

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 19th 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

108 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 anticompliment 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	
	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 lowest 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

181 percentage phagocytosis. Chromatographic 239 neutrophil lymphocyte ratio was recorded in Guduchi
 182 purification of these fraction led to the isolation of 240 supplemented cows in comparison to untreated cows
 183 seven immunomodulatory active compounds belonging 241 although plasma total antioxidant activity was similar
 184 to different classes such as N-formylannonain, 11- 242 between the two groups. Prepartum plasma
 185 hydroxymustakone, N-methyl-2-pyrrolidone, 243 progesterone concentration was significantly lowered in
 186 cordifolioside A , magnoflorine , tinocordiside 244 the treated group however there was no significant
 187 syringin by nuclear magnetic resonance and mass 245 change in peripartum plasma total estrogens and PGFM
 188 spectrometry . Cordifolioside A and syringin have been 246 levels due to Guduchi supplementation [16].
 189 reported to possess immunomodulatory activity. Other

190 five compounds showed significant enhancement in 247 **Antidiabetic effects**

191 phagocytic activity and increase in nitric oxide and 248 The stem of *T.cordifolia* has long been used in
 192 reactive oxygen species generation at concentration 0.1- 249 Indian Ayurvedic Medicine for the treatment of
 193 2.5 µg/ml [11]. 250 Diabetic mellitus. Oral administration of aqueous

194 Recently, the presence of an immunomodulatory 251 *T.cordifolia* root extract to alloxan-induced diabetic rats
 195 protein (ImP) in guduchi has been investigated. Guduchi 252 caused a significant reduction in blood glucose level
 196 ImP showed ~3-fold mitogenic activity compared to 253 and brain lipids [17]. Though the aqueous extract at
 197 untreated murine splenocytes in the 1-10 µg/mL 254 adose of 400 mg/kg could elicit significant
 198 concentration range; 5-7-fold increase in mitogenic 255 hypoglycemic effect in different animal model, its effect
 199 activity was seen in the case of murine thymocytes vs 256 was equivalent to only one unit /kg of insulin [18]. It
 200 control. The purified protein also induced nitric oxide 257 was reported that the daily administration of either
 201 production from macrophages present in isolated 258 aqueous or alcoholic extract of *T. cordifolia* decreases
 202 murine peritoneal exudates cells. Guduchi ImP displays 259 the blood glucose level and increases glucose tolerance
 203 enhanced phagocytosis of yeast cells by macrophages. 260 in rodents [19, 20].

204 Guduchi ImP does not possess haemagglutination 261 Berberine, an alkaloid obtained from the stem of *T.*
 205 activity indicating that the immunomodulatory protein 262 *cordifolia* has been tested and used successfully in
 206 is not a lectin. The confirmation of an 263 experimental and human diabetes mellitus. Berberine
 207 immunomodulatory protein in guduchi stem showing 264 has been shown to lower elevated blood glucose as
 208 lymphoproliferative and macrophage-activating 265 effectively as metformin [21]. The mechanisms of
 209 properties reinforces the rationale of the use of guduchi 266 action include inhibition of aldose reductase [22],
 210 preparations for immunomodulation [12]. 267 inducing glycolysis [23], preventing insulin resistance

211 Cordifolide A , a novel unprecedented sulfur- 268 through increasing insulin receptor expression [24], and
 212 containing clerodane diterpene glycoside, together with 269 acting like incretins [25]. Berberine also overcome
 213 other two new diterpene glycosides, cordifolides B and 270 insulin resistance via modulating key molecules in
 214 C, and four known analogues, were isolated from a 271 insulin signaling pathway, leading to increased glucose
 215 methanol-soluble extract of the stems of *Tinospora* 272 uptake in insulin-resistant cells [26]. Berberine might
 216 *cordifolia*. The structures of the new compounds were 273 exert its insulinotropic effect in isolated rat islets by up-
 217 determined on the basis of spectroscopic data 274 regulating the expression of hepatocyte nuclear factor 4
 218 interpretation, with that of cordifolide A confirmed by a 275 alpha, which probably acts solely or together with other
 219 single-crystal X-ray crystallographic analysis. All 276 HNFs to modulate glucokinase activity, rendering β
 220 isolates were evaluated for their in vitro 277 cells more sensitive to glucose fluctuation and to
 221 immunomodulatory activity using mouse bone marrow- 278 respond more effectively to glucose challenge [27].
 222 derived dendritic cells [13]. *Tinosporia cordifolia* had 279 Berberine also seems to inhibit human dipeptidyl
 223 shown a significant level of macrophages activation 280 peptidase-4 (DPP IV), as well as the pro-diabetic target
 224 leads to increase in GM-CSF which leads to 281 human protein tyrosine phosphatase 1B (h-PTP 1B),
 225 leucocytosis and improved neutrophil function [14]. G1- 282 which explain at least some of its anti-hyperglycemic
 226 4A, an immunomodulatory polysaccharide from 283 activities. Berberine suppresses intestinal disaccharides
 227 *Tinospora cordifolia*, modulates macrophage responses 284 with beneficial metabolic effects in diabetic states [28].
 228 and protects mice against lipopolysaccharide induced 285 A recent comprehensive metabolomics method,
 229 endotoxic shock and G1-4A appeared to induce 286 applied to type 2 diabetics, suggested administration of
 230 tolerance against endotoxic shock by modulation of 287 berberine down-regulates the high level of free fatty
 231 cytokines and nitric oxide [15]. 288 acids which are known to be toxic to the pancreas and

232 T.C. was evaluated for the possibility of enhancing 289 cause insulin resistance. These results suggest berberine
 233 the reproductive performance of crossbred cows by its 290 might play a pivotal role in the treatment of type 2
 234 peripartum supplementation, as the crossbred 291 diabetes [29]. Berberine has been shown to boost the
 235 periparturient cow is highly susceptible to various 292 effects of metformin and 2,4 -thiazolidinedione (THZ),
 236 diseases that effectively reduce its reproductive 293 and can partly replace the commercial drugs, which
 237 performance postpartum. A higher total leukocyte, 294 could lead to a reduction in toxicity and side effects of
 238 lymphocyte, neutrophil count along with increased 295 the latter. Berberine inhibits Foxo1, which integrates

296 insulin signaling with mitochondrial function. Inhibition³⁵⁰ (ALTC) [35]. Intra-peritoneal administration of ALTC
297 of Foxo1 can improve hepatic metabolism during³⁵¹ in DL-bearing mice not only augment the basic function
298 insulin resistance and the metabolic syndrome [30]. ³⁵² of macrophages such as phagocytosis as well as their

299 *Diabetic retinopathy*

300 *T. cordifolia* plays role in prevention and³⁵⁵ the intra-peritoneal administration of ALTC slow down
301 management of diabetic retinopathy due to its³⁵⁶ the tumor growth and increase the life span of tumor
302 antihyperglycemic, anti-angiogenic, anti-inflammatory³⁵⁷ bearing host, thus showing its anti-tumor effect through
303 and anti-oxidant properties. It also prevents the³⁵⁸ destabilizing the membrane integrity of DL cells.
304 progression of cataract and vascular changes, the³⁵⁹ *T.cordifolia* was shown effective in several other
305 important symptoms of DR. Although diabetic rats³⁶⁰ tumour models including Ehrlich ascites carcinoma
306 treated with TC do not achieve the status of normal non-³⁶¹ (EAC) in mice [36]. It induces proliferation and myeloid
307 diabetic rats, but they achieve significant levels as³⁶² differentiation of bone marrow precursor cells in a
308 compared to untreated diabetic rats. *T. cordifolia* thus³⁶³ tumor-bearing host [37], activates tumor-associated
309 acts as a potential therapeutic agent for prevention of³⁶⁴ macrophages-derived dendritic cells [38], is effective
310 the vascular complications of diabetes. ³⁶⁵ against various cancers, killing the cancer cells very

311 *Diabetic neuropathy*

312 *Tinospora cordifolia* prevents the hyperalgesia in,³⁶⁸ *Cognitive effects*
313 experimental diabetic neuropathy. It has an aldose
314 reductase inhibitory activity in vitro which may³⁶⁹ The memory impairment induced by cyclosporine
315 contribute to the beneficial effects [31]. ³⁷⁰ was successfully overcome by both the alcoholic and

316 *Diabetic foot ulcer*

317 Diabetic patients with foot ulcers on *T. cordifolia* as³⁷³ reversed the hippocampal neuronal degeneration
318 an adjuvant therapy showed significantly better final³⁷⁴ induced by cyclosporine revealed by the
319 outcome with improvement in wound healing. Reduced³⁷⁵ histopathological investigation [40]. The alteration of
320 debridements and improved phagocytosis were³⁷⁶ immune function affected learning and memory process
321 statistically significant, indicating beneficial effects of³⁷⁷ and *T. cordifolia* is a potent immunomodulator and
322 immunomodulation for ulcer healing [32]. ³⁷⁸ cognitive enhancer. The dual property of *T. cordifolia*

323 *Hypolipidemic effects*

324 Diabetics are often associated with hyperlipidemia³⁸¹ induced memory changes. Significant response has been
325 and as *T.cordifolia* been shown to have hypoglycemic³⁸² found in children with moderate degree of behaviour
326 properties, the plant was evaluated for its³⁸³ disorders and mental deficit, along with improvement in
327 hypolipidemic activity. An aqueous extract of³⁸⁴ IQ levels. The root of *T.cordifolia* is known to be used
328 *T.cordifolia* root was administered to alloxan induced³⁸⁵ traditionally for its anti-stress activity. The pure
329 diabetic rat (2.5 and 5g/kg body weight for 6 weeks)³⁸⁶ aqueous extract of the root was found to enhance verbal
330 and it reduced serum and tissue cholesterol,³⁸⁷ learning and logical memory. Both the alcoholic and
331 phospholipids, and fatty acid levels. In another study in³⁸⁸ aqueous extracts of *T.cordifolia* produced a decrease in
332 rats, the aqueous extracts also reduced levels of brain³⁸⁹ learning scores in Hebb William maze and retention
333 lipids [33]. ³⁹⁰ memory, indicating enhancement of learning and

334 *Antineoplastic effects*

335 Jagetia *et al.* have found that the guduchi killed the³⁹² *Adaptogenic effects*
336 *HeLa cells* very effectively *in vitro*. In this study, the³⁹³ The aqueous extract not only reversed the effect of
337 stem extracts were evaluated *in vitro* for their cell³⁹⁴ cisplatin on gastric emptying, but also normalized
338 killing effects [34]. When *HeLa* cells were exposed to³⁹⁵ cisplatin-induced hypermotility. The plant was also
339 various doses of the extract, a dose-dependent increase³⁹⁶ found to normalize the phagocytic function of peritoneal
340 in cell killing was observed as compared with non drug-³⁹⁷ macrophages after exposure of rats to either carbon
341 treated controls. The methylene chloride extract was the³⁹⁸ tetrachloride or serum, thus it satisfied the definition of
342 most potent. The effect of guduchi extract was³⁹⁹ adaptogen [42].

343 *Antioxidant activity*

344 thus it indicates that the plant warrants a future study as
345 anti-neoplastic agent. Further investigation were⁴⁰¹ The antioxidant properties of *T. cordifolia* roots
346 undertaken to study whether the tumor associated⁴⁰² were studied by administering the aqueous extract of
347 macrophages (TAM) of Daltons lymphoma (DL) a⁴⁰³ alloxan-induced diabetic rats. After 6 weeks, the level
348 spontaneous transplantable T-cell lymphoma, can be⁴⁰⁴ of plasma barbituric acid reactive substances,
349 activated by the aqueous liquid extract of *T.cordifolia*⁴⁰⁵ 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 500 mg/kg given orally) and formalin-induced arthritis 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), Sodiumazide, 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. 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

517 placebo group, there was relief from sneezing only in 573 gluconeogenic enzymes activity in diabetic rat kidney
518 21% patients; from nasal discharge, in 16.2%; from 574 [66]. The ethanol extracts of the roots of *T. cordifolia*
519 nasal obstruction, in 17%; and from nasal pruritis, in 575 Miers and *C. asiatica* Linn were observed to induce a
520 12%. Thus, *T. cordifolia* significantly decreased all 576 marked protective action against an 8 h restraint stress
521 symptoms of allergic rhinitis and was well tolerated 577 induced ulcerization, the activity being comparable to
522 [58]. The anti-allergic and bronchodilator properties of 578 that of diazepam [67]. Concurrent daily administration
523 an aqueous extract of the stem evaluated on histamine- 579 of *T. cordifolia* stem and leaves extract prevented the
524 induced bronchospasm in guinea pigs, capillary 580 toxic influences of lead on haematological value and the
525 permeability in mice and mast cell disruption in rats 581 results suggested that simultaneous supplementation of
526 showed that it significantly decreased bronchospasm 582 *T. cordifolia* protects against lead intoxication [68].
527 induced by 5% histamine aerosol, decreased capillary
528 permeability and reduced the number of disrupted mast 583 **Clinical uses**
529 cells.

530 Antipyretic and anti-infective activity

531 The water-soluble fraction of 95% ethanolic extract 584
532 of *T. cordifolia* plant has shown significant antipyretic 585 of medicine for the treatment of jaundice, diabetes and
533 activity [59]. In another experimental study, antipyretic 586 rheumatoid arthritis. It has also been found to posses
534 effects have been reported in the hexane- and 587 adaptogenic, anti-inflammatory, anti-neoplastic, anti-
535 chloroform-soluble portions of *T. cordifolia* stems [60]. 588 oxidant, hepatoprotective, cognitive, hypolipidemic,
536 Various studies show remarkable anti-infective and 589 antimalarial, antistress, antipyretic and immunologic
537 antipyretic properties of *T. cordifolia*. Pre-treatment 590 properties. There are limited human studies to support
538 with *T. cordifolia* was shown to impart protection 591 these use. *T. cordifolia* can also be used as an adjuvant
539 against mortality induced by intra-abdominal sepsis 592 drug in the treatment of hyper-reactive malarious
540 following caecal ligation in rats and significantly 593 splenomegaly [69]. *Tinospora cordifolia* appears to
541 reduced mortality from induced by *E. coli*-induced 594 improve surgical outcome by strengthening host
542 peritonitis in mice [61]. 595 defenses as evidenced by the study on surgical outcome
596 in patients with malignant obstructive jaundice [70].

543 Antifertility & aphrodisiac activity

544 Oral administration of 70% methanolic extract of *T.* 597 **Toxicology**
545 *cordifolia* stem to male rats at a dose level of 100 mg/d 598
546 for 60 days did not cause body weight loss but 599 The ayurvedic literature reports that *T. cordifolia*
547 decreased the weight of testes, epididymis, seminal 600 can cause constipation, if taken regularly in high doses.
548 vesicle and ventral prostate in a significant manner [62]. 601 It has no side effect and toxicity. When *T. cordifolia*
549 Gudichi is a natural aphrodisiac in females. Its 602 extract was administered to rabbit up to the highest oral
550 immunomodulatory action helps to strengthen the 603 doses of 1.6 g/kg, there were no predictable adverse
551 immune system and to make the body stronger and 604 drug effects.
552 hence make a woman more able and ready to enjoy the 605
553 sex. It is a rejuvenator and a natural herbal aphrodisiac. 606

554 Other effects

555 In a clinical evaluation, a compound preparation 607
556 'RUMALAYA' containing *T. cordifolia* was reported to 608
557 significantly reduce the pain in patient suffering from 609 potential in modern pharmacotherapeutics.
558 rheumatoid arthritis. Ether extract of the steam distillate 610
559 of aerial part of *T. cordifolia* has inhibited the *in vitro* 611
560 growth of *Mycobacterium tuberculosis* at 1:50,000 612
561 dilutions [63]. It is used for its anti-leprotic properties, 613
562 along with wide use in other types of skin disorders and 614
563 has been shown to exert antileprotic activity in a 615
564 combination formulation. Ethanolic extract of 616
565 *T. cordifolia* has exhibited significant antipyretic activity 617
566 in rats [64]. 'Septilin syrup' a compound preparation 618
567 containing *T. cordifolia* was found to elicit good clinical 619
568 response in children suffering from upper respiratory 620
569 tract infection and chronic otitis media. In a scientific 621
570 study on rats and human volunteers, *T. cordifolia* was 622
571 found to have diuretic effects [65]. It was also found 623
572 effective in modulation of morphology and some 624

604 CONCLUSION

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

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