

## 1 REVIEW ARTICLE

2 *Tinosporacordifolia*: A Potential Plant with  
3 Immunomodulatory Activity

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## 8 ABSTRACT

9 Immunomodulation is a procedure, which can alter the immune system of an organism by interfering its  
10 function. Modulation of immune system may result in suppression or stimulation of immunological  
11 reactivity. Recently the effect of immunomodulators in the treatment of various diseases is significant.  
12 *Tinosporacordifolia* is a widely used shrub in ayurvedic system of medicine. It is reported to benefit the  
13 immune system in a variety of ways. The medicinal properties incorporated with this plant are anti-  
14 diabetic, hypolipidemic, anti-neoplastic, anti-oxidant, anti-inflammatory, immunomodulatory, cognitive,  
15 adaptogenic, aphrodisiac, cardioprotective and hepatoprotective effect. Many compounds belonging to  
16 different classes such as alkaloids, diterpenoids, phenol, aliphatic compounds and polysaccharides have  
17 been isolated from this plant. But it is not well known that which of these compounds are responsible for  
18 various activities. Therefore, it needs further exploration of its components, pharmacological action and  
19 mechanism of action. This review presents a detail survey of literature on immunomodulatory properties  
20 of *T.cordifolia*. The main aim of the survey is to reinforce scientific reconfirmation of its immunological  
21 activities and human studies.

22 **Keywords:** *Immunomodulation, Immunomodulating agent, Tinosporacordifolia*

23 Advances in molecular biology have revolutionized 41 depending on the requirement of the situation.  
24 immunology and medicine. Initially the use of antibody 42 Alternative medicine is now recognized as an invaluable  
25 as therapeutic agents was limited by their purity and 43 resource even by the most intransigent clinicians of  
26 heterogeneity. Immunotherapy derives from the 44 advanced countries. Plant extracts have been widely  
27 observation from the 19<sup>th</sup> century, that cancer 45 investigated for their possible immunomodulatory  
28 sometimes regressed after acute bacterial infections, that 46 properties, *Tinospora cordifolia*, an indispensable  
29 is, there may be no specific immunostimulant effect. 47 medicinal plant, has been used for the treatment of  
30 The rapidly expanding discipline of immunology 48 various diseases and has been recommended for  
31 contributes to diagnosis, therapy and prevention of 49 improving the immune system. There is great interest in  
32 human diseases in many ways. The role of 50 development of new drugs from traditionally used  
33 immunocompetents in prevention of malignancy is 51 medicinal plants like *Tinosporacordifolia*. Ayurveda  
34 currently of great interest in experimental science as 52 refers to *Tinospora cordifolia* as 'Amruth' or the 'Nectar  
35 well as clinical medicine. Interest in the immune 53 of Immortality'. The term 'Amruth' is attributed to this  
36 response has been stimulated by the alarming increase 54 drug in recognition of its ability to impart youthfulness,  
37 in a novel epidemic form of immune deficiency, 55 vitality and longevity. Immunomodulation can be  
38 "AcquiredImmunoDeficiency Syndrome" (AIDS). 56 determined by the capacity of the compounds to  
39 Immunomodulation relates to potentiation or 57 influence the cytokine production, mitogenicity,  
40 suppression of the immune responses of the host, 58 stimulation and activation of immune effector cells.



Fig 1. *Tinospora Cordifolia* (Courtesy: KottakkalAryavaidyashala)

59 Panchabhai et al done a study “Validation of  
60 therapeutic claims of *Tinospora cordifolia*: a review “on  
61 2008 [1]. As *Tinospora cordifolia* is a plant of high  
62 pharmacological potential, day by day new studies are  
63 conducted and novel therapeutic activities are revealed.  
64 Recently, isolation and characterisation of  
65 phytoconstituents responsible for the activities are done.  
66 So, there is a scope for a new study. *Tinospora*  
67 *cordifolia* is a plant of high pharmacological potential,  
68 day by day new studies are conducted and novel  
69 therapeutic activities are revealed. Recently, isolation  
70 and characterisation of phytoconstituents responsible for  
71 the activities are done. So there is a scope for a new  
72 study. The current survey is aimed to include the  
73 updated informations available with special emphasis  
74 on immunomodulatory activity, as its name suggests  
75 “amruth”.

#### DESCRIPTION AND HISTORY

76  
77 *T.cordifolia* (Fig 1); common name *guduchi*, *amrita*  
78 of family *menispermaceae* is a perennial, wild climber,  
79 succulent, shrub often attaining a great height and  
80 sending down long thread like aerial roots. The bark is  
81 creamy white and grey, leaves are membranous and  
82 chordate. Flowers grow during the summer and fruits  
83 during the winter. The viscous sap has a yellow colour,  
84 odour and nauseating bitter [2]. It has been used in  
85 ayurvedic preparations for the treatment of various  
86 ailments throughout the centuries. Today the drug and  
87 tincture are used for the treatment of general weakness,  
88 fever, dyspepsia, dysentery, gonorrhoea, secondary  
89 syphilis, urinary diseases, impotency, gout, viral  
90 hepatitis, skin diseases and anemia. In compound  
91 formulation Guduchi is clinically used to treat jaundice,  
92 rheumatoid arthritis and diabetes. The root is considered

93 as a powerful emetic and is used for bowel obstruction.  
94 *T.cordifolia* is used as an antidote for snake bite and  
95 used in malaria, environmental illness, asthma, upper  
96 respiratory tract infection, UTI, general debility and  
97 amelioration of symptoms from chemo or radiotherapy.

#### CHEMISTRY

98  
99 A variety of constituents have been isolated from  
100 *T.cordifolia* plant. They belongs to different classes such  
101 as alkaloids, diterpenoids, lactones, glycosides, steroids,  
102 sesquiterpenoids, phenolic, aliphatic compounds and  
103 polysaccharides (Table 1). Leaves of this plant are rich  
104 in protein (11.2%), calcium and phosphorus [3].  
105 Anarabinogalactan had been isolated from the dried  
106 stem of *T.cordifolia* [4].

#### PHARMACOLOGICAL ACTIONS

##### Immunological effects

109 *T.cordifolia* benefits the immune system in variety  
110 of ways. The alcoholic and aqueous extract of this plant  
111 have been tested successfully for immunomodulatory  
112 activity [5]. Pretreatment with *T.cordifolia* lead to  
113 protection against mortality induced by intra-abdominal  
114 sepsis following caecal ligation in rats. It also  
115 significantly reduced mortality from *E. coli* induced  
116 peritonitis in mice [6]. In a clinical study, it was  
117 afforded protection in cholestatic patients against *E. coli*  
118 infection. Those activities were not due to its  
119 antibacterial activity as shown by the negative *in vitro*  
120 antibacterial activity of the plant extract. It was reported  
121 that treatment in rats had resulted in significant  
122 leucocytosis and predominant neutropenia. It has been  
123 also observed that it stimulated the macrophages as  
124 evidenced by an increase in the number and percentage  
125 phagocytosis of *S.aureus* by peritoneal macrophages in  
126 rats. The phagocytic and intercellular killing capacity of  
127 polymorphs in rats, tested at 3.5 hours after *E. coli*  
128 infection were significant. Syringin, Cordiol,  
129 Cordioside, Cordifoliosides A&B were identified as the  
130 active principle responsible for the anticcompliment and  
131 immunomodulatory activities [6]. Anarabinogalactan  
132 polysaccharide, isolated from the dried stem of  
133 *T.cordifolia* showed polyclonal mitogenic activity  
134 against beta cell [4]. It was reported that following oral  
135 treatment of mice with water and ethanol extracts of  
136 *T.cordifolia* stems, there was a significant increase in  
137 the total of count leucocytes. The aqueous extract of  
138 *T.cordifolia* was found to increase phagocytosis *in vitro*.  
139 The aqueous and ethanolic extract also induced an  
140 increase in antibody production *in vivo*. *T.cordifolia*  
141 extracts treatment cause significant reduction in  
142 eosinophil count and improved hemoglobin in HIV  
143 patients [5]. Sixty percent patients receiving TCE and  
144 20% on placebo reported decrease in the incidence of  
145 various symptoms associated with the disease. All  
146 extracts inhibited cyclophosphamide-induced

**Table 1.** Chemical composition of *T. cordifolia* plant

Types of chemicals	Active principle	Parts in which present
Alkaloids	Berberine	Stem Root
	Palmatine	
	Magnoflorine	
	Tinosporine	
	Choline	
	Isocolumbin	
Glycosides	Tetrahydropalmatine	Stem
	Magnoflorine	
	Tinocordiside	
	Cordiside	
	Syringin	
	Cordifolioside A	
	Cordifolioside B	
	Cordifolioside C	
	Cordifolioside D	
	Cordifolioside E	
Steroids	Palmatoside C	Aerial part Stem
	Palmatoside P	
	Beta-sitosterol	
	gama-sitosterol	
	20B-ecdysone	
	Ecdysone	
Diterpenoid lactones	Ecdysterone	Whole plant
	Makisterone A	
	Giloinsterol	
	Furanolactone	
	Celondane derivatives	
Sesquiterenoid	Tinosporon	Stem
	Tinosporides	
Aliphatic Compounds	Jateorine	Whole plant
	Columbin	
Miscellaneous Compounds	<i>Tincordifolin</i>	Root
	Octacosanol	
	Heptacosanol	
	Tinosporidine	
	Cordifol	
	Cordifelone	
Miscellaneous Compounds	Cordifelone	Root
	Gilonin	
	Tinosporic acid	

147 immunosuppression [7]. The polysaccharide-enriched 164 *T. cordifolia* treatment, significantly caused the  
148 fraction from this plant is found to be very effective in 165 reduction in cell count ( $p < 0.05$ ) on day 15 of the  
149 reducing the metastatic potential of B16f-10 melanoma 166 treatment period, however, reduction in total bacterial  
150 cells [8]. 167 count was observed from day 3 onwards. The

151 Sharma *et al.* (2012) evaluated the 168 phagocytic activity and lysosomal enzyme content of  
152 immunomodulatory activity of three polysaccharide- 169 milk polymorphonuclear cells enhanced in the diseased  
153 enriched immunomodulatory fractions from *Tinospora* 170 cows treated with the *T. cordifolia* extract. The IL-8  
154 *cordifolia* using the polymorphonuclear leukocyte 171 level in milk serum also increased significantly ( $p <$   
155 function test. The results confirmed the 172 0.05) in diseased cows treated with the extract. The  
156 immunomodulatory activity of the polysaccharides of 173 results suggest that the hydro-methanolic extract of  
157 *T. cordifolia*, and also it was conclude that the 174 *T. cordifolia* (stem) possesses antibacterial and  
158 polysaccharide with lowest sugar content showed 175 immunomodulatory properties [10].

159 highest activity and with highest sugar content showed 176 Sharma *et al* (2012) isolated and characterised the  
160 biological activity [9]. Mukherjee et al evaluate the 177 immunomodulatory active compounds of *Tinospora*  
161 biological activity of the *Tinospora cordifolia* extract at 178 *cordifolia*. It was found that ethyl acetate, water  
162 standardized dose against bovine subclinical mastitis. 179 fractions and hot water extract exhibited significant  
163 Intramammary infusion of hydro-methanolic extract of 180 immunomodulatory activity with an increase in

percentage phagocytosis. Chromatographic purification of these fraction led to the isolation of seven immunomodulatory active compounds belonging to different classes such as N-formylannonain, 11-hydroxymustakone, N-methyl-2-pyrrolidone, cordifolioside A, magnoflorine, tinocordiside, syringin by nuclear magnetic resonance and mass spectrometry. 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 µg/ml [11].

Recently, the presence of an immunomodulatory protein (ImP) in guduchi has been investigated. Guduchi ImP showed ~3-fold mitogenic activity compared to untreated murine splenocytes in the 1-10 µg/mL concentration range; 5-7-fold increase in mitogenic activity was seen in the case of murine thymocytes vs control. The purified protein also induced nitric oxide production from macrophages present in isolated murine peritoneal exudates cells. Guduchi ImP displays enhanced phagocytosis of yeast cells by macrophages. Guduchi ImP does not possess haemagglutination activity indicating that the immunomodulatory protein is not a lectin. The confirmation of an immunomodulatory protein in guduchi stem showing lymphoproliferative and macrophage-activating properties reinforces the rationale of the use of guduchi preparations for immunomodulation [12].

Cordifolide A, a novel unprecedented sulfur-containing clerodane diterpene glycoside, together with other two new diterpene glycosides, cordifolides B and C, and four known analogues, were isolated from a methanol-soluble extract of the stems of *Tinospora cordifolia*. The structures of the new compounds were determined on the basis of spectroscopic data interpretation, with that of cordifolide A confirmed by a single-crystal X-ray crystallographic analysis. All isolates were evaluated for their *in vitro* immunomodulatory activity using mouse bone marrow-derived dendritic cells [13]. *Tinospora cordifolia* had shown a significant level of macrophages activation leads to increase in GM-CSF which leads to leucocytosis and improved neutrophil function [14]. G1-4A, an immunomodulatory polysaccharide from *Tinospora cordifolia*, modulates macrophage responses and protects mice against lipopolysaccharide induced endotoxic shock and G1-4A appeared to induce tolerance against endotoxic shock by modulation of cytokines and nitric oxide [15].

T.C. was evaluated for the possibility of enhancing the reproductive performance of crossbred cows by its peripartum supplementation, as the crossbred periparturient cow is highly susceptible to various diseases that effectively reduce its reproductive performance postpartum. A higher total leukocyte, neutrophil count along with increased

neutrophil lymphocyte ratio was recorded in Guduchi supplemented cows in comparison to untreated cows although plasma total antioxidant activity was similar between the two groups. Prepartum plasma progesterone concentration was significantly lowered in the treated group however there was no significant change in peripartum plasma total estrogens and PGFM levels due to Guduchi supplementation [16].

#### Antidiabetic effects

The stem of *T. cordifolia* has long been used in Indian Ayurvedic Medicine for the treatment of Diabetic mellitus. Oral administration of aqueous *T. cordifolia* root extract to alloxan-induced diabetic rats caused a significant reduction in blood glucose level and brain lipids [17]. Though the aqueous extract at a dose of 400 mg/kg could elicit significant hypoglycemic effect in different animal model, its effect was equivalent to only one unit /kg of insulin [18]. It was reported that the daily administration of either aqueous or alcoholic extract of *T. cordifolia* decreases the blood glucose level and increases glucose tolerance in rodents [19, 20].

Berberine, an alkaloid obtained from the stem of *T. cordifolia* has been tested and used successfully in experimental and human diabetes mellitus. Berberine has been shown to lower elevated blood glucose as effectively as metformin [21]. The mechanisms of action include inhibition of aldose reductase [22], inducing glycolysis [23], preventing insulin resistance through increasing insulin receptor expression [24], and acting like incretins [25]. Berberine also overcome insulin resistance via modulating key molecules in insulin signaling pathway, leading to increased glucose uptake in insulin-resistant cells [26]. Berberine might exert its insulinotropic effect in isolated rat islets by up-regulating the expression of hepatocyte nuclear factor 4 alpha, which probably acts solely or together with other HNFs to modulate glucokinase activity, rendering β cells more sensitive to glucose fluctuation and to respond more effectively to glucose challenge [27]. Berberine also seems to inhibit human dipeptidyl peptidase-4 (DPP IV), as well as the pro-diabetic target human protein tyrosine phosphatase 1B (h-PTP 1B), which explain at least some of its anti-hyperglycemic activities. Berberine suppresses intestinal disaccharides with beneficial metabolic effects in diabetic states [28].

A recent comprehensive metabolomics method, applied to type 2 diabetics, suggested administration of berberine down-regulates the high level of free fatty acids which are known to be toxic to the pancreas and cause insulin resistance. These results suggest berberine might play a pivotal role in the treatment of type 2 diabetes [29]. Berberine has been shown to boost the effects of metformin and 2,4 -thiazolidinedione (THZ), and can partly replace the commercial drugs, which could lead to a reduction in toxicity and side effects of the latter. Berberine inhibits Foxo1, which integrates

296 insulin signaling with mitochondrial function. Inhibition<sup>350</sup> (ALTC) [35]. Intra-peritoneal administration of ALTC  
297 of Foxo1 can improve hepatic metabolism during<sup>351</sup> in DL-bearing mice not only augment the basic function  
298 insulin resistance and the metabolic syndrome [30]. <sup>352</sup> of macrophages such as phagocytosis as well as their

### 299 *Diabetic retinopathy*

300 *T. cordifolia* plays role in prevention and<sup>355</sup> the intra-peritoneal administration of ALTC slow down  
301 management of diabetic retinopathy due to its<sup>356</sup> the tumor growth and increase the life span of tumor  
302 antihyperglycemic, anti-angiogenic, anti-inflammatory<sup>357</sup> bearing host, thus showing its anti-tumor effect through  
303 and anti-oxidant properties. It also prevents the<sup>358</sup> destabilizing the membrane integrity of DL cells.  
304 progression of cataract and vascular changes, the<sup>359</sup> *T.cordifolia* was shown effective in several other  
305 important symptoms of DR. Although diabetic rats<sup>360</sup> tumour models including Ehrlich ascites carcinoma  
306 treated with TC do not achieve the status of normal non-<sup>361</sup> (EAC) in mice [36]. It induces proliferation and myeloid  
307 diabetic rats, but they achieve significant levels as<sup>362</sup> differentiation of bone marrow precursor cells in a  
308 compared to untreated diabetic rats. *T. cordifolia* thus<sup>363</sup> tumor-bearing host [37], activates tumor-associated  
309 acts as a potential therapeutic agent for prevention of<sup>364</sup> macrophages-derived dendritic cells [38], is effective  
310 the vascular complications of diabetes. <sup>365</sup> against various cancers, killing the cancer cells very

### 311 *Diabetic neuropathy*

312 *Tinospora cordifolia* prevents the hyperalgesia in,<sup>368</sup> *Cognitive effects*  
313 experimental diabetic neuropathy. It has an aldose  
314 reductase inhibitory activity in vitro which may<sup>369</sup> The memory impairment induced by cyclosporine  
315 contribute to the beneficial effects [31]. <sup>370</sup> was successfully overcome by both the alcoholic and

### 316 *Diabetic foot ulcer*

317 Diabetic patients with foot ulcers on *T. cordifolia* as<sup>373</sup> reversed the hippocampal neuronal degeneration  
318 an adjuvant therapy showed significantly better final<sup>374</sup> induced by cyclosporine revealed by the  
319 outcome with improvement in wound healing. Reduced<sup>375</sup> histopathological investigation [40]. The alteration of  
320 debridements and improved phagocytosis were<sup>376</sup> immune function affected learning and memory process  
321 statistically significant, indicating beneficial effects of<sup>377</sup> and *T. cordifolia* is a potent immunomodulator and  
322 immunomodulation for ulcer healing [32]. <sup>378</sup> cognitive enhancer. The dual property of *T. cordifolia*

### 323 *Hypolipidemic effects*

324 Diabetics are often associated with hyperlipidemia<sup>381</sup> induced memory changes. Significant response has been  
325 and as *T.cordifolia* been shown to have hypoglycemic<sup>382</sup> found in children with moderate degree of behaviour  
326 properties, the plant was evaluated for its<sup>383</sup> disorders and mental deficit, along with improvement in  
327 hypolipidemic activity. An aqueous extract of<sup>384</sup> IQ levels. The root of *T.cordifolia* is known to be used  
328 *T.cordifolia* root was administered to alloxan induced<sup>385</sup> traditionally for its anti-stress activity. The pure  
329 diabetic rat (2.5 and 5g/kg body weight for 6 weeks)<sup>386</sup> aqueous extract of the root was found to enhance verbal  
330 and it reduced serum and tissue cholesterol,<sup>387</sup> learning and logical memory. Both the alcoholic and  
331 phospholipids, and fatty acid levels. In another study in<sup>388</sup> aqueous extracts of *T.cordifolia* produced a decrease in  
332 rats, the aqueous extracts also reduced levels of brain<sup>389</sup> learning scores in Hebb William maze and retention  
333 lipids [33]. <sup>390</sup> memory, indicating enhancement of learning and

### 334 *Antineoplastic effects*

335 Jagetia *et al.* have found that the guduchi killed the<sup>392</sup> *Adaptogenic effects*  
336 *HeLa cells* very effectively *in vitro*. In this study, the<sup>393</sup> The aqueous extract not only reversed the effect of  
337 stem extracts were evaluated *in vitro* for their cell<sup>394</sup> cisplatin on gastric emptying, but also normalized  
338 killing effects [34]. When *HeLa* cells were exposed to<sup>395</sup> cisplatin-induced hypermotility. The plant was also  
339 various doses of the extract, a dose-dependent increase<sup>396</sup> found to normalize the phagocytic function of peritoneal  
340 in cell killing was observed as compared with non drug-<sup>397</sup> macrophages after exposure of rats to either carbon  
341 treated controls. The methylene chloride extract was the<sup>398</sup> tetrachloride or serum, thus it satisfied the definition of  
342 most potent. The effect of guduchi extract was<sup>399</sup> adaptogen [42].

### 343 *Antioxidant activity*

344 thus it indicates that the plant warrants a future study as  
345 anti-neoplastic agent. Further investigation were<sup>401</sup> The antioxidant properties of *T. cordifolia* roots  
346 undertaken to study whether the tumor associated<sup>402</sup> were studied by administering the aqueous extract of  
347 macrophages (TAM) of Daltons lymphoma (DL) a<sup>403</sup> alloxan-induced diabetic rats. After 6 weeks, the level  
348 spontaneous transplantable T-cell lymphoma, can be<sup>404</sup> of plasma barbituric acid reactive substances,  
349 activated by the aqueous liquid extract of *T.cordifolia*<sup>405</sup> ceruloplasmin and alpha tocopherol were reduced. In

addition, the level of glutathione and vitamin C were increased. The root extract at a dose of 5 g/kg was most effective one [43]. In another study, guduchi extract was shown to inhibit the lipid peroxidation superoxide and hydroxyl radical *in vitro*. Earlier studies shows that dry stem crude extract (DSCE) contains polygonal beta cell mitogen; G1-4A, DSCE as well as

G1-4A also enhance immune response in mice [44]. In order to explore the possibility of using G1-4A/pp1 to

modulate radiation-induced immune suppression, the antioxidant effect PPI from of this plant was examined against reactive oxygen and nitrogen species (ROS/RNS), generated by photosensitization/peroxynitrite. Oxidative damage induced by peroxynitrite was inhibited by PPI. The degradation of protein due to photosensitization assessed by SDS PAGE was effectively reduced by simultaneous treatment with PPI during photosensitization. Selective inhibitors of ROS-like mannitol, super oxide dismutase (SOD), Sodiunazide, ant-oxidant GSH, and vitamin C brought about significant inhibition of formation of TBARS thus indicating generation of oxygen. Thus the action of PPI may be against oxidative damage through type 1 and type 2 photosensitization mechanism. *T. cordifolia* has also been reported to elevate GSH levels, expression of the gamma-glutamylcysteine ligase and Cu-Zn SOD genes. The herb also exhibited strong free radical-scavenging properties against reactive oxygen and nitrogen species as studied by electron paramagnetic resonance spectroscopy [45].

**Cardioprotective activity**

A dose-dependent reduction in infarct size and in serum and heart lipid peroxide levels was observed with prior treatment with *T. cordifolia* in ischemia-reperfusion-induced myocardial infarction in rats [53].

The stem extract can normalize the alterations in lipid metabolism caused by diabetes mellitus in streptozotocin-induced diabetic rats, indirectly benefiting the heart [54]. Administration of the extract of *T. cordifolia* has been found to exert anti-inflammatory actions in models of acute and subacute inflammation [46]. The water extract of the stem of neem-giloe [*T. cordifolia* that grow on *Azadirachtaindica* (neem)] significantly inhibited acute inflammatory response evoked by carrageen in a dose of 50 mg/100 g given orally and intraperitoneally. A significant inhibition of primary and secondary phases of inflammation was observed in a model of adjuvant induced arthritis. It also significantly inhibited antibody formation by typhoid "H" antigen. A mild analgesic effect of its own as well as potentiation of morphine analgesia has been reported [47]. In another study aqueous extract of *T. cordifolia* showed a significant inflammatory effect in the cotton pellet granuloma and formalin induced arthritis model, its effect was comparable with indomethacin and its mode of action appeared to resemble that of non-steroidal anti-inflammatory agent. The dried stem of *T. cordifolia* produced significant anti-inflammatory effect in both acute and subacute models of inflammation. *T. cordifolia* was found to be more effective than

**Osteoprotective activity**

Rats treated with *T. cordifolia* (10 mg/kg body weight) showed an osteoprotective effect, as the bone loss in tibia was slower than that in controls. Serum osteocalcin and cross-laps levels were significantly reduced. This study demonstrates that extract of *T. cordifolia* has the potential for being used as antiosteoporotic agent [56].

**Anti-allergic activity**

*T. cordifolia* is traditionally used for the treatment of asthma, and the juice is also employed for the treatment of chronic coughs [57]. In a clinical study, 100% relief was reported from sneezing in 83% of the patients on treatment with *T. cordifolia*. Similarly, the relief from nasal discharge was reported in 69%; from nasal obstructions 61% and from nasal pruritis, in 71%. In

placebo group, there was relief from sneezing only in 21% patients; from nasal discharge, in 16.2%; from nasal obstruction, in 17%; and from nasal pruritis, in 12%. Thus, *T. cordifolia* significantly decreased all symptoms of allergic rhinitis and was well tolerated. The anti-allergic and bronchodilator properties of an aqueous extract of the stem evaluated on histamine-induced bronchospasm in guinea pigs, capillary permeability in mice and mast cell disruption in rats showed that it significantly decreased bronchospasm induced by 5% histamine aerosol, decreased capillary permeability and reduced the number of disrupted mast cells.

### Antipyretic and anti-infective activity

The water-soluble fraction of 95% ethanolic extract of *T. cordifolia* plant has shown significant antipyretic activity [59]. In another experimental study, antipyretic effects have been reported in the hexane- and chloroform-soluble portions of *T. cordifolia* stems [60]. Various studies show remarkable anti-infective and antipyretic properties of *T. cordifolia*. Pre-treatment with *T. cordifolia* was shown to impart protection against mortality induced by intra-abdominal sepsis following caecal ligation in rats and significantly reduced mortality from induced by *E. coli*-induced peritonitis in mice [61].

### Antifertility & aphrodisiac activity

Oral administration of 70% methanolic extract of *T. cordifolia* stem to male rats at a dose level of 100 mg/d for 60 days did not cause body weight loss but decreased the weight of testes, epididymis, seminal vesicle and ventral prostate in a significant manner [62]. Gudichi is a natural aphrodisiac in females. Its immunomodulatory action helps to strengthen the immune system and to make the body stronger and hence make a woman more able and ready to enjoy sex. It is a rejuvenator and a natural herbal aphrodisiac.

### Other effects

In a clinical evaluation, a compound preparation 'RUMALAYA' containing *T. cordifolia* was reported to significantly reduce the pain in patient suffering from rheumatoid arthritis. Ether extract of the steam distillate of aerial part of *T. cordifolia* has inhibited the *in vitro* growth of *Mycobacterium tuberculosis* at 1:50,000 dilutions [63]. It is used for its anti-leprotic properties along with wide use in other types of skin disorders and has been shown to exert antileprotic activity in a combination formulation. Ethanolic extract of *T. cordifolia* has exhibited significant antipyretic activity in rats [64]. 'Septilin syrup' a compound preparation containing *T. cordifolia* was found to elicit good clinical response in children suffering from upper respiratory tract infection and chronic otitis media. In a scientific study on rats and human volunteers, *T. cordifolia* was found to have diuretic effects [65]. It was also found effective in modulation of morphology and some

*T. cordifolia* is used clinically in the Indian system of medicine for the treatment of jaundice, diabetes and rheumatoid arthritis. It has also been found to possess adaptogenic, anti-inflammatory, anti-neoplastic, anti-oxidant, hepatoprotective, cognitive, hypolipidemic, antimalarial, antistress, antipyretic and immunologic properties. There are limited human studies to support these use. *T. cordifolia* can also be used as an adjuvant drug in the treatment of hyper-reactive malarious splenomegaly [69]. *Tinospora cordifolia* appears to improve surgical outcome by strengthening host defenses as evidenced by the study on surgical outcome in patients with malignant obstructive jaundice [70].

### Toxicology

The ayurvedic literature reports that *T. cordifolia* can cause constipation, if taken regularly in high doses. It has no side effect and toxicity. When *T. cordifolia* extract was administered to rabbit up to the highest oral doses of 1.6 g/kg, there were no predictable adverse drug effects.

## CONCLUSION

The pharmacological actions attributed to *T. cordifolia* in ayurvedic texts and folk medicine have been validated by a remarkable body of modern evidence suggesting that this drug has immense potential in modern pharmacotherapeutics.

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