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A REVIEW ON PHYTOCHEMISTRY AND IMMUNOMODULATORY PROPERTIES OF *TINOPORA CORDIFOLIA* (GILOY / GUDICHI / GULVEL)

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ABSTRACT

Popular medicinal plant Tinospora cordifolia (T. cordifolia) is used in numerous traditional remedies to treat a wide range of illnesses. The common names Amrita and Guduchi are members of the Menispermaceae family. It has been used to cure a variety of illnesses, including diabetes, leprosy, skin conditions, diarrhoea, and fever, and is regarded as an essential medicinal plant in the Indian system of medicine (ISM). Alkaloids, Terpenoids, Lignans, Steroids, and other chemical compounds have been documented to be present in the plant, establishing the phytochemistry and pharmacological action of Tinospora cordifolia. The plant exhibits various pharmacological activities specifically antioxidant activity, antimicrobial activity, antibacterial activity, antifungal activity, anti-diabetic activity, antistress activity, hypolipidemic effect, hepatic disorder, anticancer anti-HIV potential, antiosteoporotic effects, antitoxic effects, wound healing, and immunomodulating activity.The current review was aimed at collection and compilation of scientific information about chemistry and immunomodulatory activity of T. cordifolia.

Keywords *– Tinospora cordifolia, Guduchi, Glycosides, immunomodulator,Menispermaceae .*

1. INTRODUCTION

Herbal formulations are medical preparations made from one or more plants in precise amounts to provide benefits intended for cosmetic, diagnostic, and disease mitigation in humans and animals [1]. It is often referred to as phytomedicine or herbal medicine. Herbal medicine was the main form of treatment in the early 20th century because there were no antibiotics or analgesics. Due to the rising use of the allopathic medical system and its quick healing effects, herbal therapy has steadily lost favour with the populace. For instance, Curcuma has been utilised for more than 2000 years in Traditional Chinese Medicine to treat anti-inflammatory and potent antioxidant conditions [2, 3]. Because herbal medicines have fewer side effects and are better suited to the human body, over 70–80% of people continue to utilise them for their main health [4]. The use of herbal medicine has increased, and it is more efficient than synthetic medications.

Tinospora cordifolia is a popular medicinal plant which is used in several traditional medicines to cure various diseases.Various properties of *T. cordifolia*, described in ancient texts of Ayurveda, like Rasayana, Sangrahi, Balya, Agnideepana, Tridoshshamaka,

Dahnashaka, Mehnashaka, Kasa-swasahara, Pandunashaka, Kamla-Kushta-Vataraktanashaka, Jwarhara, Krimihara, Prameha, Arshnashaka, Kricch-Hridroganashak, etc., are acquiring scientific validity through modern research adopting "reverse pharmacological" approach.

Fig. 1 : Various parts of T. cordifolia

T. cordifolia (synonym: *Tinospora sinensis* (Lour.) Merr.) is also known as Guduchi/Amrita and its names in Latin: *Tinospora cordifolia* (Wild) Hook. f. & Thomson, English: Tinospora Gulancha/Indian Tinospora, Hindi: Giloya. It belongs to the family of Menispermaceae and is found in Myanmar, Sri Lanka, and China [5].

The plant is frequently used as conventional ayurvedic medicine and possesses a number of therapeutic benefits [6, 7] including the treatment of jaundice, rheumatism, urinary disorders, skin diseases, diabetes, anaemia, inflammation, allergic conditions, anti-periodic properties, and radioprotective effects, among other conditions. [8, 9] To treat intestinal obstruction and as a powerful emetic, Giloya (*T. cordifolia*) root is utilised. The starch from this plant reduces burning, boosts energy, and stimulates the appetite. It also works as a useful home cure for chronic fever.

In addition to helping the immune system and the body's resistance to infections, giloya is effective in the treatment of helminthiasis, heart conditions, leprosy, rheumatoid arthritis, and other conditions [10]. It also maintains normal white blood cell structure, function, and levels. Also, it aids in the treatment of digestive disorders such hepatitis and liver diseases like hyperacidity, colitis, worm infestations, lack of appetite, abdominal pain, excessive thirst, and vomiting. The chemical components of the plant, which include diterpenoid lactones, glycosides, steroids, sesquiterpenoids, phenolic compounds, essential oils, a combination of fatty acids, and polysaccharides, are what give rise to the plant's pharmacological effects [13]. These chemical constituents are also found in the root, stem, and entire body of the plant.

2. PHYTOCHEMISTRY

The chemical components of *T. cordifolia* include alkaloids, glycosides, steroids, phenolics, aliphatic compounds, and polysaccharides. The leaves also contain high levels of calcium, phosphorus, and protein (11.2%), among other nutrients. The stem comprises clerodane furono diterpene glucoside (amritoside A, B, C, and D).

The glycosyl component of a polysaccharide from *T. cordifolia* has been isolated, purified, methylated, hydrolyzed, reduced and acetylated. The partially methylated alditol acetate (PMAA) derivative thus obtained have been subjected to Gas Chromatography-Mass Spectrometry (GC-MS) studies. The following types of linkages were reported: terminal-glucose, 4-xylose, 4-glucose, 4, 6-glucose and 2, 3, 4, 6-glucose. Callus and cell suspension cultures have been established from the stem explants of the plant. Accumulation of berberine and jatrorrhizine (protoberberine alkaloids) was observed in both callus and cell suspension cultures. The signaling mechanism of the novel (1, 4)-alpha-D-glucan (RR1) isolated from *T. cordifolia* was investigated in macrophages to evaluate its immunostimulating properties. An arabinogalactan has been isolated from the dried stems and examined by methylation analysis, partial hydrolysis and carboxyl reduction. Purified polysaccharide showed polyclonal mitogenic

activity against B-cells; their proliferation did not require macrophages. Detailed chemical constitution of *T. cordifolia* is given in Table 1. [34] The structures of the active chemical components for *Tinospora cordifolia* has been shown in Fig. 2, some of the important phytoconstituents are summarised in Table 1. [14-43]

Table-1: List of Phytochemicals present in *T. Cordifolia* [44]

Chemical Class	Phytoconstituents	Present in Part
Alkaloids	Berberine, Palmatine Tembetarine, Magnofl orine, Choline, Tinosporin, Isocolumbin, Palmatine, Tetrahydropalmatine, Magnofl orine	Stem Root
Glycosides	18-norclerodane glucoside, Furanoid diterpene glucoside, Tinocordiside, Tinocordifolioside,Cordioside, Cordifolioside A, Cordifolioside B, Syringin, Syringin-apiosylglycoside, Palmatosides C, Palmatosides F, Cordifoliside A, Cordiofoliside B, Cordifoliside C, Cordifoliside D, Cordifoliside E	Stem
Diterpenoid lactones	Furanolactone, Clerodane derivatives and [(5R,10R)-4R-8R-dihydroxy-2S-3R:15,16-diepoxy-cleroda-13 (16), 14-dieno-17,12S: 18,1S-dilactone] and Tinosporon,Tinosporides, and,Jateorine, Columbin	Whole plant
Sesquiterpenoid	Tinocordifolin.	Stem
Steroids	Gβ -sitosterol, δ-sitosterol, 20 β-Hydroxy ecdysone. Ecdysterone, Makisterone A, Giloinsterol.	Aerial part, Stem
Others	Nonacosan-15-one 3,(α,4-di hydroxy-3-methoxy-benzyl)-4-(4-Compounds hydroxy-3-methoxy-benzyl)-tetrahydrofuran. Jatrorrhizine. Tinosporidine, Cordifol, Cordifelone, N-trans-feruloyl tyramine as diacetate, Giloin, Giloinin, Tinosporic acid.	Whole plant, Root Whole plant

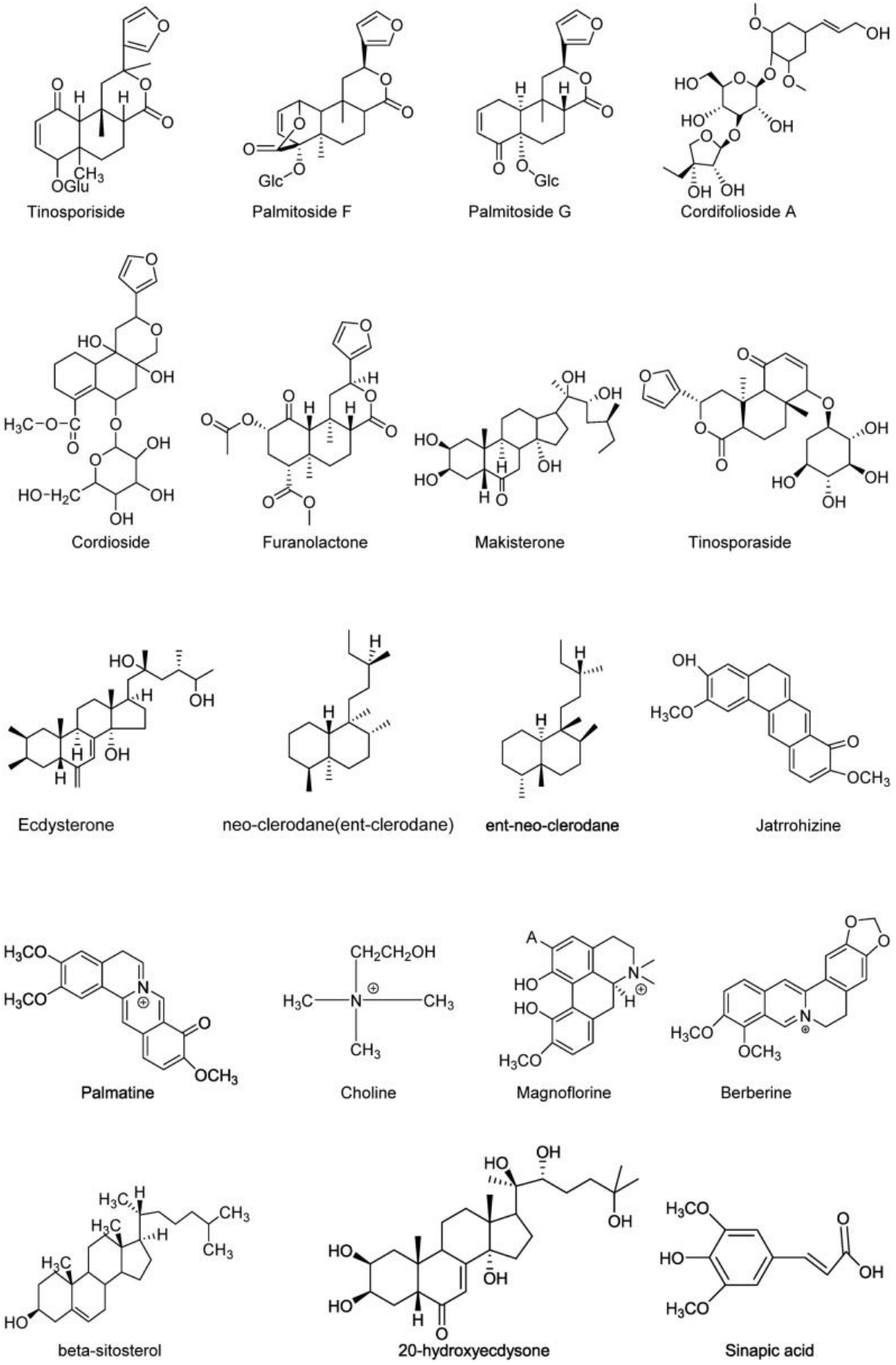

Fig. 2: Structures of chemical constituents of *T. cordifolia* [45]

3. IMMUNOMODULATORY PROPERTIES

T. *cordifolia* is thought to have a number of beneficial characteristics in Ayurveda, including rasayana (rejuvenating), balya (tonic), vayah-sthapana (anti-aging), aayushyaprada (increases lifetime), vrishya (aphrodisiac), and chakshusya (helpful in eye diseases) . The immune system is said to benefit from the alcoholic and aqueous extracts of *T. cordifolia*, which have effectively been investigated for their immunomodulatory action. [46-52]

The degradation of proteins due to photosensitization as assessed by Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was effectively reduced by simultaneous treatment with G1-4A/PPI (partially purified immunomodulator) from *T. cordifolia* during photosensitization.[53]

The novel (1,4)-alpha-D-glucan derived from the plant activates the immune system through the activation of macrophages via TLR6 signaling, NFkappaB translocation and cytokine production.[54] *Tinospora cordifolia* differentially regulate elevation of cytokines as evidenced by the increased production of antiangiogenic agents IL-2 and tissue inhibitor of metalloprotease-1 (TIMP-1) in the B16F10-injected, extract-treated animals. The observed antiangiogenic activity of the plant *T. cordifolia* is related to the regulation of the levels of cytokines and growth factors in the blood.[55]

The aqueous extract of *T. cordifolia* was found to enhance phagocytosis in vitro. The aqueous and ethanolic extracts also induced an increase in antibody production in vivo.[56] *T. cordifolia* extract (TCE) treatment caused significant reduction in eosinophil count and improved hemoglobin in HIV patients. Sixty percent patients receiving TCE and 20% on placebo reported decrease in the incidence of various symptoms associated with disease.[57]

Diabetic patients with foot ulcers on *T. cordifolia* as an adjuvant therapy showed significantly better final outcome with improvement in wound healing.[58] Administration of *T. cordifolia* (200 mg/kg body weight) 1 hour before irradiation showed recovery of spleen weight from 49% of control in irradiated group to 93%; apoptosis, from 19% to 2.8%; DNA fragmentation, from 43% to 20.4%; macrophage adherence, from 75% of control to 120%; and macrophage spread size, from 8 µ to 15µ. It also stimulated proliferation in splenocytes in a dose-dependent manner. Administration of *Tinospora cordifolia* (Tc) before irradiation also increased levels of IL-1beta and GM-CSF from 56 pg/mL and 53 pg/mL in irradiated group to 59 pg/mL and 63 pg/mL, respectively. Similarly, radiation-induced decrease of antioxidant potential of plasma [32 Fe(2+) equiv.] as compared to control [132 Fe(2+) equiv.] was countered by administration of Tc before irradiation [74.2 Fe(2+) equiv.]. RTc treatment thus suggesting its radio-protective mechanism.[59] Ten days of treatment with *T. cordifolia* (100 mg/kg/d) induced a significant ($P < 0.01$) increase in the number of (Colony Forming Units of ranulocyte-macrophage series (CFU-GM; 255 ± 49.32 vs. 38.51 ± 9.98). This suggests that activation of macrophages by *T. cordifolia* leads to increase in GM-CSF, which leads to leukocytosis and improved neutrophil function.[60].

4. CONCLUSION

A plant with as diverse a role as *Tinospora cordifolia* is a versatile resource for all forms of life. According to reports, plant extracts contain active substances in the form of alkaloids, glycosides, lactones, and steroids, as was already mentioned. All of these active substances have various immunomodulatory and physiological functions, highlighting the plant's wide range of adaptability. Research must be done to understand how the active substances alter the links between structure and function in living systems.Exploiting the molecular and signalling pathways of Tinospora's active ingredients will continue to be the review's future focus in order to facilitate efficient disease targeting. Tinosporia is a plant that has a lot to offer the scientific community in the field of medicine.

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