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Pharmacological and Phytochemical Review of Tinospora cordifolia (Willd.): A Traditional Herb with Modern Therapeutic Potential

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ABSTRACT
Tinospora cordifolia (Willd.) Miers, commonly known as Guduchi, is one of the most valued medicinal plants in the traditional Indian system of medicine, particularly Ayurveda. Over the years, it has garnered significant attention from researchers due to its broad therapeutic potential and minimal toxicity. This review compiles and critically evaluates the existing literature on the phytochemical profile, pharmacological activities, and pharmacodynamic mechanisms of Tinospora cordifolia, highlighting its relevance in modern drug discovery and integrative medicine.
Phytochemical investigations reveal that Tinospora cordifolia contains a rich spectrum of bioactive compounds including alkaloids, glycosides, diterpenoid lactones, steroids, phenolics, flavonoids, and polysaccharides. These constituents are primarily responsible for its wide-ranging biological effects. The plant exhibits multiple pharmacological activities such as antioxidant, anti-inflammatory, antidiabetic, hepatoprotective, nephroprotective, cardioprotective, immunomodulatory, anti-cancer, anti-microbial, and neuroprotective effects. Several of these effects have been validated through in vitro assays, animal models, and some preliminary clinical evaluations.
Mechanistically, Tinospora cordifolia modulates various cellular signaling pathways including NF-κB, MAPK, and Nrf2. It has been shown to regulate cytokine levels, scavenge free radicals, inhibit pro-inflammatory mediators, and improve metabolic function. Immunologically, it enhances both humoral and cell-mediated immunity, making it useful in managing conditions of immune suppression and chronic inflammation. Its adaptogenic and rejuvenating properties have led to its wide use in formulations designed for general health improvement and disease prevention.
Despite its extensive traditional use and encouraging preclinical data, challenges remain in the form of standardization, identification of active principles, pharmacokinetic profiling, and large-scale clinical trials. The lack of regulatory standards and inconsistency in extract formulations also hinder its integration into mainstream therapeutics.
In conclusion, Tinospora cordifolia is a pharmacologically versatile medicinal plant with significant therapeutic promise. It serves as a strong candidate for the development of novel phytopharmaceuticals targeting inflammatory, metabolic, and immunological disorders. Future research should focus on clinical validation, mechanistic exploration, and standardization of its extracts to realize its full potential in evidence-based medicine.
KEYWORDS: Tinospora cordifolia, Guduchi, Immunomodulatory activity, Antioxidant properties, Diterpenoid lactones, Herbal therapeutics.

I. INTRODUCTION

In the contemporary era of globalization and modernization, the rising risk of numerous diseases, both infectious and non-infectious, can be attributed to lifestyle changes (such as stress, work pressure, and climate variations) and unhealthy dietary habits among individuals.[1] The World Health Organization has indicated that 80% of the global population primarily depends on traditional medicines that utilize plant extracts or their active components. India, with its vast biodiversity and extensive knowledge of ancient traditional medical systems (including Ayurveda, Siddha, Unani, Amchi, and local health practices), offers a robust foundation for the use of a wide variety of plants in general healthcare and the treatment of common ailments.[2] Medicinal plants have served as natural remedies since prehistoric times. Various methods have demonstrated the medicinal value of plants, including the direct use of crude plant extracts due to their natural chemical constituents. A significant number of plants are employed in medicine for

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therapeutic or preventive purposes[3]. Among the extensive collection of significant plants, Tinospora cordifolia (wild) is a deciduous climbing shrub belonging to the Menispermaceae family. This family comprises approximately 70 genera and 450 species found in tropical regions. It is distributed throughout India and also in parts of Sri Lanka, Bangladesh, and China.[4] As an effective adaptogen and aphrodisiac, this climbing shrub has exhibited considerable potential for the development of biopharmaceutical products aimed at treating various diseases.[5]A range of active compounds sourced from the plant, such as alkaloids, steroids, diterpenoid lactones, aliphatics, and glycosides, have been extracted from various parts of the plant, including the root, stem, and entire plant. Recently, this plant has garnered significant attention from researchers worldwide due to its reported medicinal benefits, which include anti-diabetic, anti-periodic, anti-spasmodic, anti-inflammatory, anti-arthritic, anti-oxidant, anti-allergic, anti-stress, anti-leprotic, anti-malarial, hepatoprotective, immunomodulatory, and anti-neoplastic properties[6].

Tinospora cordifolia is one of the most commonly utilized herbs in Ayurvedic medicine, having been extensively employed by communities and tribes as a healing herb for various ailments. Tinospora cordifolia holds significant value in Ayurveda due to its diverse medicinal attributes, including rejuvenation, immune enhancement, anti-rheumatic effects, and detoxification properties.

In contemporary medicine, the herb has undergone extensive evaluation and research, and most recently, the drug has been utilized to alleviate the adverse effects of chemotherapy. This review emphasizes the phytochemical analysis, pharmacological factors, and its potential for scientific inquiry to advance further in the realm of traditional medicine.

PHARMACOGNOSTIC DESCRIPTION:

It is a sizable deciduous climbing shrub that spreads extensively, featuring multiple coiled branches exhibiting various morphological types. The plant's stem is slender, fleshy, and climbing in nature, while the bark ranges from white to gray[7].The powder derived from the stem is either creamish brown or dark brown in color, has a distinctive odor, a bitter taste, and is utilized for treating dyspepsia, fever, and urinary disorders[8].The starch derived from the stem is referred to as "Guduchi-satva." It possesses high nutritional value and aids digestion. The leaves of this plant are simple, arranged alternately, and have long petioles (about 15 cm); they are round, pulvinate, heart-shaped, and partially twisted. The lamina is ovate, measuring 10–20 cm in length, has seven nerves, is deeply cordate at the base, and is membranous[9].The leaves are a vibrant dark green color. Further, its lamina is showing multicoated reticulate venation.The bark is juicy, featuring deep grooves and large rosette-shaped lenticels. Its color ranges from creamy white to grey. Long, thread-like aerial roots emerge from the branches. The branches themselves are elongated and have a dirty white or light greyish-brown hue. Flowers are unisexual, small, and exhibit a greenish-yellow color on auxiliary and terminal racemes. Male flowers are found in clusters, while female flowers typically appear in solitary inflorescences. Each flower consists of six sepals, which are free and arranged in two series of three, along with six petals that are also free, smaller than the sepals, and have an ovate, membranous structure[8].Flowers bloom in the summer months (March to June), whereas fruits mature in the winter (November). The fruits are orange-red in color, fleshy, and consist of 1-3 ovoid, smooth droplets attached to a thick stalk with sub-terminal style scars[10].The curved seed and embryo have been detailed in guduchi[11]. Therefore, this family is referred to as the moonseed family.

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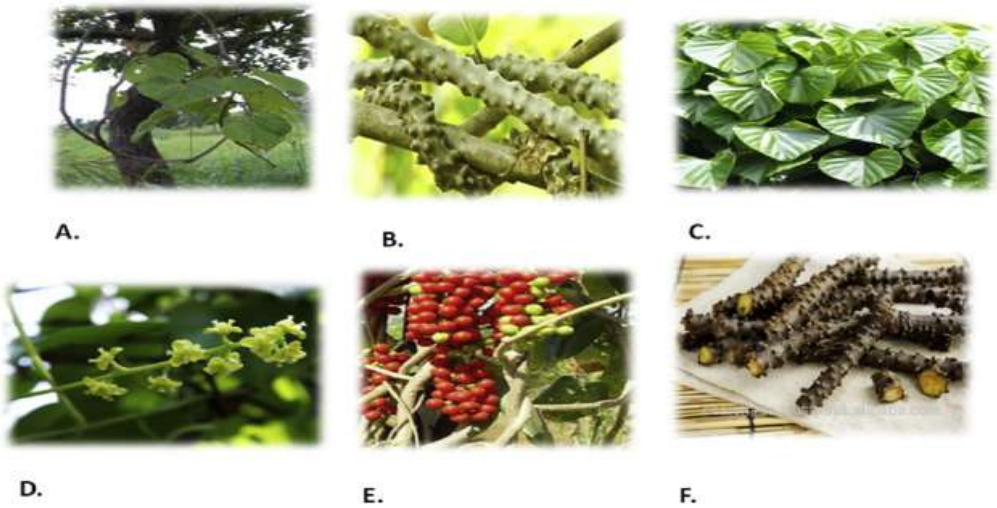

Fig. 1 Morphology of Tinospora cordifolia A) steam B) root C) leaves D) flower E) fruit F) seed.

TAXONOMY[12]

Kingdom	Plantae-Plant
Subkingdom	Tracheobionta-Vascular plant
Super division	Spermatophyta-Seed bearing plant
Division	Magnoliophyta – Flowering
Class	Magnoliopsida – Dicotyledons
Sub-class	Polypetalae – Petals are free
Series	Thalamiflorae – Many stamens and flower hypogynous
Order	Ranales
Family	Menispermaceae – The Moonseed family
Tribe	Tinosporeae
Genus	Tinospora
Species	cordifolia

Tab 1: Taxonomical classification of Tinospora cordifolia

VERNACULAR NAMES[13]

Language	**Names**
Telugu	Guduchi, Iruluchi
Arabic	Gilo
Assamese	Amarlata
French	Culancha
English	Tinospora
Sanskrit	Guduchi, Amrita
Hindi	Gulancha
Kannada	Amrutaballi, Madhuparni
Malayalam	Amrytu, Chittamritam
Gujarati	Gado,galo, gulo
Bengali	Gadancha, guluncha
Oriya	Gulochi
Tamil	Amridavalli, Niraidarudian
Urdu	Guruch

Tab 2: Different names of Tinospora cordifolia

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PHYTO ACTIVE COMPOUNDS OF Tinospora cordifolia

T. cordifolia (Guduchi) primarily comprises alkaloids, glycosides, steroids, diterpenoid lactones, sesquiterpenoid, aliphatic compounds, essential oils, and a blend of fatty acids, calcium, phosphorus, protein, and polysaccharides[14].

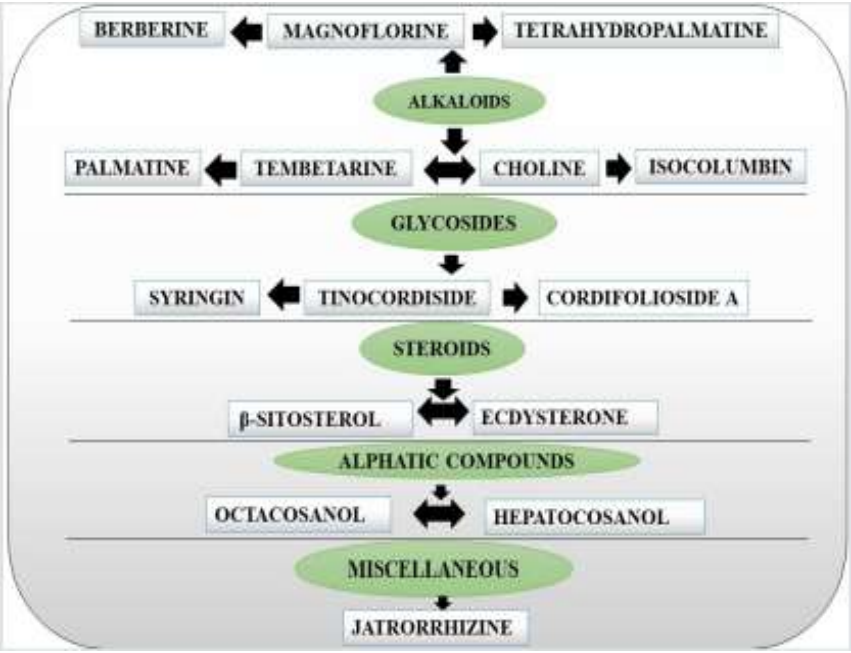

Fig 2 Phyto active compounds of Tinospora cordifolia

ACTIVE COMPOUNDS AND THERAPEUTIC ACTIVITY OF Tinospora cordifolia

CLASS	CHEMICAL CONSTITUENTS	USES	PLANT PARTS
Alkaloids[15-20]	Berberine, Magnoflorine, CholinePalmatin, Tembetarine, Tinosporine, Isocolumbin, Aporphine alkaloids, Jatrorrhizine, Tetrahydropalmatine	Anti-viral infections Neurological, Immunomodulatory anti-diabetes, Anticancer	Stem and root
Steroids[21-23]	20 δ -Hydroxyecdysone, δ sitosterol, β –sitosterol, Giloinsterol Ecdysterone, Makisterone A	Inhibits TNFα, IL-1 β, IL-6 and COX2. inflammatory arthritis, IgA neuropathy	Shoot
Glycosides[24-27]	Tinocordiside, Tinocordifolioside, Cordioside, 18-norclerodane glucoside, Cordifolioside Syringin, Syringinapiosyl glycoside, Furanoid diterpene Glucoside, Palmatosides, Cordifolioside A, B, C, D and E, Pregnane glycoside	Anticancer activities Treats neurological disorders like ALS, Parkinsons, Dementia	Stem
Diterpenoid lactones[28-32]	Furanolactone , Tinosporon, Tinosporides , Columbin, Clerodane derivatives, Jateorine	Anti-inflammatory, anti-microbial, anti-viral, Anti hypertensive, Vasorelaxant Induce apoptosis in leukemia by activating caspase-3and bax, inhibits bcl- 2	Whole plant
Sesquiterpenoid	Tinocordifolin	Antiseptic	Stem

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Aliphatic compounds[33-35]	Heptacosanol, Octacosanol, Nonacosan-15-one dichloromethane	Anti-inflammatory, Protection against 6- hydroxy dopamine induced parkinsonism's in rats	Whole plant
Miscellaneous compound[36-37]:	3,(α,4-di hydroxyl-3-methoxybenzyl)-4-(4- Compounds hydroxyl-3- methoxy-benzyl)-tetrahydrofuran ,Giloinin, Tinosporic acid, Tinosporidine, Cordifol, Cordifelone, Jatrorrhizine, Ntrans-feruloyltyramineas diacetate	Protease inhibitors for HIV and drug-resistant HIV.	Whole plant & Root

Tab 3: Phytohemical constituents and their Pharmacological activity of Tinospora cordifolia

THERAPEUTIC ACTIVITY OF Tinospora cordifolia

Tinospora cordifolia has long been acknowledged as one of the most widely utilized plants in traditional medicine due to its spasmolytic, allergen-free, and anti-diabetic properties. This plant plays a significant role in enhancing the immune system. It is endowed with numerous beneficial attributes. The root is particularly noted for its ability to relieve stress and combat malaria, while the stem is employed as a bitter stomachic and diuretic. It promotes biliary secretion, enriches the blood, and helps in the treatment of jaundice. The primary biological activities of Tinospora cordifolia are as follows.

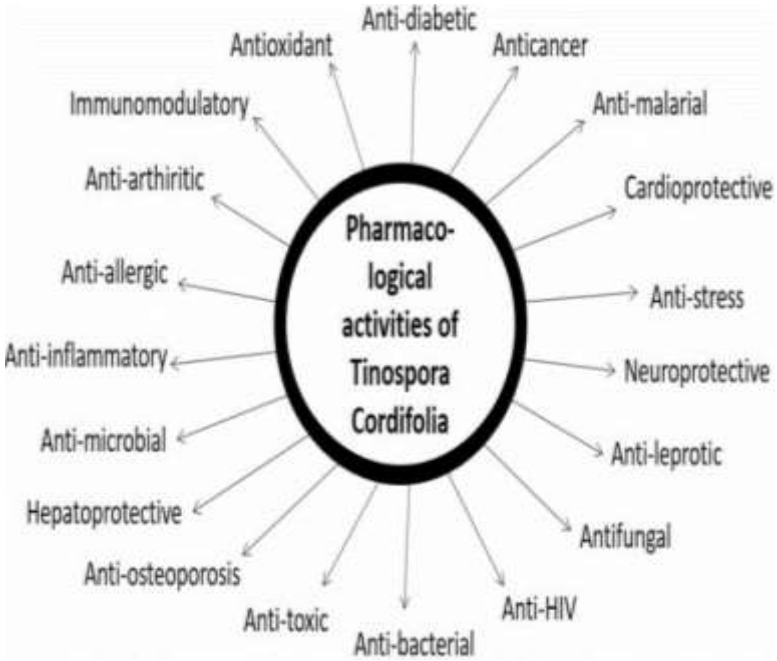

Fig 3: Pharmacological activity of Tinospora cordifolia

Anti-diabetic activity

In a diabetic rat model, extracts from the root of guduchi have been shown to reduce brain-mediated lipid levels and lower both blood and urinary glucose levels, underscoring their anti-diabetic and lipid-lowering effects38. The root extract of guduchi exhibits an antihyperglycemic effect in an alloxan-induced diabetic model by normalizing the elevated glucose levels found in both urine and blood[39]. The anti-diabetic properties of Tinospora cordifolia, along with its active compound palmatine, primarily operate through an insulin-dependent pathway, while also enhancing the expression of Glut-4 and PPAR. Berberine, a close analogue of palmatine, has been demonstrated to exert its effects by facilitating Glut-4 translocation and increasing AMP-activated protein kinase (AMPK) activity in L6 myotubes, as

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well as modulating lipogenic genes to reduce lipid accumulation in 3T3-L1 cells[40]. The crude extract of the stem, when analyzed in ethyl acetate, dichloromethane (CDM), chloroform, and hexane, was evaluated for its ability to inhibit the alpha-glucosidase enzyme. This enzyme's activity was found to inhibit hypoglycemic action in both diabetic and normal animals. In studies involving rats, the aqueous extract was administered without the addition of Tinospora cordifolia extract, resulting in a 21.3% increase in glucose, a 51.5% rise in insulin, a 54.12% increase in triglycerides, and a 59.8% rise in the glucose-insulin index when the plant-containing extract was given. Additionally, the fructose-induced liver abnormalities related to lipid peroxidation, protein carbonyl groups, GSH levels, and enzymatic antioxidants were found to decrease[9]. extracts from Tinospora cordifolia stems can enhance glucose uptake via glucose transporters 1 (GLUT1) and 3 (GLUT3), which are essential for basal glucose absorption. Therefore, we selected Ehrlich ascites tumor (EAT) cells as a model, as they express both GLUT1 and GLUT3, and we assessed glucose uptake using the fluorescent analog 2-[N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino]-2-deoxy-D-glucose (2-NBDG). The results indicated that various solvent extracts of Tinospora cordifolia stems, particularly those using water, ethanol, and methanol, exhibited glucose uptake activity. This uptake was observed to increase in a dose-dependent manner at concentrations ranging from 1 to 100 µg. Interestingly, the glucose-stimulating effect does not appear to be solely attributed to the polyphenol content, as the methanol extract, which contains a significant amount of polyphenols (9.5±0.1 gkg−1), did not demonstrate a higher glucose uptake compared to the water extract[41].

Anti-oxidant activity

The dried leaves of Tinospora cordifolia were powdered and extracted using chloroform, methanol, ethanol, hexane, and water. Antioxidant assays were conducted through various in-vitro models, including lipid peroxidation inhibitory activity, DPPH radical scavenging, and superoxide radical scavenging activity. Other solvent extracts exhibited weak antioxidant activity, while the ethanol extract demonstrated high antioxidant activity. The findings indicated that the antioxidant compounds are more effective in the ethanol extract, and there is a direct correlation between the total polyphenols extracted and their antioxidant activity[42]. The administration of ethanolic extract of Tinospora cordifolia (EETC) in male Wistar albino rats with liver cancer induced by Nnitroso diethylamine (DEN) restored the levels of lipid peroxidation (LPO) and both enzymatic and non-enzymatic antioxidants to nearly normal[43].

Anti-HIV activity

Pepsin was used as a substitute for HIV-protease to evaluate inhibitory activity of these extracts, as pepsin has close resemblance with HIV-protease in proteolytic activity. Extracts of O. sanctum and Tinospora cordifolia showed potent inhibitory activity with IC50 values of 123.73 and 11.20 µg/ml respectively. In our earlier study, these extracts exerted their anti-HIV activity via multiple mechanisms of action; viz., interference with the gp120 / CD4 interaction and inhibition of HIV-reverse transcriptase[44]. The n-hexane and n-butanol crude extracts of Tinospora cordifolia showed moderate cytotoxic activities against PBMCs with CC50 values ranging from 5.7-12.0 µg/ml. In the HIV-1 reverse transcriptase assay T. cardifolia plant extracts showed good inhibitory activity, which was near that of the reference drug. Ethyl acetate extract shows 85 percentage of HIV-1 RT inhibition activity at a concentration of 20 mg/ml[45].

Anti-cancer activity

Tinospora cordifolia shows anti-cancer activity, this activity is mostly shown in animal models. The extraction of alkaloid palmatine from Tinospora cordifolia by using response surface methodology (RSM) clearly indicate the anticancer potential in 7,12- dimethylbenz(a)anthracene DMBA induced skin cancer model in mice. A single application of Tinospora cordifolia extract at a dose of 200, 400 and 600 mg/kg dry weight, 24 hrs prior the i.p. administration of cyclophosphamide (at the 50 mg/kg), significantly prevented the micronucleus formation in bone marrow of mice, in a dose dependent manner. C57 Bl mice when received 50% methanolic extract of Tinospora cordifolia at a dose 750 mg/kg body weight for 30 days showed increase in life span and tumor size was significantly reduced as compared to control [46].The various phytocomponents identified from the studies analyzed in the systematic review included berberine, new clerodane furanodiptherine ,glycosidae, elligic acid, kaempferol, N-formylannonain,magnoflorine, jatrorrhizine palmatine, 11-hydroxymustakone, cordifolioside A, tinocordiside, yangambin, anthraquinones, terpenoids, saponins and phenol,

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pyrrole-based small molecules, quercetin and rutin, arabinogalectian, palmatine, clerodane-derived di-terpenoids and hexane fractions. These phytocomponents induced anticancer effect via mitochondrial-mediated apoptosis, cytotoxic activity, mutagenic activity, reduction in tumor size, triggering reactive oxygen species, decreased gene expression of the cell cycle, effectively inhibiting cancer proliferation. Berberine (BBR) is a natural active principle with potential antitumor activity. The compound targets multiple cell signaling pathways, including proliferation, differentiation, and epithelial–mesenchymal transition. BBR treatment resulted in a time- and dose-dependent down regulation of 33 genes differently involved in cell cycle, differentiation, and epithelial–mesenchymal transition[47]. The presence of BBR in Tinospora cordifolia extract plays a significant role in its antiproliferative activity. One study demonstrated that the extract of Tinospora cordifolia can inhibit the expression of various genes associated with the development and progression of colon cancer. The effects observed from Tinospora cordifolia treatment were closely mirrored by pure Berberine (BBR). This evidence indicates that the primary effects of Tinospora cordifolia are mediated by Berberine (BBR). The capacity to markedly reduce the expression of genes related to proliferation, differentiation, cell motility, and EMT suggests the need for further research to investigate the potential of these substances as chemotherapeutic agents in colorectal cancer[48].

Immunomodulatory activity

Tinospora cordifolia is well known for its immunomodulatory response. Ethyl acetate, water fractions and hot water extract exhibited significant immunomodulatory activity with an increase in percentage phagocytosis. Chromatographic purification of these fraction led to the isolation of a mixture of two compounds 2, 3 isolated for the first time from natural source and five known compounds 1, 4–7 which were characterized as 11-hydroxymustakone (2), N-methyl-2-pyrrolidone (3), N-formylannonain (1), cordifolioside A (4), magnoflorine (5),tinocordiside (6), syringin (7) by nuclear magnetic resonance (NMR) and mass spectrometry (MS) and comparing the spectral data with reported one. Cordifolioside A and syringin have been reported to possess immunomodulatory activity. Other five compounds showed significant enhancement in phagocytic activity and increase in nitric oxide and reactive oxygen species generation at concentration 0.1–2.5 g/ml[49]. The immunomodulatory activity of Tinospora cordifolia ethanolic extract (100 mg/Kg/p.o.) stem through altering the concentration of antioxidant enzymes, increasing T and B cells and antibody which play an important role in immunity, enhancing the concentration of melatonin in pineal gland and increasing the level of cytokines like IL-2, IL-10 and TNF-α which plays an important role in immunity[50].

Anti-microbial activity

The presence of biologically active phytocompounds like berberine, an alkoloidic compound and the bitter compounds like tinosporin, tinosporic acid, tinosporal, a complex mixture of fatty acids and essential oils that are responsible for the expression of the antibacterial or the general antimicrobial activity of the plant extract. At a concentration of 3 mgs., the zone of inhibition of 25.6 mm was found with Tinospora cordifolia, followed by 15.8 mm with O. tenuiflorum against S. mutans, and 0.12% chlorhexidine, at 21.7 ± 0.43 mm. A zone of inhibition of 23 mm and 22.9 mm was observed in both Tinospora cordifolia and O. tenuiflorum against C. albicans, respectively. Positive control of nystatin showed 26.1 ± 0.46 mm[51].The larger zones of inhibition exhibited by Tinospora cordifolia extract may be due to the presence of variety of active secondary metabolites such as tannins, cardiac glycosides, saponins, and others in plant extracts which are responsible for their antimicrobial activity[52]. The active compound [(5R, 10R)-4R, 8R-Dihydroxy-2S, 3R:15, 16-diepoxycleroda13 (16), 17, 12S, 18, 1S-dilactone] was isolated from ethanol extract of Tinospora cordifolia stem showed activity against bacteria and fungi. The lowest MIC values were observed against Enterococcus faecalis (125 µg/ml) and Bacillus subtilis (200 µg/ml). The compound also showed activity against fungi; the lowest minimum inhibitory concentration values were seen against Trichophyton simii (31.25 µg/ml), Trichophyton rubrum 57 (62.5 µg/ml), Trichophyton rubrum 296 (62.5 µg/ml) [53].

Anti-arthritic activity

The polyphenols present in Tinospora cordifolia extract(TCE) were identified through HPLC analysis. TCE significantly reduced the levels of pro-inflammatory mediators (IL-6, TNF-α, PGE2, and NO) in LPS-stimulated RAW 264.7 cells. Additionally, the elevated expression of

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COX-2 and iNOS that occurred after LPS stimulation was also diminished by TCE. Moreover, TCE affected the upstream kinases of the JAK/STAT pathway, which is a vital inflammatory pathway. The expression of VEGF, an important angiogenic factor and inflammatory mediator, was also lowered after pre-treatment with TCE. The anti-arthritic properties of TCE (150 mg/kg) were assessed in the CIA model as well. Histopathological results indicated that oral administration of TCE effectively alleviated clinical symptoms of arthritis, including paw edema, erythema, and hyperplasia. In vivo findings corroborated the in vitro results, showing a significant decrease in serum levels of pro-inflammatory cytokines and mediators (IL-6, TNF-α, IL-17, NO, and PGE2). Furthermore, the phosphorylation of STAT3 and the expression of VEGF were also reduced following TCE treatment[54].

Anti –allergic activity

The anti-allergic properties of an aqueous extract of the stem of Tinospora Cordifolia was evaluated on histamine induced bronchospasm in guineapigs, capillary permeability in mice and mast cell disruption in rats. The aqueous extract of Tinospora cordifolia demonstrated an average protection rate of 95fl.09 against 5% histamine aerosol-induced broncho-constriction in guinea pigs. This result was comparable to the average protection rate of 78f4.6 provided by pheniramine maleate, the standard antihistamine medication. Additionally, Tinospora cordifolia exhibited a notable protective effect on mast cells in rats. It resulted in a 22.8%f2.23 disruption of mast cells, in contrast to 85.5f8.17 observed in the control group. Finally, the aqueous extract significantly reduced capillary permeability in mice. The extract significantly decreased the bronchospasm induced by 5% histamine aerosol, decreased capillary permeability and reduced the number of disrupted mast cells in the above experimental animals respectively[55]. Tinospora cordifolia significantly reduced all allergic rhinitis symptoms while also being well-tolerated. The anti-allergic and bronchodilator properties of an aqueous extract of the stem were tested on histamine-induced.

Anti-inflammatory activity

The anti- inflammatory properties of an aqueous extract of the stem of Tinospora Cordifolia was evaluated on Carrageen an induced paw edema rats. Animals were divided in three groups, having six animals in each. Group A received test drug, Group B received market sample at a dose of 50 mg/kg orally, while Group C (control group) received tap water. Reduction in edema was observed in Group A and B at 3 h interval by 33.06% and 11.71% respectively. Group A showed significant effects ($P < 0.05$) in comparison to control group. These experimental results have shown anti-inflammatory activity of Guduchi Ghana[56]. The anti inflammatory activity of Tinospora cordifolia is due to the presence of flavanoids, alkaloids and phenols which decrease the production of inflammatory mediators like IL-6, Cox, and bradykinins[57].

Hepato-protective activity

Tinospora Cordifolia extract also deleted the immunosuppressive effect of CCl4, since a significant increment in the functional capacities of rat peritoneal macrophages (PM phi) was observed following Tinospora Cordifolia treatment[58]. Tinospora Cordifolia extract is a potent hepato-protective agent. It is assumed that this hepato-protective effect of Tinospora Cordifolia may be due to several reasons such as antioxidant and/or free radical scavenger property and ability to induce hepatic regeneration.

Anti-osteoporosis

Cell morphology studies clearly indicated the increase in cell numbers and absence of adverse change in the cell morphology on treatment with the extract. Tinospora cordifolia extract has a potential influence on osteogenesis and hence its use could be explored as a potential anti-osteoporotic agent.The evaluation of effects of the alcoholic extract of Tinospora cordifolia (TC) on the proliferation, differentiation and mineralization of bone like matrix on osteoblast model systems in vitro and hence its possible use as a potential anti-osteoporotic agent. Two in vitro osteoblast model systems were used in the study viz., human osteoblast-like cells MG-63 and primary osteoblast cells isolated from femur of rats. Cell growth and viability was assessed by standard colorimetric assays like MTT assay. The cell differentiation into osteoblastic lineage was evaluated by the activities of bone marker alkaline phosphatase. The effect of the extract on matrix mineralization was assessed by alizarin red-s staining and Von kossa staining. Cell morphology was studied by phase contrast microscopy and light microscopy (Giemsa/crystal violet staining). Results indicate that the alcoholic extract of TC at a dosage of 25 g/ml stimulated the

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growth of osteoblasts, increased the differentiation of cells into osteoblastic lineage and increased the mineralization of bone like matrix on both the osteoblast model systems used in the study. Cell morphology studies clearly indicated the increase in cell numbers and absence of adverse change in the cell morphology on treatment with the extract. TC extract has a potential influence on osteogenesis and hence its use could be explored as a potential anti-osteoporotic agent[59].

Anti-fungal activity

Methanolic leaves and stem extracts of Tinospora cordifolia has higher antifungal activity in comparision to ethanolic leaves and stem extracts against test fungal species in the form of inhibition zone[60]. Leaves of T.cordifollia are rich in protein and fairly rich in Ca and P.Anti-fungal chemical constituents such as giloin, columbin, chasmanthin, palmatin, isocolumbin, tembetarine, cordioside, palmatin, tinosporin, tinosporic acid have been isolated from different parts of Tinosporacordifolia[61].

Neuro protective activity

Tinospora cordifolia extract in STZ induced neurotoxicity and evaluating mechanisms responsible for attenuating neuropathic pain. Leaf extract significantly relieved thermal hyperalgesia and allodynia by increasing the antioxidant enzymelevels, decreasing the lipid peroxidation and by increasing the Nerve growth factor (NGF) expression in diabetic rat sciatic nerves[62]. Tinospora cordifolia ethanol extract (TCEE) exhibited significant neuroprotection by increasing the dopamine levels (1.96 ± 0.20 and 2.45 ± 0.40 ng/mg of protein) and complex I activity (77.14 ± 0.89 and 78.50 ± 0.96 nmol/min/mg of protein) at 200 and 400 mg/kg respectively when compared with negative control group. Iron asymmetry ratio was also significantly attenuated by TCEE at 200 (1.57 ± 0.18) and 400 mg/kg (1.11 ± 0.15) when compared with negative control group. Neuroprotection by TCEE was further supported by reduced oxidative stress and restored locomotor activity in treatment groups. The increased levels of dopamine by the treatment of TCEE might be due to decreased metabolism of dopamine or due to increased biosynthesis of dopamine by the dopaminergic neurons present in SN. The increased dopamine levels by TCEE is further supported by the anti-stress and anti-depression activity of Tinospora cordifolia root extract in which dopamine levels were normalized after treatment[63].

Anti-stress activity

The serum glucose, lipid like triglyceride, cholesterol, cholesterol and psychological parameters like anxiety, depression were significantly increases in patients with chronic mental stress. However following treatment with Tinospora cordifolia associated with practice of yoga significantly reduced various stress induced psychological and biochemical parameters ($P< 0.001$)[64]. In Ayurveda Tinospora cordifolia (Willd.) Miers, has been used for its Rasayana, Deepana, Jwaranashana, TridoshaSha maka properties. It is an immunomodulator, useful in stress. It is found to be safe on hematological and biochemical organ function tests and has muscle strengthening, lipid lowering action in healthy individuals. It has been shown that the immune system can function as a neuroendocrine organ since it can synthesize not only hormones and neuropeptides but also cytokines that have an impact on the neuroendocrine system. Tinospora cordifolia improved physical performance and suppressed over activation of the sympathetic nervous system showing its adaptogenic property[65]

Cardioprotective activity

Cardiovascular disease is currently the most common disease globally, exerting a heavy personal and economic toll. The drugs used in the treatment for the cardiac arrhythmia are called anti-arrhythmic drugs such as quinidine, amiodarone, propafenone, veramapril and lignocaine, which are some of the examples of anti-arrhythmic drugs. Very few anti-arrhythmic drugs have been successful in the last few decades due to safety concerns or limited benefits in comparison to existing therapy . The present study investigated the antiarrhythmic activity of alcoholic extract of T. cordifolia (Tinospora cordifolia) in CaCl2 induced arrhythmia. CaCl2 (25 mg/kg) was administered by intravenous infusion (iv) to produce arrhythmia in rats. The animals were then treated with Tinospora cordifolia extract (150, 250, and 450 mg/kg) and verapamil (5 mg/kg,iv). Lead II electrocardiogram was monitored. Plasma calcium, sodium and potassium levels were measured. In CaCl2 induced arrhythmia, heart rate was decreased by 41.10%, T. cordifolia at 150, 300, and 450 mg/kg decreased the heart rate by 26.30%, 29.16%, and 38.29%, respectively, and verapamil reduced the heart rate by 9.70% compared to the normal group. The PQRST waves were normalized and atrial and ventricular fibrillation was controlled in rats treated

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with verapamil and Tinospora cordifolia. $CaCl_2$ increased calcium and sodium levels and decreased potassium levels in blood. Tinospora cordifolia dose-dependently decreased calcium and sodium levels and increased potassium levels. Hence, Tinospora cordifolia can be used in anti-arrhythmic clinical settings and beneficial in atrial and ventricular fibrillation and flutter and may be indicated in ventricular tachyarrhythmia[66]. The methanolic extract of Tinospora cordifolia in the dose of 350 mg/kg and 650 mg/kg body weight was administered orally for 28 days before isoprenaline administration to test their cardio protective effect. Isoprenaline (85 mg/kg) was administered subcutaneously on days 29th and 30th, respectively in order to induce myocardial infarction. The parameters for evaluation of cardio protective activity were the physical parameters and the biochemical estimations. The physical parameters were gross examination of heart, heart weight/body weight ratio and histopathology examination. In biochemical estimations, the activity of various cardiac enzymes such as aspartate transaminase, alanine transaminase, creatinine kinase, lactate dehydrogenase, and the gold marker troponin-I were determined. The levels altered by isoproterenol were restored significantly by the administration of the both doses of test extract especially at higher dose. The result of this study shows that methanolic extract Tinospora cordifolia has significant cardioprotective activity against isoprenaline induced myocardial infarction[67].

II. CONCLUSION

Tinospora cordifolia (Willd.) Miers, a prominent medicinal plant in Ayurveda, demonstrates a broad spectrum of pharmacological properties due to its rich repository of bioactive compounds including alkaloids, glycosides, steroids, diterpenoid lactones, sesquiterpenoids, and polysaccharides. As reviewed, various parts of the plant particularly the stem and root—have shown significant therapeutic activities such as anti-diabetic, anti-inflammatory, anti-oxidant, immunomodulatory, anti-cancer, anti-viral, antimicrobial, hepatoprotective, neuroprotective, and cardioprotective effects.

The pharmacological potential of Tinospora cordifolia is supported by extensive in vitro and in vivo studies, which reveal mechanisms of action involving modulation of cytokines, antioxidant pathways, glucose metabolism, apoptotic signaling, and gene expression related to inflammation, immunity, and cell proliferation. Notably, compounds like berberine, palmatine, cordifoliosides, and magnoflorine contribute significantly to its bioactivity.

Despite its widespread traditional use and encouraging experimental evidence, challenges remain in translating these findings into clinical applications. Variability in plant sources, lack of standardized extraction protocols, and limited high-quality clinical trials hinder the development of Tinospora cordifolia-based therapeutic agents. Furthermore, detailed pharmacokinetic, toxicological, and dose-optimization studies are imperative to ensure reproducibility, efficacy, and safety in human subjects.

Future research should focus on the standardization of extracts, elucidation of molecular targets, and rigorous clinical validation. With integrated efforts combining traditional knowledge and modern pharmacological science, Tinospora cordifolia holds considerable promise as a phytopharmaceutical for managing various chronic and infectious diseases.

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