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Phytochemical compounds and their pharmacological activity on *Tinospora cordifolia*

Praveen Garg[1], Jyoti Pandey[2] , Ashwini A. Waoo*3
[1,2] Department of Science, VIMS, Satna (M.P.)
***3Department of Biotechnology, Faculty of Life Sciences and Technology, AKS University, Satna, MP**

Corresponding Author: Dr. Ashwini A. Waoo

Email: ashwiniwaoo@gmail.com

ORCID: 0000-0002-8772-3847

Abstract: Herbal medicines are the most important traditional medicine all over the world. *Tinospora cordifolia* has been an important medicinal plant since the beginning of human civilization. *Tinospora cordifolia* contains different phytochemicals having pharmacological activity, as presented in this review study. *Tinospora cordifolia* is also known as Guduchi, Giloya (Hindi), Amrita (Sanskrit), Giloe, Galo (Gujrati), and Heartleaf moonseed (Hindi). Teppatige (Telugu). It is a shrub generally used in Ayurvedic medicine. Different qualitative analytical methods were used for the phytochemical analysis of *Tinospora cordifolia.* Here, in this review to compile all the updated information on phytochemical and pharmacological activities of *Tinospora cordifolia*, which were performed by 'Kokate' methods. The medicinal properties of *Tinospora cordifolia* are anti-diabetic, anti-malarial, anti-spasmodic, anti-inflammatory, anti-oxidant, anti-arthritic, anti-allergic, anti-leprotic, anti-stress, hepatoprotective, immunomodulatory activity. Under these studies, we are trying to promote the use of herbal medicine and to determine its potential as a source of new drugs.

Keywords: Phytochemical compounds, Pharmacological property, Tinospora cordifolia.

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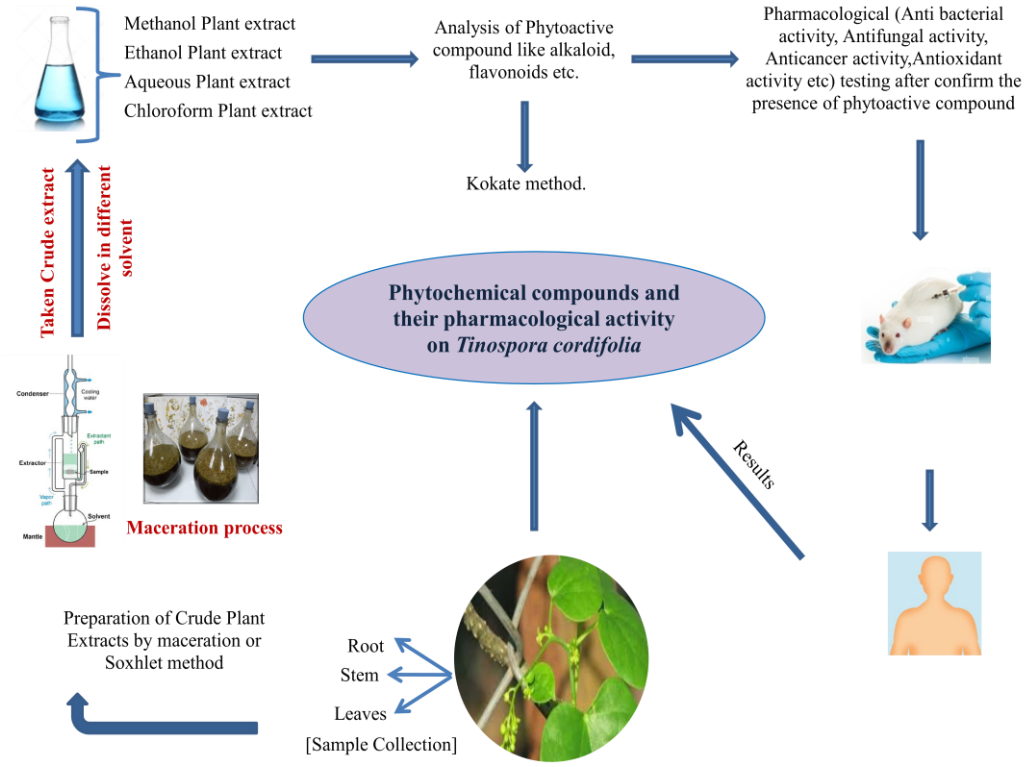
Graphical Abstract



Introduction

Herbal medicines are one of the most important areas of traditional medicine all over the world. Medicinal plants are used to prepare herbal medicine and determine their potential for new drugs. [1] *Tinospora cordifolia* is mostly referred to as Guduchi, Amrita, Giloe, Gulancha, Giloya, Galo, Teppatige, and Heartleaf moonseed. [2] It is a genetically diverse, large, deciduous climbing shrub with green-yellow flowers that belongs to the *Menispermaceae* family found at higher altitudes. [3–5] The male flowers are in cluster form and female flowers are in solitary form in racemes or racemose panicles. The season of flowering expands during summers and winters. [6] This plant is used to treat various diseases such as jaundice, gout, skin diseases, diabetes, etc. It has been established for traditional medicine practices in the history. [7] Guduchi is examined as a nectar plant and known as amrita for recognition of its detoxifying, rejuvenating, and immune-boosting properties. [8] This review focussed on the study of phytochemical and pharmacological properties and its scope in the field of traditional medicine for further improvement.

Botanical Description

It is widely distributed in the areas of India, Myanmar, China, Bangladesh, Sri Lanka, Thailand, Malaysia, Philippines, Indonesia, Vietnam, Borneo, North Africa, West Africa and South Africa.

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[9-12]. Its scientific nomenclature is given in Fig 1. *T. cordifolia* is a climbing shrub that climbs in various types of trees found in tropical areas of the Indian subcontinent. [13] These are usually climbing or twining shrubs and rich sources of alkaloid and terpene chemicals. [14]

Kingdom	**Plantae**
Division	*Magnoliophyta*
Class	*Magnoliopsida*
Order	*Ranunculales*
Family	*Menispermaceae*
Genus	*Tinospora*
Species	*T. cordifolia*
Scientific Name	*Tinospora cordifolia*

Fig 1: Classification of *Tinospora cordifolia*

Morphology

Tinospora cordifolia is a dioecious perennial deciduous climber grown on a wide range of shrubs and trees. It is reported to bear distinct male and female flowers. [15-17] The leaves are simple, heart-shaped, and dark green. It is alternate and entire and the lamina is mostly oval, length is 10 to 12cm and width is 8 to 15 cm showing reticulate venation. [18] The surface of the stems is closely covered with watery tubercles and is longitudinally fissured, 3 to 5cm in length and 3 to 8mm in diameter. [19, 20] Bark act as succulents having deep clefts spotted and large rosette-like lenticels. The bark color is creamy white or gray. Many aerial roots arise from the branches that look like long threads. Branches are long and dirty white or light brown. [21] Flowers are small, uni-sexual, greenish-yellow on auxiliary and terminal racemes. One flower has six sepals, free in

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two series of three each, and six petals which are free, ovate, and membranous smaller than sepals. [22] The male flowers are small, yellow, or green and occur in clusters form in the axils of small subculate bracts. Sepals are very small, yellow, ovate, acute, membranous, elliptical, and concave in shape. Petals are equal, and spathulate, each loosely taking on a stamen, claw cuneate, reflexed margin to apex, and pistillode. Female flowers are normally solitary, with green sepals, margins not reflexed, short staminode, and linear similar to male flowers. Carpels are separated on the short fleshy gynophores, dorsally convexed, and scarlet. Flowers grow during the summer while fruits develop during the winter. Fruits are orange or red in color, fleshy, ovoid, smooth, droplets on thick stalks with sub-terminal-style scars and form curved seeds and embryos. [23-24] The best synergy between these two distinct bitter plants is supposed to be found in neem trees, which increases the effectiveness of Guduchi, according to herbalist Sebastian Pole. According to custom, Guduchi satva is derived from the Guduchi plant that grows on neem trees. *(Azadirachta indica)* is bitterer and more efficacious and is said to incorporate the medicinal values of neem. [25,135]

HISTORY AND AYURVEDIC ASPECTS

T. cordifolia is usually known as "Rasayana" in Ayurveda which implies circulation of rasa the nutrient in Sanskrit. 'Charaka' the ancient Indian physician, described rasayana as anti-aging, higher life span, promotes intelligence, increased memory, and free from diseases, indicating an immunostimulant effect [26] and also used as an antispasmodic and an antidiarrhoeal agent. [27] Indian scriptures known as 'The Vedas', a 5,000-year-old system of Ayurveda medicine rooted in three elemental substances Kapha, Vata, and Pitt. In 'Sushurta Samhita', it was traditionally used for the treatment of several diseases such as Svasa (asthma), Maha Jvara (fever), Aruci (anorexia), and kustha (leprosy).[28] There is big evidence for the treatment of various diseases like Jvara (fever), Vat Rakta (gout), and Kamala (jaundice) in "Ashtang Hridaya and Charak Samhita".[29,30] In 'Bhavya Prakash', it is described as a diuretic, bitter tonic, astringent, and potential curative and aphrodisiac against diabetes, jaundice, dysentery, chronic diarrhea, and skin infections. [31] In 'Dhanvantri Nighantu', it has been described for the treatment of piles bleeding, curing the itching, and cellulitis (skin infection), and promoting longevity. [32]

Medicinal properties of *T. cordifolia* are currently applied in modern medicine for the treatment of cold and flu prevention, liver disorders, skin disorders, immune support, arthritis, and gout, and lately to overcome the adverse effects of chemotherapy. [33] So, now it is clear that *T. cordifolia* is the most important medicinal herb considered by the ancient rishis in Vedic times with great potential (medicinal qualities) of curing several diseases. *T. cordifolia* has been described in Ayurveda in various dosage forms. These include Swaras (juice from the fresh stem (10 to 20 microliters/day), Kalka (fresh stem paste 10 gm per day), Churna (made by Dry stem powder 1 to 3 gm/day), Kwatha (hot water extract from ground dried stem dosage 20–30 ml 2 to 3 times a day), Fant (hot water infusion, 10 to 20 ml/day), Arishta, (stable processed synthesized

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from a decoction of *T. cordifolia*, which containing self-generated alcohol), Satwa (made by sedimented starchful extract of the stem- 750 mg to 2 gm/day) Together with lipid formulations of *T. cordifolia* processed in ghee or oil (Guduchi Ghrita: 10–20 grams per day) and Guduchi Taila (for external application), Ghana (it is a solidified aqueous extract) using a day 500 mg to 1 gm three or four times). [34]

Phytochemistry

The different types of phytochemical compounds found in this plant are classified into several groups such as alkaloids, terpenoids, steroids, glycosides, polysaccharides, and aromatic and aliphatic compounds that occur in their active form responsible for the broad range of medicinal and therapeutic properties (Fig 2). These phytochemical compounds mostly occur in different parts of the plant but highly occur in the stem, leaves, and root parts of the plant. [35] *T. cordifolia* contains mainly alkaloids, steroids, glycosides, aliphatic compounds, essential oils, a mixture of fatty acid, protein and polysaccharides, calcium, and porous. [36] The alkaloids contain bitter gilonin, berberine, and non-glycoside gilonin gilosterol. [37]

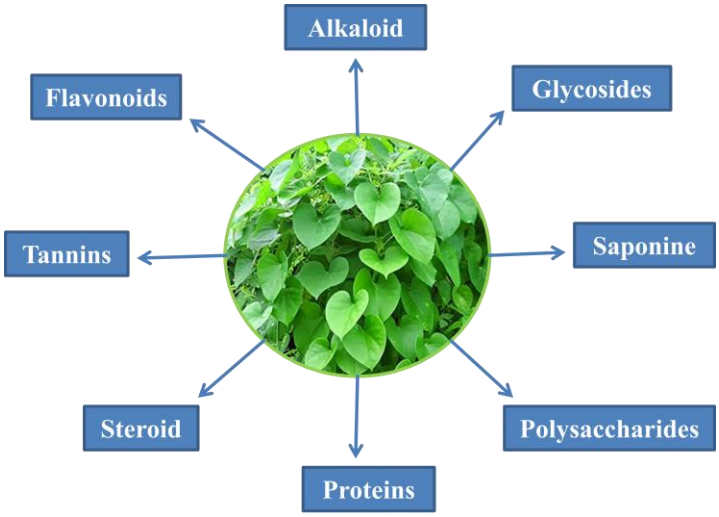

Fig 2: Phytochemical component of *Tinospora cordifolia*

Alkaloids are present in the stem and root of *T. cordifolia* as active constituents. These are named choline, terbutaline, berberine, magnoflorine, isocolumbin, tinosporin, palmetine, aporphine alkaloids, jatrorrhizine, tetrahydropalmatine which showed anti-cancer, anti-viral, anti-diabetes, anti-psychiatric, anti-inflammatory and immunomodulatory action. [38-43] *T. cordifolia* plants contain furanolactone, Codeine derivatives, diterpenoid Lactones, columbine tinosporides, jateorine, and tinosporin. These chemicals represent various biological actions like anti-inflammatory, vasorelaxant, anti-microbial, anti-hypertensive, and anti-viral. [44-47] The Stem part of *T. cordifolia* mainly contains steroids, glycosides, sesquiterpenoids, and tinocorfifolin. Steroids are effective in glucocorticoid-induced osteoporosis in early

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inflammatory arthritis. [48-49] Glycoside plays a role in immunomodulation in Parkinson's disease, dementia, neurological disorders, and motor and cognitive disorders. [50-52] Sesquiterpenoids and Tinocordifolin exhibit antiseptic activity. [53] The other parts of *T. cordifolia* con contain active phytoconstituents e.g. diasporic acid, Jatrorrhizine, tetrahydrofuran, N-trans-feruloyl tyramine as diacetate, groin showed a protective effect against HIV (human immunodeficiency virus). [54-55]

Pharmacological Properties

Tinospora cordifolia has been extensively used in the traditional medicine system (Fig 3). This plant possesses several useful properties that significantly improve the immune system. [56] *T. cordifolia* is also known essential chemical constituent, which includes a combination of fatty acids, alkaloids, glycosides, steroids, phenols, terpenoids, and essential oils, all constituents are separated during the first screening process. The supply of active phytochemical components such as b-sitosterol, columbin, tinosporine, tinosporide, tinosporaside, heptacosanol, and furano diterpene is these vital major phytoconstituents of T. cordifolia. [57, 136] The major biological activities of *T. cordifolia* include the following.

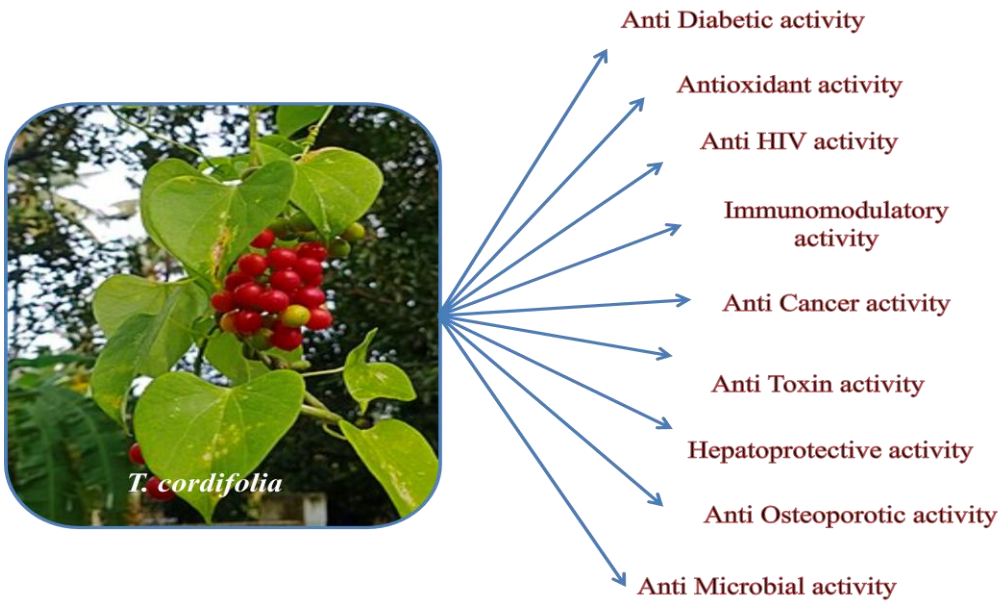

Fig 3: Pharmacological properties of *Tinopora cordifolia*

Anti- Diabetic Property

The stem of Tinospora cordifolia is predominantly used in the treatment of diabetes, where it effectively regulates blood glucose levels in traditional medicine. Various phytochemicals isolated from Tinospora cordifolia, such as alkaloids, glycosides, flavonoids, tannins, and

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steroids, possess anti-diabetic activity [58]. Alkaloids, for instance, have been found to exhibit insulin-like activity, demonstrating actions mediated by insulin [59]. Studies have shown that administering T. cordifolia to diabetic pregnant rats as part of their regular daily diet provides a protective effect, reducing the incidence of diseases and any birth defects [60].

The anti-diabetic properties of Tinospora cordifolia function through several mechanisms: it reduces oxidative stress (OS), enhances insulin secretion, and inhibits gluconeogenesis and glycogenolysis processes [61]. Research indicates that the alkaloid fraction extracted from the stem contains compounds such as palmatine, magnoflorine, and jatrorrhizine, which demonstrate both insulin-mimicking and insulin-releasing effects in laboratory and animal studies [58]. Additionally, extracts from the roots of Tinospora cordifolia have shown antihyperglycemic effects, effectively lowering excessive glucose levels in urine and blood to normal ranges in diabetic models induced by alloxan. These extracts have also been observed to reduce levels of glycosylated hemoglobin, plasma thiobarbituric acid reactive substances, ceruloplasmin, hydroperoxides, and vitamin E in diabetic rats. The phytochemical activity of the plants grown under salinity stress was estimated by using an appropriate biochemical assay. Comparative analysis of the photochemical activity of the test plants in comparison with the control revealed that various phytochemicals were increased in response to salt stress (Gupta and Waoo 2022).

The root extract of Tinospora cordifolia has been shown to increase body weight and total hemoglobin content, along with enhancing hepatic hexokinase activity [62]. Additionally, it decreases hepatic glucose-6-phosphatase activity, as well as serum levels of acid phosphatase (ACP) and lactate dehydrogenase (LDH) in diabetic rats, thereby producing hypoglycemic and hypolipidemic effects [63] [64]. The extract of T. cordifolia is rich in antioxidants and enzyme molecules, which exhibit protective effects [65]. Studies have reported that stem extracts of T. cordifolia possess anti-diabetic potential by enhancing insulin secretion from pancreatic beta cells and promoting pathways that inhibit glucose formation through increased glycogenesis, thereby reducing endogenous glucose levels [66]. Furthermore, oral administration of leaf extracts from T. cordifolia has demonstrated anti-diabetic effects in diabetic rat models induced by streptozotocin. This effect operates through various peripheral pathways, including enhanced glycogen storage, improved glucose transportation, and other mechanisms [67].

Immunomodulatory Property

T. portfolio plant contains several active compounds like 11-hydroxymustakone, N-formylannonain, N-methyl-2-pyrrolidone, magnoflorine, cordifolioside A, tinocordiside, etc. [67] has been reported to have lots of potential for cytotoxic effects and immunomodulatory. [54,68–70] *T. cordifolia* stems highlight the immune-protective role, maintaining the immune strength and altering the enzyme levels such as catalase, which stimulates lymphocyte cells. [71] When *T. cordifolia* extract is exposed to macrophage cells, it increases the production of myeloperoxidase enzymes, improves the anti-microbial activity to protect immunity, and increases the phagocytic activity of macrophages. It has been reported that stimulated

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splenocytes and macrophage cells produce reactive oxygen species (ROS) in neutrophil cells of humans, enhancing nitric oxide (NO) production, which indicates anti-tumor effects as well as immuno-protective activity. The extracts of *Tinospora cordifolia* have been reported to enhance the production of cytokines, mitogenicity, activation, and stimulation of effector cells of the immune system. [72-73] It has been stated that the lotion of *T. cordifolia* causes a decline in interleukin level i.e. IL-1 and IL-6 in scabies contagious disease. It inhibits hyperkeratosis and infiltration of inflammatory cells into a scabietic person and develops its anti-scabies activity. [74] In the case of mice, extract of *Tinospora cordifolia* controls the level of IL-6 cytokine, consequential acute reactions such as any injury, inflammation in tissues, activation as well as differentiation of both Tc-cells, (cytotoxic T-cell) and B cells. *T. cordifolia* increases the immune cell response and neutrophil activity acts as an effective factor for the treatment of immune susceptible diseases. [75] Aqueous extracts of *T. cordifolia* contain active compounds like alkaloids, glycosides, steroids, phenolics, di-terpenoid lactones, sesquiterpenoid, aliphatic compounds, or polysaccharides [76] responsible for their cytotoxic action in an experimental rat model. A polysaccharide compound known as G1-4A obtained from *T. cordifolia* enhances the proliferation and differentiation of T-cell and B-cell combined with the expression of anti apoptotic gene. [77] Orally administration of alcoholic extract of *T. cordifolia* (100mg/kg) initiates an increase in foot pad thickness and white blood cell count. Bone marrow cells show a potent immunomodulatory activity which represents a stimulatory effect on the overall haemopoetic system. [78, 134] The cytotoxic and immunomodulatory properties of 11-hydroxymustakone, N-methyl2-pyrrolidone, N formylannonain, cordifolioside, magnoflorine, tinocordiside, and also syringing have been documented. [2023]

Anti Cancer property

The anti-cancer properties of *Tinospora cordifolia* are widely studied in animals. *T. cordifolia* extracts have been shown a radioprotective role and protect to mice from the gamma radiation radiated on the testes. When extracts of methylene chloride from *T. cordifolia were* then exposed to the cultures HELA cells in different concentrations like 0,5,10,25,50,100 µg/ml, it increased cell death in comparison to untreated cultured cells. [79] *T. cordifolia* extracts affected radiation in pre-irradiated mice induced lipid peroxidation and decline of GSH concentration in testes.[80] *T. cordifolia* extracts treated with HeLa cells to reduce the cell life, enhance lactate dehydrogenase (LDH) and decrease Glutathione (GSH) S-transferase activity.[81] Extract with dihydrotestosterone (DHT), stimulates the growth and also proliferation of the Human LNCaP cells (These cell lines are human prostate cancer cells that are sensitive to androgen). [82] Recently, isolated substances, such as 8R-dihydroxy-2S, 3R-15,16-diepoxycleroda, dilactone, and a diterpenoid, have been shown to have chemopreventive potential in diethylnitrosamine (DEN)-induced hepatocellular carcinoma (HCC) in rats. It decreased anti-oxidant activities and serum transaminase levels, confirming its anti-tumor effects and working as an effective chemo-preventive drug for HCC. [48] It studied that, the hydroalcoholic root extract of *T. cordifolia* on exposure or contact with the liver and extrahepatic organs of mice shows an increased Glutathione (GSH) and other metabolizing enzymes level. There is a decrease in the level of malonaldehyde (MLD) production, which represents a decreased level of free radical formation and produces an antioxidative state in the cell. [83] Dichloromethane (DCM) extract of *T.*

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cordifolia has been reported its radio sensitive activity in Ehrlich ascite carcinoma (EAC) of mice which decreases the level of GSH and glutathione S transferase by increasing the level of lipid peroxidase and damaging DNA of tumor cells enable tumor-free survival. [41,42,84] In EAC mice TCE of hexane blocks the G1 phase of the cell cycle and causes apoptosis by nuclear condensation, creation of apoptotic bodies, caspase-3 activation, decreased number of cells, increased pro-apoptotic gene expression (*Bax*) and decreased anti-apoptotic (*Bcl-2)* gene expression. TCE reduces the tumor yield, tumor weight, tumor burden, and papilloma formation while increasing the level of detoxifying enzymes in skin carcinoma animals. [84-85] Palmatine extract of *T. cordifolia* indicates the anti-cancer property in a Dimethyl benzanthracene induced (DMBA) skin cancer model in mice. [86] There are many phytochemicals such as mangnoflorine, tinocordiside, jatrorrhizine, palmatine, and yangambin isolated from Tinospora as secondary metabolites having anti-cancer properties were tested in different types of tumor cells. 'Palmatine' and 'Yangambin' were reported to treat keratin-forming tumor cell lines while tinocordiside was for colon cancer cell and oral cancerous cell treatment. [89] Apart from this, most of the chemotherapeutic drugs have several adverse and severe toxic effects which is very less in *T. cordifolia* herbs. So, it can be observed that *T.cordifolia* is used as a 'safe drug' for treating cancer patients. [137, 138].

Anti Toxin Property

It has been reported that extracts of *T.cordifolia* show scavenging free radicals activity during aflatoxicosis. [89] It alters the level of different hormones and mineral and show a protective effect. It can decrease the level of Thiobarbituric Acid Reactive Substances and also enhance the level of glutathione (GSH), protein, ascorbic acid, and activities of anti-oxidant enzymes for example superoxide dismutase (SOD), CAT, and glutathione reductase (GR) and Glutathione S-transferase (GST) in kidney. *T. cordifolia* contains alkaloids like choline, isocolmbin, magnoflorine, tinosporin, palmatine, and tetrahydropalmatine show protective activity against aflatoxin-induced nephrotoxicity. *T. cordifolia* can revert the toxic property of aflatoxin in the kidney where, it increases the glutathione hormone level and catalase, glutathione enzyme reductase activity, and decreases the amount of reactive oxygen species (ROS). All these anti-toxin activities are effective by the plant alkaloids. [89] Generally, the toxicity of lead nitrate in mice shows a decreased value of erythrocytes and leucocytes in blood. Despite that, the leaves and stem extract of Guduchi reduce the lead toxicity and overcome the hematological value. [90]

Hepatoprotective Activity:

T. cordifolia has been shown to hepatoprotective effect in mice (Male: swiss albino) against toxicity of lead nitrate in stem and leaf extract. [91] Oral administration of Tinospora plant extracts prevents the damage of the liver by lead nitrate. [90] Lead toxicity in mice causes decreased levels of CAT, and SOD and increased levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), acid phosphatase (ACP), and alkaline phosphatase (ALP).

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[90] Administration of aqueous stem and leaf extract along with lead nitrate increased the SOD and CAT activities and decreased the ACP, ALT, AST, and ALP enzyme levels.[90] The protective role of *Tinospora cordifolia* aqueous leaves and stem extract overcome the toxic effects of lead and change the hematological values. [91]

Antioxidant Activity:

T. cordifolia extracts exhibit anti-oxidant properties by scavenging the free radicals compound and other reactive species. [92] *T. cordifolia* minimizes the process of lipid peroxidation regulation thus decreasing the free radical level in a model of diabetic rat (alloxan-induced diabetes) and regulates catalase and glutathione antioxidant enzymes indicating its anti-oxidant results. [93, 94] It has been shown that the extract exhibits an antioxidant effect by enhancing GSH levels and reducing the inducible nitric oxide synthase gene expression. It is also useful in cataract treatment by inhibiting the aldol reductase enzyme. [95,96] According to the study, ethanol extracts of bark *T. cordifolia* show the maximum free radical scavenging activity and more phenolic content as compared to the methanol extracts. [97] *T. cordifolia* stem methanolic extracts show antioxidant activity when administered orally by increasing the activity of lipid peroxidase and catalase. Its extracts reduce the SOD, and GPx activities in alloxan-induced diabetic rats. [97,98] *T. cordifolia* extracts have aldose reductase inhibitors and anti-oxidant agents [99] thus inducing free radicals component by reducing chemotoxicity. [101] *T. cordifolia* decreases the malondialdehyde and ROS levels and increases the GSH and total thiol levels. [102] *Tinospora cordifolia* restored glycogen amounts in the liver by repressing the level of glucose 6-phosphatase & fructose 1 6-diphosphatase enzymes and regulated blood glucose levels. [103] *T. cordifolia* aqueous extract has a radio-protective activity that enhanced the mice's survival against a lethal dose of gamma radiation. [104,105] *T. cordifolia* was more effective in elevating the level of GSH, look of the gamma-glutamylcysteine ligase, Cu-Zn SOD genes. [106] *Tinospora cordifolia* aqueous extract inhibited radiation effect mediated by 2-deoxyribose degradation by inhibiting the formation of (Fe^{2+})-bipyridyl complex formation to produce radio-protective effects. [107] *T. cordifolia* contains arabinogalactan polysaccharides having a defense not in favor of free radicals in a rat model which means it indicates anti-oxidant activity. [108] Antioxidant & hydroxyl radical scavenging activities caused by the presence of alpha-glucosidase inhibitor characterized as saponarin (apigenin-6-C-glucosyl-7-O-glucoside) in the leaf extract of *Tinospora cordifolia*. [109] The powder form of leaves of *T. cordifolia* extracted with chloroform, ethanol, methanol, hexane, and as well as in water perform strong antioxidant activity by assay in different *in-vitro* models that show lipid peroxidation inhibitory activity and superoxide radical scavenging activity. The study revealed that the antioxidant activity of *Tinospora cordifolia* mostly occurs in ethanolic extract due to the presence of a polyphenol compound. [110,133]

Anti HIV activity

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Tinospora cordifolia extract has been shown to reduce the level of frequent infection of HIV by improving the therapeutic effect. The root extract of *Tinospora cordifolia* affects the immune system of HIV patients. The stem extracts of *Tinospora cordifolia* decrease the number of eosinophil cell count, hemoglobin level, and polymorphonuclear leucocytes, stimulating B cells. [111,112] The anti-HIV activity of *Tinospora cordifolia* declines the level of infection by decreasing eosinophil count and increasing the CD4 T-cells in HIV-positive patients. *Tinospora cordifolia* extracts markedly enhanced intracellular bactericidal and phagocytic activity and stimulated peritoneal macrophage.

Antimicrobial Activity

Tinospora cordifolia has good antifungal and antibacterial activity with different solvents on different micro-organisms. It has been reported that methanolic extracts of *Tinospora cordifolia* have potential against microbial infections. [113] The extract of *Tinospora cordifolia* possesses antibacterial activity against *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Salmonella typhi, Proteus vulgaris, Shigella flexneri, Salmonella typhimurium, Pseudomonas aeruginosa, Salmonella paratyphi, Enterobacter aerogene,* and *Serratia marcesenses* (Gram-positive bacteria). [114] Tinospora cordifolia extract can enhance neutrophil phagocytic and intracellular bactericidal capabilities in mice by aiding in the clearance of germs. It has been found that TCE stimulates macrophage immunity. [115] *Klebsiella pneumonia* and *Pseudomonas aeruginosa* are both urinary pathogens were suppressed their activity through the acetone, and ethanol-based extract of *T. cordifolia*. [116] The stem of *T. cordifolia* possesses antibacterial activity due to the presence of silver particles besides the different strains of bacteria. [117] The antifungal activity of the aqueous extract *T. cordifolia* was determined by using the agar plate well diffusion method reported by Allemailem *et al.*, against *Aspergillus flavus, and Aspergillus nigar*. [118] Khan *et al.*, studied the antifungal activity of *T. cordifolia* aqueous extract (TCAE) was tested *in vitro* against the different species *of Aspergillus* isolates. Different dosages, such as 10, 25, and 50 mg per kg of *T. cordifolia* aqueous extract were administered orally in *A. fumigates* infected mice for the estimation of activity in the condition of *in vivo* for seven days. The aqueous extract is effective on the basic survival/endurance rate in the kidney of mice. [119] Prasad *et al.* reported the phenolic extract of *T. cordifolia* stem and root possesses anti-oxidant and antimicrobial properties. The ethanolic extract showed maximum free radical scavenging activity about H_2O_2 and hydroxyl free radicals. [120] The hydroalcoholic extract of *T. cordifolia* was effective in enhancing the granulocyte activity in the mammary inflammation known as mastitis. Mastitis occurs due to the infection of *Streptococcus aureus.* This plant has antimicrobial activity against *S. aureus* that prevents the inflammation. [121-122] The importance of guduchi is decreasing the resistance power to different antibiotic therapy. Guruchi has urinary pathogens and it can check microbial infectivity. [123] The stem and leaves of the *T. cordifolia* plant showed higher

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inhibitory action against clinical urinary pathogens like *Klebsiella pneumoniae* and *Pseudomonas aeruginosa and* prevent urinary tract infections. [124,132,138]

Anti-Osteoporotic Activity

According to studies, understand that the alcoholic extract of *T. cordifolia* can increase the rate of proliferation and discrimination of the osteoblast cells which present in humans and rats. It is also involved in the calcification process by producing minerals from bone-forming cells and regulates bone mineralization. [125] *T. cordifolia* possesses a steroid i.e. 'Beta Ecdysone' or 20 hydroxyecdysones, which promotes the muscle tissue formation in the mesenchymal stem cells in its model of mouse and prevents osteoporosis. [126,127] Ecdysteroids isolated from the plant showed anti-osteoporotic effects in the mammals. Beta-ecdysone (Ecd) induces the thickness of joint cartilage and in mouse mesenchymal stem cells cures osteoporosis through an osteogenic differentiation process. [128]. *T. cordifolia* plants showed anti-osteoporotic effects due to the presence of 20-OH-β-Ecd thus playing a major role in the treatment of osteoporosis and osteoarthritis [129-130]. *T. cordifolia* combines with *Zingiber officinale* for the treatment of rheumatoid arthritis. [131]

CONCLUSION:

Recently, the demand for phytopharmaceuticals has been increasing all over the world because there are more side effects caused by allopathic drugs. This provides the selection of plants for further investigation of phytochemical and pharmacology activity. In this review, the pharmacological and clinical studies of *Tinospora cordifolia* confirm their therapeutic value. The presence of phytochemical compounds indicates that the plant serves as a "lead" for disorder in the coming year for the development of novel agents. It is necessary to explore *Tinospora cordifolia* for its efficiency in preventing and treating diseases. So, the current review provides a direction for upcoming investigations to carry out research on this plant and get some medically important drugs. *T. cordifolia* being an ingenious plant constitutes numerous bioactive compounds having therapeutic potential. There are various reports available in pharmacological and clinical studies that authenticate the curative and preventive role of this plant against different illnesses. The different phytoactive compounds for example glycosides, steroids sesquiterpenoids, etc. have potential applications mainly as immunomodulators and anti-oxidant agents. The various studies conducted on *T. cordifolia* revealed that it is a magnificent drug and does not have any toxic effects. Overall, the present review provides knowledge about the antidiabetic, anti-toxin, anticancer, antioxidant, immunomodulatory, and antimicrobial activity of *T. cordifolia* that can be used in further investigations for the development of novel drugs. *T. cordifolia* is a plant that has flexible resources for life. It has been already discussed that the plant extracts of *T. cordifolia* have phytoactive compounds such as alkaloids, lactones, glycosides, steroids, etc. All these phytoactive compounds have various pharmacological roles, which enable the plant used in the treatment of different diseases. There is a further need to study

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how the phytoactive compounds truly interact with living organisms and show an effect on the functional relationships. The future aspect of this review remains in the biochemical pathways of signaling of phytoactive compound contained by *T. cordifolia* therefore enabling the effective mechanism against targeting disease. The plant Tinospora strictly acts as an incredible source in the scientific world of medicine.

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