

The genus *Tinospora* having 32 species distributed in tropical Africa, Madagascar, Asia, Australia and the Pacific Islands[6-8]. In India, the genus is represented mainly by 4 species.Out of 4 two species as*T. cordifolia* (Thunb.)Miers and *T. sinensis* (Lour.) Merr occurs in South India and other two namely *T. crispa* (L.) Hook.f. & Thomson and *T. glabra* (Burm. F.) Merr reported in Northeast India and the Andaman Islands[9]. *Tinopora cordifolia, T. uliginosa, T. malabarica, T. tomentosa, T. crispa* are medicinally important species of genus.

T. cordifolia is deciduous plant of dry forest distributed throughout tropical Indian subcontinent and China hight up to 300 m. It contains alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides[10]. Protoberberinealkaloids, terpenoids and polysaccharides are 3 major groups of compounds considered as putative active constituents[11-12].

BOTANICAL DESCRIPTION

T. cordifolia is glabrous, deciduous, perennial climber, bearing distinct male and female flowers (flowering in month of March to June) grow as wide range of hedges and trees with coiling branches[1, 13, 14]. Stem is succulent, long, filiform and fleshy with gray or creamy white barkwhich have large rosette shaped lenticels on its surface. The wood is white, soft and porous; but when it exposed to air become yellow tint. The fresh stem is covered by green succulent thin brown bark which normally separate from the wood when the stem dry or shrink. Arial roots arise from the branches and characterized by tetra to penta-arch as primary structure.The inner soft parenchymatous cortex is covered by outer thick walled[15-16].

Branches are coiled and pendulous; fleshy roots covered by striate, tubercled, pale-shining or glabrous bark. Leaves are simple, membranous, alternate, exstipulate, long petiolated (2.5-7.0 cm),

chordate in shape with multicoated reticulate venation (7-9 nerved). Small yellowish to greenish unisexual flowers emerge from leafless plant in summer.

Female flowers are solitary while males are found in cluster (terminal racemes). Six petals arranged equally in two whorls, broadly spathulate, claw cuneate, reflexed to apex, pistillode. Six sepals arranged in two whorls of 3 each, outer is very small, ovate-oblong, acute but the inner whorl has 3 sepals larger, membranous, broadly elliptical, concave and yellow. Solitary female flower has green sepals without reflex margins, staminode short, linear. Carpels 1-3, widely separated on the short fleshy gynophores, dorsally convexed and scarlet in colour[14].

Red fruits are found in cluster with fleshy thick stalk and sub terminal style scars [17]. The fruits (drupes) are ovoid, pea-sized; glossy became redand mucilaginous when ripe in month November-January[18-19].The embryo is curve automatically due to the curvature in seed (moonseed family). The endocarp is ornamented (taxonomic characters).

Common Name(s): Guduchi, Amrita (Sanskrit), Gadancha, Giloe, Gulancha (Bengali), Giloya, Giloe, Gulbel, Gurcha (Hindi), Gulo, Gado, Galo (Gujarati), Heartleaf Moonseed, Tinospora (English), Gilo (Arabic); Amarlata (Assamese); Amrytu, Sittamrytu (Malayalam); Ambarvel, Giroli, Gulvel (Marathi), Garjo (Nepali); Gulancha (Oriya); Gulbel (Persian); Gilo (Punjabi, Kashmiri), Gurjo (Sikkikim); Shindila Kodi, Amridavalli, Niraidarudian (Tamil); Duyutige, Teppatige, Guduchi, Iruluchi (Telugu), Guruch (Urdu), Amrutha Balli (Kannada), Brotowali, Andawali, Putrawali (Indonesia), Makabuhay (Tagalog), Paliaban, Pañgiauban (Bisaya), Taganagtagua & Boraphet (Thailand), K'uan Chu Hsing (Chinese) and Culancha (French)[1,13,20].

DISTRIBUTION:The plant is indigenous to India, Myanmar, Sri Lanka, China, Thailand, Philippines, Indonesia, Malaysia, Borneo, Vietnam, Bangladesh, North Africa, West Africa and South Africa[21-23]. In Indian subcontinent, it is found as climber on *Jatropha curcas*, *Azadirachta indica*, *Moringa oleifera* and other olants which provide support to it[24, 25]. When it climbs on Neem (*Azadirachta indica*) as a climber it is called Neem giloy having combination of chemical constituents of both neem and giloy (tinospora) [26].

Growth Requirement-The plant prefers wide range of soil; acid to alkaline with moderate soil moisture. It can grow in almost all climates but it prefers warm climate. Plantation in the months of July-August in well drained medium black or red soil with rich organic matter is good for plant growth. It is propagated by seeds, vegetative cuttings or clonal propagation[27].

Nutritive composition- *T. cordifolia* contains high fibre (15.9%), protein (4.5%-11.2%), carbohydrate (61.66%) and low fat (3.1%) with 292.54 calories as nutritive value (per 100 g). It contains high amount of potassium (0.845%) and chromium (0.006%); sufficient amount of iron (0.28%) and calcium (0.131%) [28].

ETHNOBOTANICAL AND TRADITIONAL USES

Different tribal or ethnic groups have their own tradition, folk language, beliefs and knowledge to use natural resources as medicines[29]. All the plant parts of *T. cordifolia* are documented to be useful in ethno botanical surveys[30-31]. The plant is used in folkloric veterinary medicine and traditional ayurvedic medicine or reported to widely used for anti-inflammatory and anti-arthritic problems[24, 21].

The leaves used in the treatment of gout and ulcer. Stem stimulates bile secretion, diuretic, enriches the blood, cures jaundice and useful in skin diseases. Extract of stem used to treat chronic diarrhea, chronic dysentery, and intestinal problems and improve digestion [32]. The juice of stem used to cure diabetes, vaginal and urethral discharges, low fevers and enlarged spleen[13]**.** Stem decoction used to washing sore eyes, syphilitic sores, antipyretic and anti-malarial.

In folk medicine the whole plant or powdered root and stem bark, root and stem decoction, juice of the root, paste of the leaves and stem used to treat various disease disorder*viz.* fever, jaundice, diarrhea, dysentery, general debility, cough, asthma, leucorhea, skin diseases, fractures, eye disorders and bites of poisonous insects. The combination of stem root with other drugs is used as antidote to snake bite and scorpion sting[18, 33, 34]. Dried fruits in combination of ghee or honey are used as tonic to cure jaundice and rheumatism.

PHYTOCHEMISTRY

Stem contains several bioactive compounds like alkaloids *viz.* berberine, palmatine-D, choline-D, tinosporine, magnoflorine, tetrahydropalmatine, isocolumbin[35-40], 18-norclerodane glycoside[41]. Furanoidditerpene glycoside[42,43]as tinocordiside[44,45], syringin[46,47] syringin-apiosylglycoside[41,42] tinocordifolioside, cordioside, cordifolioside A, cordifolioside B, palmatoside-C31, palmatoside-F31, cordiofoliside-B2, cordifoliside-D2, cordifoliside[43,44-48,49]and sesquiterpenoid tinocordifolin[50]. The root contains palmatine as an important alkaloid[38,51].The whole plant contains diterpenoid lactones, furanolactone, tinosporon, columbin[52-53]; aliphatic compound as octacosanol, heptacosanol[54] and other miscellaneous compound are nonacosan-15-one 3, (a-4-dihydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxy-enzyl)-tetrahydrofuran, tinosponidine, 6-cordifol, 6-

cordifelone, 6-jatrorrhizine[55,56]. The aerial plant parts have steroids b-sitosterol, d-sitosterol, g-sitosterol b-hydroxyecdysone, ecdysterone, makisterone, giloinsterol jateorine and columbin[51, 57].

USES IN INDIAN SYSTEM

The stems, leaves and roots of guduchi are used in various medicines[58, 59]. In Hindu mythology giloy means heavenly elixir which saved celestial beings from old age and kept them eternally young[10]. In Ayurveda, various dosages in form of Swaras, Kalka, Churna, Kwatha, Fant, Arishta, Satwa, Ghana, Guduchi Ghrita and Guduchi Taila used for treatment of diseases [60]. It is used as Chhinnaruha/Chhinnodbhava (plant's capacity to grow from the cut side), Vatsadini (eaten by grazing animals), Pittaghni (bile destroying), Amruta (imparts immortality), Rasayana (capacity to improve quality of rasa, the primordial tissue which strengthens all other tissues), Chakrangi/Chakra-akshana (wheel-like appearance), Jwaranashi/ Jwarari (potent antipyretic), Vayastha (prevents ageing), Amrutsambhava (ambrosia), Bhishakpriya (favourite of physicians), Saumya (not harmful) and Tikta (bitter taste).

Guduchi used as several formulations to treat general weakness, fever, dyspepsia, skin diseases, anaemia, dysentery, asthma, anorexia, jaundice, gout, diabetes, gonorrhoea, secondary syphilis, urinary diseases, impotency, gout, viral hepatitis, leprosy, chronic diarrhoea and dysentery[61-70].

Charaka described guduchi rasayana as antiaging, immunostimulant, life span booster, promotses intelligence, memory enhancer, resistence, anti-spasmodic and anti-diarrhoeal[71, 72], anti-stress; promote longevity and adaptogen[17, 24, 73-75]. In Sushruta Samhitaa guduchi described it as antiseptic, febrifuge, appetizer, abdominal dropsy, haemoptysis, urinary, vaginal disorders, skin diseases and oedema. It is component of various ointments used for healing of wounds and burns. It is used to treat hyperacidity, colic pain, sprue, dysentery, rheumatism and cellulitis. A crude aqueious dry stem starch preparation is used to cure gastrointestinal disorders or as a tonic in debilitating diseases[76]. The commercially available products to cure various diseases or as suppliment to cure various diseases are Tinospora Pellets, Cirrholiv-DS syrup, Mussaffen, Madhu Mehari, Guduchi, Abhaibhubejhr, Safe herb, Brave Heart capsule, Cirrholiv capsules, Tonoplex, giloya vati and Rebuild[27].

PHARMACOLOGICAL ACTIVITIES

Recently guduchi extracts/fractions used in various forms (aqueous, alcoholic or methanolic, chloroform, ether, petroleum ether, acetone) or chemical constituents used in numerous pharmacological, pre-clinical and clinical investigations.The active adaptogenic constituents in plant

are diterpene compounds alkaloid, Giloinin(glucosidal bitter principle), polysaccharides, Picrotene and bergenin[17, 74]. It has anti-inflammatory, anti-oxidant, anti-pyretic and immunomodulatory activities[17, 73-75]. Bark of plant is anti-allergic, anti-spasmodic, anti-leprotic or used to treat urinary diseases, syphilis, skin diseases, bronchitis[77], promote longevity and increase body's resistance[77-81] or induce the immunity[82-84].

Guduchi has immunomodulatory and cytotoxic affects due to various compounds[82, 85-97]. Both humoral and cell-mediated immunity enhanced in a dose-dependent manner[47]. An immunologically active arabinogalactan identified from dried stem[11]. These natural compounds improve the phagocytic activity of macrophages, enhancement in nitric acid production by stimulation of splenocyte and production of reactive oxygen species (ROS) in human neutrophil cells[27, 98-99]. The aquous extract improve phagocytic and intracellular bacterial capacities of neutrophils in mice reported against bacterial growth[100].

The plant has various properties *viz.* antioxidant[23, 101-107], anti-hyperglycaemic[108-111], anti-cancerous or antitumor[80, 89,104,112-115].

1. The stem used to cure diabetes due to the presence of alkaloids (Magnoflorine, Palmetine and Jatrorrhizine) tannins, glycosides, flavonoids, saponins, steroids by promoting insulin secretion or by inhibiting gluconeogenesis and glycogenolysis[116-118]. The stem extract in various organic solvents like ethylacetate, dichloromethane, chloroform and hexane inhibits the enzymes like salivary amylase and glucosidase resulting increase in post-prandialglucose level and shows potential activities to cure diabetes mellitus disease[119]. The root extract also has anti-diabetic properties, reduce the level of glycosylated haemoglobin, hydroperoxidase and vitamin E[111, 120-122]. Oral dose (aq.) of roots significantly reduce in thiobarbituric acid and increase in reduced glutathione, catalase and superoxide dismutase in alloxan diabetic rats[89]. Arabinogalactan polysaccharide protect against iron-mediated lipid peroxidation of rat brain homogenate (also vide infra) [96].

The plant has antipyretic, analgesic, antiicteric[80,104], antigonorrhoeal[120-122], antifertility[123], anticancer[112,114,124,125], anti-stress[127], hypolipidaemic[104,128-129], antimalarial[120-122,130], anti-allergic[105,131], antiamoebic, antiatherogenic, antihelmentic[80,120-122], antigout, antiasthmatic, antiperiodic, androgenic[78], anticoagulant, antimicrobial properties[104]. It help to dissolve urinary calculi[132], infections[133], phagocytes[134], memory booster[135], anti-ischemic[136], anti-leprotic[29], antiulcer[137,138], hepatoprotective[89,139], cure splenic injury[95,130] and anti-inflammatory[29,80,105,140-145].

Stem extract (aqueous) exhibit adaptogenic properties[146]. In rat, it evidented that liver damage by carbon tetrachloride (0.7 ml/kg/7 days) as evidenced by higher levels of enzymes (SGOT, SGPT,

AP) and serum bilirubin. When these rats treated with stem extract (100 mg/kg) for 15 days found significant reduction in the serum levels of these enzymes and bilirubin was observed[95]. In a clinical study of 30 patients (who received surgical treatment for extra hepatic obstructive jaundice) given aqueous extract (16 mg/kg/day/oral) of guduchi stem with usual medication showed a far superior postoperative survival rate[83].

Aqueous extract of stem showed antinflammatory, analgesic and antipyretic actions in rats. The extract @ 500 mg/kg (oral) significantly inhibited acute inflammatory response evoked by carrageenan. It is reported that syringin and cordiol found in stem extract have potent anticomplement properties[147]. In asthma, stem extract significantly reduced bronchospasms (allergic) induced by 5.0% histamine acrosol in guinea pigs and capillary permeability in mice[79].

Plant has anti-neoplastic[112, 148], antiasthmatic, antiperiodic, antiemetic, radioprotective[149], anti-depression[150]and obstructive jaundice properties[83, 151].

It has protected effect by lowering the concentration of thiobarbituric acid and enhancing the glutathione, vitamin-C and protein, antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase, glutathione S-transferase), glutathione reductase in kidney[152]. In male albino, leaf and stem extract hepatoprotective effect against lead nitrate induced toxicity. Oral dose of plant extract showed prohibited the lead nitrate induced liver damage[53].

Root extract shown radio protective activity due to extensively increase in body weight, tissue weight and tubular diameter. Dichloromethane extracts of guduchi shows cytotoxic effects owing to lipid peroxidation and release of LDH and decline in GSH[125]. In pre-irradiating mice, root extract has widely affected radiation, induced rise in lipid peroxidation and resulted in the decline of GSH in testes[154]. Most of the synthetic chemotherapeutic agents laid toxic side effects on the living organisms[155].

In a study methylene dichloride extract of stem showed significant anticancer activity against cultured HeLa cells. Antineoplastic activity of extract was comparable to that of doxorubicin. Aqueous and alcoholic extracts of plant was also active, but less potent than the methylene dichloride extract[112]. A polysaccharide fraction from the plant was demonstreated inhibitory in experimental metastasis in mice[105].

Methanolic extract of guduchi has antimicrobial activities and reported against *Staphylococcus aureus, Salmonella paratyphi, S. typhimurium, Klebsiella pneumonia, Escherichia coli, Enterobacter aerogene, Proteus vulgaris, S. typhi, Shigella flexneri, Pseudomonas aeruginosa* and *Enterobacter aeruginosa*[156-158].

Methanolic extract of stem increase the erythrocytes, membrane lipid peroxide and catalase activity and decreases the activity of SOD, GPx in alloxan induced diabetic rats[159-160]. Leaf extract

have an alpha-glucosidase inhibitor, characterized as saponarin was found to be also significant antioxidant and hydroxyl radical scavenging activity[155]. Aqueous extract has a radio protective activity, enhancing the survival of mice against a sub-lethal dose of gamma radiation[153, 161].

Purified polysaccharide fraction of stem showed photo-protective and effectively quenched free radicals generated by photons which protect the tissues against oxidative damage[162]. Stems extract (aq.) has radioprotective activity and inhibited radiation mediated 2-deoxynbose degradation in a dose-dependent manner[161].

ACKNOWLEDGEMENT

An author is grateful to all the scientists whom work is cited and could not acknowledge unknowingly and persons that directly or indirectly engaged in writing in this review.

Conflict of intrest

There is no conflict of intrest in writing this review.

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