

# Phytochemistry and Pharmacology of *Tinospora cordifolia*: A Review

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## ABSTRACT

The use of indigenous drug industry in India has been widely expanded in recent years. *Tinospora cordifolia* (Guduchi) belonging to family Menispermaceae has a wide array of bioactive principles in exploring nutraceuticals from plant materials. It is a versatile resource for all forms of life and can be an alternative for synthetic drugs considering their adverse effects and also for economic purposes. *T. cordifolia* is considered as an important herbal drug of Indian System of Medicines (ISM). The herb is known for its therapeutic efficacy and used in treatment of dyspepsia, diabetes, fever, urinary problems, jaundice, chronic diarrhoea, cardiac disease, dysentery, helmenthiasis, skin diseases, leprosy and many more diseases. Present review highlights the classical anti-toxin, anti diabetic, anticancer, immunomodulatory, antioxidant, antimicrobial, hepato-protective activity of Guduchi and their validation through existing literature. The plant is reported to contain

alkaloids, glycosides, steroids and terpenoids. The current study is undertaken to explore and establish the phytochemistry and pharmacological activity of *T. cordifolia*.

**Key words:** Bioactive compounds, Guduchi, Menispermaceae, Pharmacological action, *Tinospora cordifolia*.

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## INTRODUCTION

*T. cordifolia* commonly called as Guduchi is a natural herbal shrub that belongs to the moonseed family Menispermaceae. This plant is useful in treatment of several diseases like jaundice, skin diseases, gout, diabetes etc. which has been established in the history of traditional medicine practices.<sup>1</sup> In this perspective, guduchi is considered to be a nectar plant and has been called as amrita in Sanskrit in recognition of its detoxifying, rejuvenating, and immune boosting properties.<sup>2</sup> In modern medicine, the herb has been evaluated and studied more profoundly and most recently the drug is implemented to mitigate the negative effects of chemotherapy. The review focuses on the phytochemical study, pharmacological aspects and its scope for the scientific investigation for further progress in the field of traditional medicine.

## METHODOLOGY

We have exhaustively reviewed many published literature on recent developments in research of *T. cordifolia*, including original articles and papers as secondary data from various search engine such as Pubmed, Pubmed Central Databases, Google Scholar, Crossref, WorldCat, Harvard library, Mendeley, Scilit, Cite factor, Shodhganga, Science Central, AYUSH Research Portal, Open J-Gate, Biblioteca were taken into consideration for the report. Medical advancements and the effects of *T. cordifolia* observed with different experiments were collected for the review purpose.

## PLANT DESCRIPTION

Guduchi is a large extensively spreading glabrous, perennial deciduous twine with succulent stems and papery bark which is widely found in India, Myanmar and Sri Lanka. It is native to the tropical region of India ascending to an altitude of 500 metres in the temperature range of 25 to 45 °C.<sup>3</sup> The leaves are simple, heart shaped and dark bright green in colour. Further, it is alternate, estipulate, entire and the lamina is broadly ovate 10-12 cm long and 8-15 cm broad showing multicoated reticulate venation.<sup>4</sup> The surface of the stems appears to be closely studded with warty tubercles and the surface skin is longitudinally fissured, having 3-5cm

length and 3-8mm in diameter.<sup>5,6</sup> Bark is succulent, with deep clefts spotted and large rosette-like lenticels. The colour of bark is creamy white or grey. Long thread-like aerial roots arise from the branches. Branches are long and dirty white or light greyish brown in colour.<sup>7</sup> Flowers are unisexual, small, and greenish yellow on auxiliary and terminal racemes. Male flowers are clustered whereas female flowers usually exist in a solitary inflorescence. A flower has six sepals, free in two series of three each and six petals which are free and smaller than sepals, ovate and membranous.<sup>8</sup> Flowers grow during the summer (March to June) while fruits develop during the winter (November). Fruits are orange-red in colour, fleshy, aggregate of 1-3 ovoid, smooth, droplets on thick stalk with a sub terminal style scars.<sup>9</sup> Curved seed and embryo have been described in guduchi.<sup>10</sup> Hence, the family is named as moonseed family. Moreover, the endocarp is variously ornamented (Figure 1).

## HISTORY AND AYURVEDIC ASPECTS

Ayurveda a 5,000-year-old system of medicine, names three elemental substance such as Kapha, Vata and Pitta rooted in Indian scriptures known as The Vedas. As per Ayurvedic text viz: Ashtang Hridaya and Sushrut, Charak and other treaties like Bhava Prakash and Dhanvantri Nighantu *T. cordifolia* named as : Amara, Amritvalli, Chinmarrhuha, Chinnodebha and Vatsadani etc, and most commonly recognised as Guduchi or Amrita.<sup>11-15</sup> In Sushurta Samhita, under Tikta-SakaVarga, it is traditionally claimed for the treatment of several diseases like Svasa (asthma), Maha Jvara (fever), Aruci (anorexia) and kustha (leprosy).<sup>14</sup> In context of Ashtang Hridaya and Charak Samhita, there is also a great evidence for the treatment of different diseases like Jvara (fever), Vat Rakta (gout) and Kamala (jaundice).<sup>13,15</sup> In Bhavya Prakash, it is considered as diuretic, astringent, bitter tonic and potential curative and aphrodisiac against jaundice, diabetes, chronic diarrhea, dysentery and skin infections.<sup>16</sup> In Dhanvantri Nighantu, it has been depicted for treatment of bleeding piles, curing itching, erysipelas and promoting longevity.<sup>17</sup> Additionally, guduchi has been shown as: Deepanam (kindles digestive fire), Laghu (light), Dhatukrit (builds the seven bodily

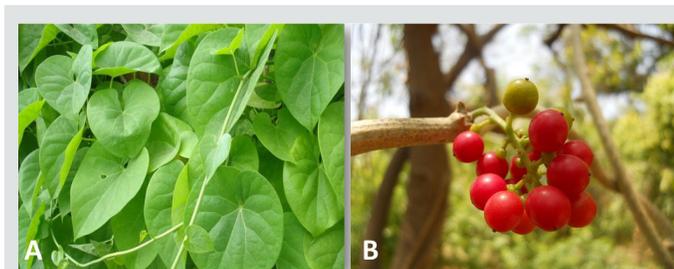


Figure 1: A: Whole plant, B: Stem part of the plant.

tissues), Chakshushyam (good for the eyes), Bayasthaapankarakam (maintains youthfulness and longevity) and Medhayam (rejuvenating for the mind).<sup>18</sup>

Guduchi has been considered by European practitioners in India as a major source of medicament like tonic, diuretic and antiperiodic and further it was comprised in Bengal Pharmacopoeia of 1868.<sup>19</sup> According to Ayurvedic literature *T. cordifolia* is a major constituent of formulations used for the treatment of several disease such as dyspepsia, urinary related diseases debility and fever. Some of the imperative formulations prepared from *T. cordifolia* are: Guduchi taila, Sanjivani vati, Kanta-Kari avaleha, Guduchyadi churna, Chyavnaprasha, Guduchu ghrita, Guduchi satva, Brihat guduchi taila, Amrita guggulu, amritashtaka churna and many more.

*T. cordifolia* is the mostly used herbs of Ayurvedic medicine that, has been widely used by folks and tribal as a remedial herb for the treatment of various diseases. *T. cordifolia* is highly valuable in Ayurveda for its numerous medicinal properties like rejuvenating, immune-boosting, anti-rheumatic and detoxifying properties. Medicinal properties of *T. cordifolia* is presently applied in modern medicine for treatment of cold and flu prevention, skin disorders, liver disorders, immune support, gout, arthritis and lately to overcome the adverse effects of chemotherapy.<sup>18</sup> So, now it is clear that *T. cordifolia* is most important medicinal herb considered by the ancient rishis in Vedic times with a great potential (medicinal qualities) of curing number of diseases.

## PHYTOCHEMISTRY

*T. cordifolia* (Guduchi) mainly consists of alkaloids, glycosides, steroids, aliphatic compounds, essential oils, mixture of fatty acid, calcium, phosphorous, protein and polysaccharides (Figure 2).<sup>20</sup>

## ACTIVE COMPONENTS AND THERAPEUTIC ACTIVITIES OF *TINOSPORA CORDIFOLIA*

Stem and root part of *T. cordifolia* contain alkaloids as active constituents. These are tembetarine, choline, magnoflorine, berberine, tinosporin, isocolumbin, palmetine, jatrorrhizine, aporphine alkaloids, tetrahydropalmatine which showed anti-cancer, anti-diabetes, anti-viral, anti-inflammatory, anti-psychiatric and immunomodulatory action.<sup>21-26</sup>

Further, whole plant of *T. cordifolia* contain furanolactone, diterpenoid Lactones, Cleodrane derivatives [(5R, 10R)-4R-8R-dihydroxy-cleroda-13(16), 14-dieno-17, 12S:18, 1S-dilactone], columbin tinoporides, tinosporin, jateorine. They showed biological actions such as Vasorelaxant, anti-inflammatory, anti-microbial, anti-hypertensive and anti-viral.<sup>27-31</sup> Shoot part of *T. cordifolia* contains Steroids (B-sitosterol,  $\delta$ -sitosterol, 20  $\beta$ -hydroxyecdysone, giloinsterol, Makisterone A, Ecdysterone). They are effective in glucocorticoid induced osteoporosis in early inflammatory arthritis. They induce cell cycle arrest in G2/M phase and inhibits TNF- $\alpha$ , IL-1  $\beta$ , IL-6 and COX-2 and apoptosis through c-Myc suppression.<sup>32-34</sup>

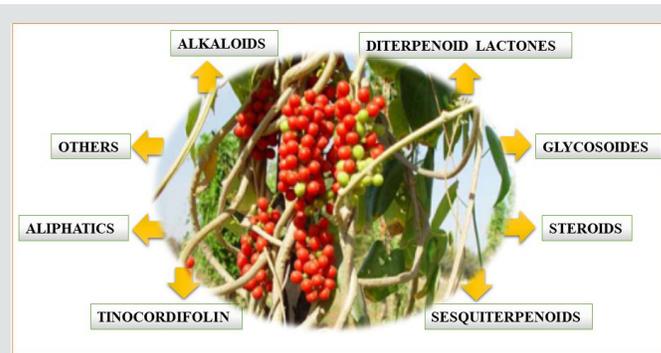


Figure 2: Active Compounds of *T. Cordifolia*.

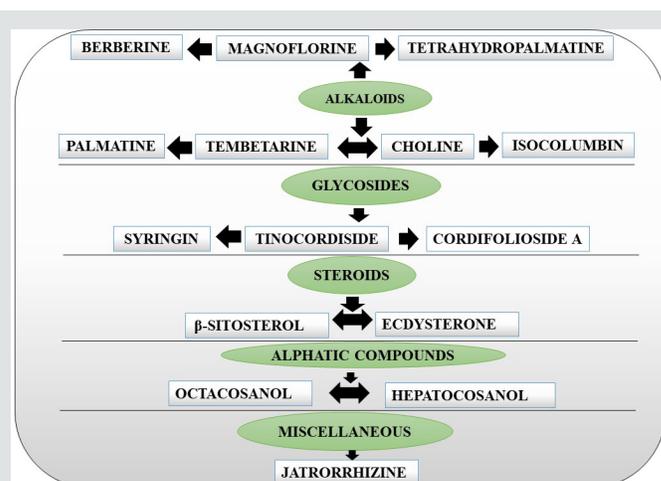


Figure 3: Phytoactive Constituents of *T. cordifolia*.

Stem part of *T. cordifolia* contain Glycosides. Their active constituents are 18-norcleodrane glucoside, Tinocordifolioside, Cordioside, cordifolioside A, B, C, D and E, Furanoid diterpine glucoside, Syringin, pregnane glycoside Syringing-apiosylglycoside, palmatosides. They showed immunomodulation in Parkinson's disease, dementia, motor and cognitive disorder, neurological disorders like ALS. They inhibit NF-k Band to show anti-cancer properties.<sup>35-41</sup> Whole plant of *T. cordifolia* contain aliphatic compounds. The active constituents are Octacosanol, Nanocosanol-15-one dichloromethane, Heptacosanol. They showed anti-nociceptive and anti-inflammatory activity. They also inhibit TNF- $\alpha$  from binding to the DNA and provide protection against 6-hydroxydopamine induced Parkinsonism in rats.<sup>42-44</sup>

Stem part of *T. cordifolia* contain Sesquiterpenoids and Tinocordifolin which exhibits an antiseptic activity.<sup>45</sup> The other parts of *T. cordifolia* contain active constituents such as Jatrorrhizine, Tinosporic acid, 3, (a, 4-dihydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxy-benzyl) tetrahydrofuran, N-trans-feruloyltyramine as diacetate, Giloin. They showed a protective effect against HIV (human immunodeficiency virus).<sup>46,47</sup> The chief Phytoconstituents of *T. cordifolia* are diterpenoid furano lactone, cordifolide, cordifol, heptacosanol, tinosporide,  $\beta$ -sitosterol, tinosporine, clerodane furano diterpine, tinosporaside, and columbin respectively (Figure 3). Alkaloids such as magniflorine, Berberine, palmetine, non-glycoside gilonin gilosterol, tembetarine, choline and tinosporin has been reported from the stem part of the *T. cordifolia*.<sup>48</sup>

## PHARMACOLOGICAL ASPECTS

*T. cordifolia* has been recognised as most extensively used plant since ages in traditional system of medicine for its spasmolytic, allergen-free and anti-diabetic property. The plant significantly improves immune system. This plant possesses many useful properties. Its root part is known for its stress relieving and antimalarial properties while its stem is being used as bitter stomachic and diuretic. It stimulates biliary secretion, enrich the blood and cure jaundice. The major biological activities of *T. cordifolia* include the following.

### ANTI-CANCER/ANTI-TUMOR ACTIVITY

Various experimental models of animal have been taken to show the anti-cancer activity of plant guduchi. The radio protective property is well characterized by this plant as it considerably increases the weight of various tissues as well as body weight. In addition to this, it also protects from the gamma radiation (sub-lethal range) radiated on the testes of mice (Swiss Albino). The cultured HeLa cells when exposed to different concentration of methylene chloride extracts of *T. cordifolia* such as 0.5, 10, 25, 50, and 100 µg/ml; it showed an increase in cell death or cell killing as compared to untreated cultured cell (control) in a dose-dependent manner.<sup>49</sup> A study has also reported that, the hydroalcoholic extract of roots (aerial) of *T. cordifolia* on exposure to the liver as well as extrahepatic organs of mice (Swiss Albino) at 50 and 100mg/kg body weight shows an increase in Glutathione (GSH) level and other metabolizing enzymes. In addition to this, there is a significant decrease in production of malonaldehyde (MLD) level representing a decrease in free radical formation providing an antioxidative state of cell.<sup>50</sup>

An exposure of hexane extract of guduchi on mice having Ehrlich ascites tumor shows an inhibition of the proliferation of these tumor cell (G1 phase) and simultaneously it enhances the expression of 'Bax' gene (pro-apoptotic) leading to apoptosis principally brought by caspases.<sup>51</sup> Guduchi has been reported to possess a potent anti-tumor activity through a two-stage skin carcinogenesis model conducted in mouse. It shows a decrease in papillary tumors, its weight and its occurrence while it also brings up the level of phase-II enzymes in the treatment group correspondingly.<sup>52</sup>

*T. cordifolia* exhibited an add-on effect when combined with  $\gamma$ -radiation on mice introduced with cultured Ehrlich cells by decrease in Glutathione (GSH) level causing oxidative damage to these cancerous cells.<sup>53</sup> Guduchi extract in researcher's skin cancer model has shown to prevent the degree of micronucleus production in bone marrow cell and hence, increase the survival time in mice. However, *T. cordifolia* in combination with cyclophosphamide drug exhibits a cumulative effect in tumor inhibitory rate and survival percentage respectively.<sup>54</sup> An extract of the isolated active constituent palmatine of plant *T. cordifolia* clearly indicates the anti-cancer potential in a Dimethylbenzanthracene induced (DMBA) skin cancer model conducted in mice (Swiss Albino).<sup>55</sup> *T. cordifolia* also possesses anti-neoplastic property as it has significant ability in treating the brain tumor in C-6 glioma cell by decreasing the proliferation and differentiation rate as reported.<sup>56</sup>

The anti-cancer activity of secondary metabolite (such as magnoflorine, palmatine, jatrorrhizine, yangambin etc.) isolated from guduchi were tested in different type of tumor cells and among them 'palmatine' and 'yangambin' reported to treat KB cells while tinocordiside for colon cancer cell and oral cancerous cell (KB) respectively.<sup>57</sup> On the contrary, most of the chemotherapeutic agents are synthetic by nature and have a number of adverse as well as severe toxic effects which is very minimal in case of herb *T. cordifolia*. So, it can be considered as a 'safe drug' for treating cancer disease as far as patient health is concerned.

### ANTI-TOXIN ACTIVITY

Guduchi have a potential ability to scavenge free radical and shows a protective effect by altering different hormone and mineral levels. *T. cordifolia* has reported to reverse the toxicity caused by aflatoxin in kidney (Swiss albino mice) where, it substantially elevates the hormone level (such as Glutathione) and enzyme activities (such as catalase, glutathione reductase); and decreases the reactive oxygen species (ROS). And this anti-toxin activity is primarily brought by the alkaloids of this plant.<sup>58</sup> Lead nitrate toxicity in swiss albino mice shows a decreased value in erythrocyte and leucocyte count in blood serum.

However, the leaf and stem extract of guduchi works against these changes by overcoming the lead induced toxicity over haematological value.<sup>59</sup> This herbal plant extract when given orally has also reported to counter the toxic effects caused by lead nitrate in mice (swiss albino) liver. The study shows a decrease in level of the enzymes like glutamic pyruvic transaminase (GPT) or alanine aminotransferase (ALT) and aspartate aminotransferase (AST) and a rise in the enzyme responsible for scavenging free radical such as catalase.<sup>60</sup> *T. cordifolia* has found its importance in overcoming cyclophosphamide induced toxicity by substantially elevating the level of lowered GSH content, cytokines and gradually declining inflammatory cytokines (Tumor necrosis factor) level in urinary-bladder and hepatic cell preventing the damage which confirms its anti-toxin activity.<sup>61</sup>

### ANTI-DIABETIC ACTIVITY

The compounds such as alkaloids, cardiac glycosides, saponins, flavonoids, tannins and steroids isolated from guduchi possess anti-diabetic property. Hence, it makes possible to have wide application in clinical as well as experimental study. Alkaloids from guduchi stated to possess the effect like insulin hormone and shows insulin mediated actions.<sup>26</sup> Gestational Diabetes can increase the GSH content and other reactive species that can act as a threat to the mother as well as fetus. However, a study stated that when *T. cordifolia* has been given in daily diet to a diabetic-pregnant rat (streptozocin induced diabetes), it shows a protective effect by reducing the oxidative load thereby preventing the relative incidence of diseases and any sort of birth defect.<sup>62</sup> In diabetic rat model, root extracts of guduchi attenuate the brain mediated lipid level and downregulates the blood glucose and urinary glucose level emphasizing its anti-diabetic and lipid lowering activity.<sup>63</sup>

The root extract of guduchi shows antihyperglycemic effect in alloxan induced diabetic model by decreasing its excess glucose level in urine as well as in blood to a range of normal.<sup>64</sup> Medicinal herbal preparations like Ilogen-Excel, Hyponidd and Dihar consist of number of herbal plants including guduchi. When these preparations have been tested in diabetic rat models, it was seen that the anti-diabetic activity is solely due to *T. cordifolia*. The effects by Ilogen Excel reported to turn down the level of excess glucose in blood and enhance the insulin efficiency by increasing its amount in the systemic circulation. Hyponidd is reported to maintain the oxidative load by decreasing reactive species and reduced the glucose mediated haemoglobin count. 'Dihar' when tested for one and half month in streptozotocin induced diabetic model decreased the urea as well as creatinine amount in blood with subsequent increase in enzyme activities.<sup>65-67</sup>

The stem extract of *T. cordifolia* is reported to have anti-diabetic potential by enhancing the insulin efficiency through its secretion from beta pancreatic cell and promoting various anti-diabetic pathway such as inhibiting glucose formation by enhancing glycogenesis etc. thereby decreasing the endogenous glucose.<sup>68</sup> Extract of guduchi in a clinical study is reported to inhibit the glucosidase enzyme which thereby decreases the post meal increased glucose level.<sup>69</sup> Oral administration of

leaf extracts of *T. cordifolia* has also found anti-diabetic potential when tested in diabetic rat model (streptozotocin induced diabetes) through different peripheral pathways such as glycogen storage, transportation of glucose and other mechanisms.<sup>70</sup>

## IMMUNOMODULATORY ACTIVITY

Isolated chemical compounds such as cordifolioside A and syringin of guduchi are reported as immunomodulating agent in the clinical study.<sup>71</sup> *T. cordifolia* stem alters the level of enzymes such as catalase and stimulates lymphocyte cells maintaining the immune strength, thus highlighting the immuno-protective role of this shrub.<sup>72</sup> Macrophage cell when exposed to *T. cordifolia* extract, increases the production of different enzymes including 'myeloperoxidase' that enhances the anti-microbial action so as to protect the immunity.<sup>73</sup> On the other hand, it also increases the phagocytic activity of macrophages. Additionally, it stimulates splenocytes and macrophages. Because of enhanced nitric oxide production signifying anti-tumor as well as immuno-protective activity.<sup>74</sup> A clinical study stated that, *T. cordifolia* lotion causes a decline in the level of interleukin i.e. IL-1 and IL-6 in scabies animal model. It inhibits hyperkeratosis and infiltration of inflammatory cells into scabetic gash, showing its anti-scabies activity.<sup>75</sup> Aqueous extract induces cellular mitosis, stimulates the production and activation of cytokine and immune effector cells.<sup>74</sup>

*T. cordifolia* is also able to increase the response of immune cell and neutrophil activity highlighting it as a potent agent for the prophylaxis of immune susceptible diseases.<sup>76</sup> Compounds of guduchi including alkaloids, steroids, aliphatic compounds etc when tested preclinically in rat model has shown a potent immuno-protective activity.<sup>77</sup> A polysaccharide compound obtained from *T. cordifolia* recognised as G1-4A enhances the proliferation and differentiation of immune cells i.e. T-cell and B-cell associated with the expression of the anti-apoptotic gene.<sup>78</sup> The compound  $\alpha$ -D-glucan obtained from TC has shown to maintain the body physiology by activating the cells of lymphocytes.<sup>79</sup> Polymorphonuclear leucocyte (PMN) cells are important components of the host defense system. Extracts of *T. cordifolia* stimulated the PMN cells for phagocytosis.<sup>80</sup> Oral administration of *T. cordifolia* alcoholic extract (100mg/kg) initiates an increase in foot pad thickness as well as in white blood cell (WBC) count and bone marrow cells indicating a stimulatory effect on haemopoietic system which shows a potent immunomodulatory action.<sup>81</sup> A classical preparation of an aqueous extract of *T. cordifolia* named as 'Ghana' in Ayurveda when tested on the edema rat model, it reduced the edematogenic agents and thus has a potent immunostimulatory action.<sup>82</sup>

## ANTI-MICROBIAL ACTIVITY

A study reported that silver nanoparticles synthesized from the stem of *T. cordifolia* possess good antibacterial activity against the bacteria *Pseudomonas aeruginosa* found in the patient suffering from burn injury.<sup>83</sup> Various bacterial strains such as *S.typhi*, *K.Pneumoniae*, *E.coli*, *Aeruginosa* and other bacteria have been tested against extracts of *T. cordifolia* and showed potential anti-bacterial activity by either inhibiting their growth or mitigating the very existence of these bacteria.<sup>84,85,86</sup> An active chemical compound that has been found from the stem of *T. cordifolia* as reported, found to be effective against bacteria like *E.faecalis* and *B.subtilis* and fungus like *T. Simii* and *T.rubrum*.<sup>87</sup> A hydro alcoholic extract of *T. cordifolia* was effective in the mammary inflammation induced in bovine model by enhancing the activity of granulocyte. As mastitis is due to the infection of *S. aureus*, prevention of this inflammation showed the antimicrobial activity of this plant.<sup>47,88</sup>

The stem and leaves of this plant showed maximum inhibitory activity against the clinical urinary pathogens such as *Klebsiella pneumoniae* and

*Pseudomonas aeruginosa*. Thus, it prevents the urinary tract infections.<sup>89</sup> Carbapenamases being a hydrolytic enzyme hydrolyzes the  $\beta$ -lactam antibiotics and turns out to be ineffective. So, when the extract of this plant tested against penicillinase resistant  $\beta$ -lactam antibiotic (methicillin) and carbapenamase enzyme producing bacteria it shows high rate of inhibition as compared to the referral microbial strain.<sup>90</sup> Guduchi has also found its importance by decreasing the resistance to different antibiotic therapy by the urinary pathogens and thus check the microbial infectivity.<sup>91</sup>

## ANTI-OXIDANT ACTIVITY

Various extracts of *T. cordifolia* exhibits an anti-oxidant potential by scavenging the free radicals and other reactive species respectively.<sup>92</sup> *T. cordifolia* significantly reduces the regulation of lipid peroxidation process thereby decreasing the level of reactive free radical species in a diabetic rat model (alloxan induced diabetes) and up regulates anti-oxidant enzymes like catalase and glutathione indicating its anti-oxidant effects.<sup>65,93,94</sup> A clinical research has reported that the extract shows anti-oxidant effect by raising the level of GSH and reducing the expression of inducible nitric oxide synthase gene, while it is also useful in treatment of cataract by inhibiting the enzyme aldol reductase.<sup>95,96</sup> A study also suggests that TC bark extracts (ethanol) shows the higher free radical scavenging activity as well as the highest phenolic content compared to the methanol extracts.<sup>97</sup>

The plant derived polysaccharide compound named as 'arabinogalactan' shows a protection against free radicals in rat model indicating its anti-oxidant action.<sup>98</sup> *T. cordifolia* is reported to modify the levels of different enzymatic system which then controls the production of these reactive species and thereby maintains the oxidative load by regulating the lipid peroxidation process and glutathione level.<sup>99</sup> This plant also protects the mice from  $\gamma$ -radiation due to its anti-oxidant property<sup>100-101</sup> by inhibiting the ferrous sulphate generated lipid peroxidation.<sup>102</sup> In Ayurveda medicine, Pepticare a herbomineral formulation which includes *T. cordifolia* has also been reported to possess potent anti-oxidant effect in rat model.<sup>103</sup>

## ANTI-HIV ACTIVITY

*T. cordifolia* has been evaluated to found its importance in treating HIV positive patients by decreasing the patient's resistance to the retroviral regimen.<sup>104</sup> The anti-HIV activity of *T. cordifolia* uncovers its application in managing the disease by increasing the CD4 T-cells count and decreasing eosinophil-(a type of WBC) count in HIV positive patients. *T. cordifolia* extract showed significantly enhanced phagocytic and intracellular bactericidal activity. *T. cordifolia* also stimulated peritoneal macrophage. Furthermore, *T. cordifolia* increases phagocytosis and intracellular killing property. *T. cordifolia* significantly stimulates B-lymphocytes, polymorph nuclear leucocytes and macrophages.<sup>101,105,106</sup>

## ANTI-OSTEOPOROTIC ACTIVITY

An in vitro study suggests, that the alcoholic extract of guduchi is found to enhance the degree of proliferation and differentiation of the osteoblast cells of both human and rats. Over and above it also take part in the calcification process by producing minerals by these bone forming cell models regulating the bone mineralization.<sup>107</sup> A steroid named 'Beta-Ecdysone' (Ecd) or 20-hydroxyecdysone isolated from *T. cordifolia* showed to promote the building of muscle tissue in mesenchymal stem cells model of mouse preventing the incidence of osteoporosis.<sup>108,100</sup>

In addition to the above, some of the other important therapeutic activity associated with *T. cordifolia* are briefly summarised in the following Table 1.

**Table 1: Table Shows the Therapeutic activity of *Tinospora cordifolia*.**

Activity	Part/Extract	Animal Model/Cell Lines	Reference
Cardioprotective effect	Whole plant/ Alcohol extract	Calcium chloride administrated by intravenous infusion to produce arrhythmia in rats	24
	Whole plant/ Ethanol and		109
Antiulcer activity	Aqueous extracts	Albino rats using pylorus ligation induced ulcer.	
	Whole plant/Ethanol and		109
Antidiarrheal activity	Aqueous extract	Castor oil and Magnesium sulphate induced diarrhea in albino rats.	
Analgesic activity	Whole plant/Ethanol extract	Hot plate and abdominal writhing method in albino rats.	110
Aphrodisiac property	Aqueous and hydroalcoholic extract	Adult albino rats of wistar strain.	111
Immunomodulatory activity	Whole plant/Aqueous extract	Swiss male albino mice.	112
Antidyslipidemic activity	Stem Extract	Alloxan induced diabetic male adult rats of charles foster strain.	113
	Aerial parts/		114
Neuroprotective effect	Ethanol extracts	6-hydroxy dopamine lesion rat models of Parkinson's disease.	
Anti-inflammatory activity	Stem/Aqueous extract	Carrageenan induced paw edema model in rats.	115
Gastroprotective activity	Whole plant	Indomethacin induced gastric ulcer in rats.	116
Antioxidant activity	Whole plant/Ethanol extract	N-nitrosodiethylamine induced liver cancer in male wistar albino rats.	117
Radio protective and Cytoprotective activity	Stem/Ethanol extract	4 Gy- $\gamma$ radiation in albino mice and cyclophosphamide induced genotoxicity.	118
Antifeedant activity	Whole plant/ Chloroform Extract	Microorganism used: <i>Earias vitella</i> , <i>Plutella xylostella</i> , <i>Spodoptera litura</i> .	119
Ameliorative effect	Root/Ethanol extract	Male swiss albino mice exposed to aflatoxin B1.	24
Hepatoprotective activity	Whole plant/ Aqueous Extract	Bile duct ligation induced jaundice in rats.	120
Nootropic effect	Whole plant/Ethanol extract	Amnesic rats using radial arm maze task performance and barnes maze test.	121
Hypoglycemic activity	Stem/ Aqueous Extract	Insulin released effect was detected in vitro using rat pancreatic $\beta$ -cell lines.	26
Antipsychotic activity	Aqueous and Ethanol extract	Amphetamine challenged mice model.	122
Antidepressant activity	Petroleum ether extract	Swiss albino mice and activity was evaluated using tail suspension test and forced swim test.	123
Antiosteoporotic activity	Stem/Ethanol extract	Female sprague-dawley rats.	124
Antineoplastic activity	Aerial parts/DCM extract	Mice transplanted with ehrlich ascites carcinoma.	25
Antifertility effect	Stem/Methanol extract	Male rats.	125
Antiasthmatic activity	Stem/Hydroalcoholic Extract	Mice were sensitized with intraperitoneal ovalbumin followed by intranasal ovalbumin in vivo asthma model.	126
Antitumor activity	Aqueous alcoholic extract	C6 glioma cells were used, extract reduced the cell proliferation in dose dependant manner.	127
Allergic rhinitis	Aqueous extract	Double blind placebo-controlled trial.	128
Diabetic neuropathy	Stem/aqueous extract	Streptozotocin induced wistar albino diabetic rats and in vitro aldose reductase inhibition assay and in vivo results were analysed with Mann whitney Test.	129
Antimalarial activity	Stem/ Ethanolic extract	Microorganism used <i>Plasmodium berghei</i> on white swiss mice models.	130
Hepatocellular carcinoma	Aerial parts/ Ether extract	Diethyl nitrosamine induced hepatocellular carcinoma in male wistar rats.	130
Anticancer activity	Aqueous and Ethanolic extract	IMR 32 human neuroblastoma cell lines as a model system.	131
Antibacterial activity	Stem/ Aqueous and Ethanolic Extract	Microorganisms used: <i>E. coli</i> , <i>P. vulgaris</i> , <i>E. faecalis</i> , <i>S. typhi</i> , <i>S. aureus</i> , <i>S. marcescens</i> .	132

## CONCLUSION

*T. cordifolia* being a resourceful plant constitute innumerable biologically active compounds that have been reported to have a therapeutic potential. There are reports in pharmacological and clinical studies which validate the curative and remedial role of this plant to combat different ailments. The different bioactive compounds including alkaloids, steroids, glycosides, sesquiterpenoids etc found to have potential application especially as immunomodulator and anti-oxidant agent. The various studies that have been conducted on *T. cordifolia* reveals that it is an excellent drug and does not have any adverse or toxic effects till now. Overall, this review gives information about the classical anti-toxin, antidiabetic, anticancer, immunomodulatory, antioxidant, antimicrobial activity of *T. cordifolia* and can be used for further research investigations in development of novel drug.

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## CONFLICT OF INTEREST STATEMENT

We declare that we have no conflict of interest.

## ABBREVIATION USED

**HIV:** Human Immunodeficiency Virus; **GSH:** Glutathione Stimulating Hormone; **DMBA:** Dimethylbenzanthracene; **ROS:** Reactive Oxygen Species; **GPT:** Glutamic Pyruvic Transaminase; **ALT:** Alanine amino Transferase; **AST:** Aspartate amino Transferase; **PMN:** Polymorphonuclear leucocytes; **WBC:** White Blood Cell; **MIC:** Minimum Inhibitory Concentration.

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## GRAPHICAL ABSTRACT



## SUMMARY

- The plant constituents, pharmacological actions and ayurvedic aspects of *Tinospora cordifolia* is reviewed.
- The plant contains active constituents like alkaloids, terpenoids etc.
- The plant possesses antidiabetic, anticancer, antioxidant, antitoxin, hepatoprotective and immunomodulatory activities etc. These activities are correlated with the active constituents.
- Its use in ayurvedic system of medicine also reported.

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