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REVIEW ARTICLE

Tinospora cordifolia and its therapeutic properties - A Review

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ABSTRACT
Tinospora cordifolia is an important medicinal plant. It is a large, glabrous, deciduous climbing shrub which belongs to the family Menispermaceae. It is distributed throughout tropical Indian subcontinent and China. Many phytochemicals have been isolated from various parts of T. cordifolia which belong to different classes such as alkaloids, steroids, glycosides, diterpenoid lactones, sesquiterpenoid, phenolics, aliphatic compounds polysaccharides essential oils and mixture of fatty acids. T. cordifolia possesses various notable therapeutic properties like anti-hyperglycemic, anti-inflammatory, anti-microbial, anti-oxidant, immunomodulatory, wound healing etc. The aim of this paper is to give critical review about T. cordifolia and its therapeutic properties.
Key words: *Tinospora cordifolia, Phytochemistry, Therapeutic properties*

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INTRODUCTION

Modern therapeutic medicines are very expensive and have various side effects. Therefore, there is a need of safer and affordable alternatives with minimal side effects and which can be taken for long durations in treatment of various diseases. Recently, there has been increasing interest in the use of medicinal plants as a safer and cost effective alternative to modern therapeutic agents. *Tinospora cordifolia* is one of them. *T. cordifolia* is a large, glabrous, deciduous climbing shrub (Fig. 1a) which belongs to the family Menispermaceae. It is commonly known as *Tinospora* in English and Ambervel, Gulancha, Guduchi or Giloya in Hindi. The stem (Fig. 1b) of *T. cordifolia* is succulent with long filiform fleshy aerial roots from the branches. The bark is creamy white to grey. The leaves (Fig. 1c) are membranous, cordate and heart shaped. The flowers are small and greenish yellow. The flowers grow during summer and fruits during winter. It is distributed throughout tropical Indian subcontinent and China [1]. *T. cordifolia* is considered to be having greater medicinal properties. Pharmacological actions attributed to Tinospora cordifolia in Ayurvedic texts have evidences suggesting that this shrub has immense potential in modern pharmacotherapeutics [2]. *T. cordifolia* is a widely used shrub in folk and Ayurvedic systems of medicine all over India [3]. Though almost all of its parts are used in traditional systems of medicines, leaves stem and roots are the most important parts which are used medicinally. Extracts from various parts of *T. cordifolia* have medicinal applications from time immemorial. It can be an important therapeutic agent which can prevent and treat different diseases. *T. cordifolia* has a wide array of bioactive principles as well as it has been proven medicinally important even though it has not received considerable scientific attention. A variety of constituents have been isolated from different parts of *T. cordifolia* belonging to different classes. Recent scientific studies have emphasized the possible use of *T. cordifolia* in modern medicine. The present paper is a review of its therapeutic properties and potential prospects for further scientific investigation in development of effective therapeutic compounds.

PHYTOCHEMISTRY

Various phytochemicals have been isolated from leaves, stem and roots of *T. cordifolia* belonging to different classes such as alkaloids, steroids, glycosides, diterpenoid lactones, sesquiterpenoid, phenolics,

aliphatic compounds polysaccharides essential oils and mixture of fatty acids. The major phytochemicals isolated from *T. cordifolia* are tinosporine, tinosporide, tinosporaside, cordifolides A to E, cordifol, heptacosanol, clerodane furano diterpene, diterpenoid furanolactone tinosporidine, columbin, sitosterol, choline, berberine, giloin, gilenin, crude giloinin, arabinogalactan polysaccharide, picrotene, bergenin, gilosterol, tinosporol, cordifol, octacosonal, columbin, chasmanthin, palmarin, palmatosides C and F, amritosides, cordioside, tinosponone, palmatine, ecdysterone, makisterone A, hydroxyecdysone, magnoflorine, jatrorrhizine, tembetarine, syringine, glucan polysaccharide, tetrahydropalmaitine, isocolumbin and apiosylglycoside [4,5,6].

Fig. 1: a. *Tinospora cordifolia* shrub **b.** Stem **c.** Leaves

THERAPEUTIC PROPERTIES

Tinospora cordifolia possesses following therapeutic properties-

1. **Anti-hyperglycemic:** *Tinospora cordifolia* is widely used in Indian ayurvedic medicine for treating diabetes mellitus [7,8,9,10]. Oral administration of aqueous extract of *T. cordifolia* root in alloxan induced diabetic rats caused a significant reduction in blood glucose and brain lipids [11]. It has been reported that the daily administration of either alcoholic or aqueous extract of *T. cordifolia* decreased the blood glucose level and increased glucose tolerance in rodents [12]. Aqueous extract also caused reduction in blood sugar in alloxan induced hyperglycemia in rats and rabbits in the dose of 400 mg/kg. The possible mode of action of the plant is through glucose metabolism as histological examination of pancreas has not revealed any evidence of regeneration of β-cells of islets of Langerhans [13]. The aqueous extract has also exhibited some inhibitory effect on adrenaline-induced hyperglycemia. Ethyl acetate extract of its roots has yielded a pyrrolidine derivative with hypoglycemic activity in rabbits [14,15]. Another study has also revealed significant hypoglycemic effect of extract of leaves in normal and alloxan induced diabetic rabbits. However, the extract had no significant effect on total lipid levels in normal or treated rabbits [16,17]. Sharma *et al.* [18] reported that *T. cordifolia* mediates its antidiabetic potential through myriad of biologically active phytochemicals isolated from different parts of plant, including alkaloids, tannins, cardiac glycosides, flavanoids, saponins and steroids. Kannadhasan and Venkataraman [19] reported that 30 days treatment of sedimental extract of *T. cordifolia* (1000 mg/kg/p.o) on diabetic subjects was proven for its efficacy and clearly establishes the antidiabetic activity with antiobese body built. It has been reported that phytochemicals of *T. cordifolia* regulate the blood glucose levels by reducing oxidative stress, promoting insulin secretion by inhibiting gluconeogenesis and glycogenolysis which is attributed to alkaloids (Magnoflorine, Palmetine, Jatrorrhizine) [20,21], tannins, cardiac glycosides, flavonoids, saponins and steroids [22].

2. **Anti-inflammatory:** Various studies revealed that *T. cordifolia* has a significant anti-inflammatory activity. The aqueous extract of the stem of *T. cordifolia* has been studied for anti-inflammatory activity in albino rats. It has significantly inhibited acute inflammatory response evoked by carrageenin when administered orally and intraperitoneally [23]. It has also shown a significant anti-inflammatory effect on cotton pellet granuloma and formalin induced arthritis models. Its effect was comparable with indomethacin and its mode of action appeared to resemble that of a non-steroidal anti-inflammatory agent [24]. The dried stem of *T. cordifolia* produced significant anti-inflammatory effect in both acute and subacute models of inflammation. *T. cordifolia* found to be more effective than acetylsalicylic acid in acute inflammation [25]. In a clinical evaluation, *T. cordifolia* significantly reduced the pain in patients suffering from rheumatoid arthritis [26].
3. **Anti-microbial:** *Tinospora cordifolia* has been reported to have antimicrobial properties. Pretreatment with *T. cordifolia* has been reported to impart protection against mortality induced by intra-abdominal sepsis and *E. coli* induced peritonitis [27]. It has been observed that it stimulates the macrophages as evidenced by an increase in the number and percent phagocytosis of *S.aureaus* by peritoneal macrophages in rats. The phagocytic and intracellular killing capacity of polymorphs in rats, tested after *E. coli* infection has been found significant [28]. Its extract has been reported against bacterial growth and improved phagocytic and intracellular bacterial capacities of neutrophils in mice [29]. Antibacterial activity of *T. cordifolia* extract has been bio assayed against *Escherichia coli, Staphylococcus aureus, Klebsiella pneumonia, Proteus vulgaris, Salmonella typhi, Shigella flexneri, Salmonella paratyphi, Salmonella typhimurium, Pseudomonas aeruginosa, Enterobacter aeruginosa, Enterobacter aerogene* [30,31,32] and and *Serratia marcesenses* (Gram-positive bacteria) (30). Aqueous, ethanol and acetone extracts of leaves and stem of *T. cordifolia* have shown maximum inhibitory activity against on clinical isolates of urinary pathogens Klebsiella pneumoniae and Pseudomonas aeruginosa [33]. Silver nanoparticles synthesized from stem of *Tinospora cordifolia* possess very good antibacterial activity against multidrugresistant strains of Pseudomonas aeruginosa isolated from burn patients [34]. The ethanolic extract of *T. cordifolia* has shown activity against bacteria and fungi which is attributed to active compound [(5R, 10R)-4R, 8R-Dihydroxy-2S, 3R:15, 16-diepoxycleroda- 13(16), 17, 12S, 18, 1S-dilactone] [35]. *T. cordifolia* has also shown a higher inhibitory activity against methicillin-resistant Staphylococcus aureus (MRSA) and carbapenemase producing Klebsiella pneumoniae [36].
4. **Anti-oxidant:** Aqueous and alcoholic extracts of *T. cordifolia* have shown notable antioxidant potential [37]. The aqueous extract of roots of *T. cordifolia* has shown the anti-oxidant action in alloxan induced diabetes rats [10]. Methanolic extract of stem of *T. cordifolia* has been reported to anti-oxidant activity, by increasing the erythrocytes membrane lipid peroxide and catalase activity. It also decreases the activity of SOD, GPx in alloxan induced diabetic rats [38,39]. Extract of *T. cordifolia* has been reported its free radical scavenging properties [40]. Phytochemicals from *T. cordifolia* have been reported to have an alpha-glucosidase inhibitor, characterized as saponarin was found to be also significant antioxidant and hydroxyl radical scavenging activity [41]. Essential oil isolated from leaf of *T. cordifolia* has shown strong 2, 2- diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity [42]. The administration of ethanolic extract of *T. cordifolia* (EETC) in N-nitrosodiethylamine (DEN) induced liver cancer in male Wister albino rats reverted the lipid peroxidation (LPO) levels, enzymic and nonenzymic antioxidants to near normal [43]. Alkaloids such as choline, tinosporine, isocolumbin, palmetine, tetrahydropalmatine and magnoflorine from *T. cordifolia* showed protection against aflatoxin induced nephrotoxicity [44]. Furthermore *T. cordifolia* shows protective effect by lowering the concentration of thiobarbituric acid reactive substance (TBARS) and enhancing the glutathione (GSH), ascorbic acid, protein and the activities of antioxidant enzymes viz. superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase, glutathione S-transferase (GST) and glutathione reductase (GR) in kidney [44]. The treatment with crude powder of *T. cordifolia* has been reported to reduce the toxicities of L-DOPA therapy for Parkinson's disease [45].
5. **Immunomodulatory:** *Tinospora cordifolia* is well known for its immunomodulatory response. It benefits the immune system in a variety of ways [46,47]. The alcoholic and aqueous extracts of *T. cordifolia* have been evaluated successfully for immuno-modulatory activity [48,49,50]. Studies have shown that alcoholic extracts of *T. cordifolia* enhanced the bone marrow cellularity as well as α-esterase activity in rats which indicates its immunomodulatory activity [51]. It has shown pronounced immunomodulating effect on inter abdominal sepsis to elucidate host defense mechanism to counter infective stresses. The compounds which are responsible for immunomodulatory and cytotoxic effects are 11- hydroxymuskatone, N-methyle-2-pyrrolidone, Nformylannonain, cordifolioside A, magnoflorine, tinocordioside and syringin [52]. These compounds

improve the phagocytic activity of macrophages, enhance nitric acid production by stimulating splenocyte [53]. It has also been reported that *T. cordifolia* shows its immunomodulatory effect through altering the concentration of antioxidant enzymes, increasing T and B cells and antibody which plays an important role in immunity, enhancing the concentration of melatonin in pineal gland and increasing the level of cytokines like IL-2, IL-10 and TNF-α which plays an important role in immunity [54]. Polymorphonuclear leucocytes (PMN) cells are an important component of the host defence system. Extracts of *T. cordifolia* were able to stimulate the PMN cells for phagocytosis of added Candida cells through an in vitro slide method of phagocytosis [55]. Aqueous extract of *T. cordifolia* has been also reported to influence the cytokine production, mitogenicity, stimulation and activation of immune effector cells [53]. Castillo *et al.* [56] has also reported the immunomodulatory effect of aqueous extract of Tinospora cordifolia in down regulation of Interleukin 1, 6 and 8 levels in scabies infestation inhibits hyperkeratosis and infiltration of inflammatory cells into scabietic lesion. The modulation effect of the Tinospora lotion on interleukin levels reinforces its anti-scabies activity.

6. **Anti-pyretic:** The extract of stem and roots of *T. cordifolia* has shown significant antipyretic effect in yeast provoked elevation of body temperature in rats and this effect is comparable to that of paracetamol [57]. In another study its extract has exhibited significant antipyretic activity in experimental rats [58]. Ashok *et al.* [59] reported the anti-pyretic activity of ***Guduchi ghrita*** (*T. cordifolia*) formulations in albino rats against yeast induced pyrexia. Studies have shown insignificant antipyretic effects in the hexane and chloroform soluble fractions of the stem of *T. cordifolia* [60].
7. **Wound healing:** Wound healing properties of *T. cordifolia* has already been reported [61,62]. It promoted healing of the wound in animal models and increased the tensile strength which may be attributed to the promotion of collagen synthesis [63]. Hashilkar *et al.* [64] reported that *T. cordifolia* significantly promotes wound healing in animal models viz. enhanced wound contraction and decreased days for complete epithelization in excision wounds, increased breaking strength in resutured incision wound and increased granulation tissue with cellular.
8. **Hepatoprotective:** Bishayi *et al.* [65] have reported the hepatoprotective actions of T. cordifolia. Extract of *T. cordifolia* has exhibited *in vitro* inactivating property against Hepatitis B and E surface antigen in 48-72 hrs [66]. *T. cordifolia* have shown significant clinical and hemato-biochemical improvement in carbon tetra chloride (CCl_4) induced hepatopathy. Its phytochemicals exert their protective action against CCl_4 induced hepatocellular alterations through synthesis of proteins, or due to bioactivation of CCl_4 and accelerated detoxification. The plant extract prohibited the lead nitrate induced liver damage on oral administration. Similarly leaf and stem extract *of T. cordifolia* has been reported to show hepatoprotective effect in male albino mice against lead nitrate induced toxicity [67]. *T. cordifolia* minimizes the effects of free radicals including the peroxy radicals and its antioxidant activity in association with the inhibition of lipid peroxidation. Its hepatoprotective actions are attributed to the combined synergistic effect of its constituents and micronutrients rather than any single factor through free radicals activity [68].
9. **Anti-arthritic and anti-osteoporotic:** In traditional medicine, *T. cordifolia* is used for the treatment of rheumatoid arthritis as a single or synergistic formulation with Zingiber officinale [69]. It affects the proliferation, differentiation and mineralization of bone like matrix on osteoblast model systems *in vitro*. Its alcoholic extract has been reported to stimulate the growth of osteoblasts, increasing the differentiation of cells into osteoblastic lineage and also increasing the mineralization of bone like matrix. Ecdysteroid, 20-OH-β-Ecd isolated from *T. cordifolia* has been reported to have anti-osteoporotic activity [70]. Beta-Ecdysone induces a significant increase in the thickness of joint cartilage, induces the osteogenic differentiation in mouse mesenchymal stem cells and relieves osteoporosis [71].
10. **Anti-neoplastic:** *Tinospora cordifolia* has been reported to have anti-cancer activity [72]. Jagetia *et al*. [73] found that it killed the HeLa cells very effectively *in vitro*. The extraction of alkaloid palmatine from *T. cordifolia* has shown anticancer potential in 7,12- dimethylbenz (a) anthracene (DMBA) induced skin cancer model in mice [74]. A single application of *T. cordifolia* extract, prior the intraperitoneal administration of cyclophosphamide significantly prevented the micronucleus formation in bone marrow of mice, in a dose dependent manner. C57/ BL mice when received 50% methanolic extract of *T. cordifolia* at a dose 750 mg/kg body weight for 30 days showed increase in life span and tumor size was significantly reduced as compared to control [75]. Mishra and Kaur [76] reported the anti-brain cancer potential of 50% ethanolic extract of *T. cordifolia* using C6 glioma cells. It significantly reduced cell proliferation in dose dependent manner and induced differentiation in C6 glioma cells. Two molecules from hexane and methanol fractions (T1 and T2) from the *T. cordifolia* showed that in MCF-7 cells, T1 treatment significantly suppressed the proliferation, migration and

invasion of MCF-7cells when compared to that of T2. Epithelial–mesenchymal transition related genes, Twist and Snail, were downregulated by T1 with increased transcription of E-cadherin [77]. Eight secondary metabolites from *T. cordifolia* have been evaluated against four different human cancer cell lines, KB (human oral squamous carcinoma), CHOK-1 (hamster ovary), HT-29 (human colon cancer) and SiHa (human cervical cancer) and murine primary cells respectively. All extracts and fractions were active against KB and CHOK-1 cells whereas among the pure molecules palmatine was found to be active against KB and HT-29; tinocordiside against KB and CHOK-1; yangambin against KB cells [78].

11. **Diuretic and calculolytic:** *Tinospora cordifolia* also has diuretic property [79]. The aqueous extract of the stem of *T. cordifolia* was experimentally evaluated for dissolution of urinary calculi [80]. In a scientific study on rats and human volunteers, ***T. cordifolia*** was found to have diuretic effects [79]. It was also found effective in modulation of morphology and some gluconeogenic enzymes activity in diabetic rat kidney [81].
12. **Anti-hyperlypidaemia:** The administration of the extract of *T. cordifolia* roots resulted in a significant reduction of serum and tissue cholesterol, phospholipids and free fatty acids in alloxan induced diabetic rats [38,82].
13. **Anti-allergic:** The anti-allergic properties of an aqueous extract of the stem of *T. cordifolia* were 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. [83,84]. Sharma *et al.* [52] have also reported anti-allergic properties of *T. cordifolia*.
14. **Anti-stress and cognitive enhancer:** The anti-stress and tonic property of the *T. cordifolia* was clinically evaluated and it was found that it brought about good response in children with moderate degree of behaviour disorders and mental deficit. It has also significantly improved the I.Q. levels. Studies have shown that *T. cordifolia* helps in cognitive enhancement by immunostimulation and synthesis of acetylcholine. Thus contributing in increased choline level which shows that it has memory enhancing property for learning and memory in normal and memory deficit animals [85].
15. **Antagonist:** The aqueous extract of the stem of *T. cordifolia* antagonizes the effect of 5-hydroxytryptamine, histamine, bradykinin and prostaglandins E 1 and 2 on the rabbit smooth muscle, relaxes the intestinal, uterine smooth muscle and inhibits the constrictor response of histamine and acetylcholine on smooth muscle [86].
16. **Anti-HIV:** Root extract of *T. cordifolia* has shown its activity against HIV [87]. This anti HIV effect was exposed by reduction in eosinophil count, stimulation of B lymphocytes, macrophages, level of hemoglobin and polymorphonuclear leucocytes [87,88].
17. **Anti-leprotic:** The stem extract *T. cordifolia* is useful in skin diseases [89,90]. Zhao *et al.* [91] reported the anti-leprotic effect of T. cordifolia. It has also shown anti-leprotic activity in a combination formulation [92].
18. **Anti-spasmodic:** Nayampalli *et al.* [79] and Upadhyay *et al.* [24] have reported antispasmodic activity of *T. cordifolia.* Chaudhari and Shaikh [60] have also reported antispasmodic activity of its dry bark.
19. **Radiation protective:** *Tinospora cordifolia* aqueous extract has a radio protective activity, enhancing the survival of mice against a sub-lethal dose of gamma radiation [93]. In pre-irradiating mice, root extract has widely affected radiation, induced rise in lipid peroxidation and resulted in the decline of GSH in testes [53].
20. **Antidote**: *Tinospora cordifolia* is also used as antidote to snake bite and scorpion sting [94,95,91].
21. **Stomachic:** Nayampalli *et al.* [79] reported stomachic property of *T. cordifolia*. Sharma *et al.* [96] have also confirmed its stomachic property.
22. **Anti-malarial:** Anti-malarial property of *T. cordifolia* has also been reported [97,91].
23. **Anti-epileptic:** Murthy *et al.* [98] reported that T. cordifolia possess significant anticonvulsant property.

CONCLUSION

This is evident from the review of literature that *T. cordifolia* is rich in many phytochemicals and has a vast therapeutic potential. Very little work has been done on the biological activities and plausible medicinal applications of these phytochemicals. Therefore, an extensive investigation is needed to exploit their therapeutic potential to combat diseases. Hence, this review can be used for further research and clinical purposes.

COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES

1. Raghu, A.V., Geetha, S.P., Martin, G., Balachandran, I. and Ravindran, P.N. (2006). In vitro clonal propagation through mature nodes of *Tinospora cordifolia* (Willd.) Hook. F. & Thoms.: An important ayurvedic medicinal plant. In Vitro Cell Dev. *Biol.-Plant,* 42: 584-88.
2. Kavya, B., Kavya, N., Ramarao, V. and Venkateshwarlu, G. (2015). Tinospora cordifolia (Willd.) Miers.: Nutritional, Ethnomedical and therapeutic utility. *Int. J. Res. Ayurveda Pharm.,* 6 (2), 195-198.
3. Reddy, N. M. and Reddy, R. (2015). *Tinospora cordifolia* chemical constituents and medicinal properties: a review. *Sch Acad J Pharm*, 4(8), 364-369.
4. Hanuman, J. B., Bhatt, R. K., and Sabata, B. (1988). A clerodane furano-diterpene from Tinospora cordifolia. *Journal of Natural Products*, 51(2), 197-201.
5. Ghosal, S. and Vishwakarma, R. A. (1997). Tinocordiside, a new rearranged cadinane sesquiterpene glycoside from Tinospora cordifolia. *Journal of Natural Products*, 60(8), 839-841.
6. Singh, S. S., Pandey, S. C., Srivastava, S., Gupta, V. S., Patro, B. and Ghosh, A. C. (2003). Chemistry and medicinal properties of *Tinospora cordifolia* (Guduchi). *Indian journal of pharmacology*, 35(2), 83-91.
7. Mathew, S. and Kuttan, G. (1997). Antioxidant activity of *Tinospora cordifolia* and its usefulness in the amelioration of cyclophosphamide-induced toxicity. *J. Exp. Clin. Cancer. Res.,* 16: 407-11.
8. Prince, P. S. and Menon, V. P. (1999). Antioxidant activity of *Tinospora cordifolia* roots in experimental diabetes. *J. Ethnopharmacol*., 65:277-81.
9. Stanely, M., Prince, P. and Menon, V. P. (2001). Antioxidant action of *Tinospora cordifolia* root extract in alloxan diabetic rats. *Phytothe.r Res.,* 15: 213-8.
10. Rathi, S. S., Grover, J. K. and Vikrant. V. (2002). Prevention of experimental diabetic cataract by Indian Ayurvedic plant extracts. *Phytother. Res*., 16: 774–7.
11. Dhaliwal, K. S. (1999). Method and composition for treatment of diabetes. *US Patent.,* 5886029.
12. Grover, J. K., Vats, V., Rathi, S. S., Dawar, R. (2001). Traditional Indian anti-diabetic plants attenuate progression of renal damage in streptozotocin induced diabetic mice. *J. Ethnopharmacol.,* 76: 233-8.
13. Raghunathan, K. and Sharma, P. V. (1969). Effect of *Tinospora cordifolia* Miers (Guduchi) on induced Hyperglycemia. *J Res Indian Med.,* 3: 203.
14. Grover, J. K., Vats, V., Rathi, S. S. (2000). Anti-hyperglycemic effect of Eugenia jambolana and *Tinospora cordifolia* in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism. *J. Ethnopharmacol.,* 73: 461-70.
15. Stanely, M., Prince, P. and Menon, V. P. (2000). Hypoglycaemic and other related actions of *Tinospora cordifolia* roots in alloxan-induced diabetic rats. *J. Ethnopharmacol.* 70: 9-15.
16. Wadood, N., Wadood, A. and Shah, S. A. (1992). Effect of *Tinospora cordifolia* on blood glucose and total lipid levels of normal and alloxan-diabetic rabbits. *Planta Med*., 58: 131-6.
17. Basnet, P., Kadota, S., Pandey, R. R., Takahashi, T., Kojima, Y., Shimizu, M., Takata, Y., Kobayashi, M. and T. Namba. (1995). Screening of traditional medicines for their hypoglycemic activity in streptozotocin (STZ)-induced diabetic rats and a detailed study on Psidium guajava. *Wakan. Iyakugaku. Zasshi*., 12: 109-7.
18. Sharma, R., Amin, H. and Prajapati, P. K. (2015). Antidiabetic claims of *Tinospora cordifolia* (Willd.) Miers: critical appraisal and role in therapy. *Asian Pacific Journal of Tropical Biomedicine*, 5(1), 68-78.
19. Kannadhasan, R. and Venkataraman, S. (2012). Antidiabetic And Antihyperlipidaemic Activity Of Sedimental Extract Of *Tinospora cordifolia* In Streptozotocin Induced Type 2 Diabetes. *Int J Pharm Pharm Sci,* 4(3), 520-527.
20. Patel, M.B. and Mishra, S. (2011). Hypoglycemic activity of alkaloidal fraction of *Tinospora cordifolia*. *Phytomedicine,* 18:1045-1052.
21. Sangeetha, M. K., Raghavendran, H. R. B., Gayathri, V. and Vasanthi, H. R. (2011). Tinospora cordifolia attenuates oxidative stress and distorted carbohydrate metabolism in experimentally induced type 2 diabetes in rats. *Journal of Natural Medicines*, 65(3-4), 544-550.
22. Sudha, P., Zinjarde, S. S., Bhargava, S. Y. and Kumar, A. R. (2011). Potent α-amylase inhibitory activity of Indian Ayurvedic medicinal plants. *BMC complementary and alternative medicine*, 11(1), 5.
23. Pendse, V.K., Dadhich, A.P., Mathur, P.N., Bal, M.S. and Madam, B.R. (1977). (Anti-inflammatory, immunosuppressive and some related pharmacological actions of the water extract of Neem Giloe (*Tinospora cordifolia*)- A preliminary report). *Indian J Pharm,* 9: 221-24.
24. Upadhyay, A.K., Kumar, K., Kumar, A. and Mishra, H. S. (2010). *Tinospora cordifolia* (Willd.) Hook. f. and Thoms. *(Guduchi)* – validation of the Ayurvedic pharmacology through experimental and clinical studies. Int. J. Ayurveda. Res., 1(2), 112–121.
25. Utpalendu, J., Chattopadhyay, R. N. and Badri, P. S. (1999). Preliminary studies on anti-inflammatory activity of Zingiber officinale Rosc., Vitex negundo Linn and *Tinospora cordifolia* (willid) Miers in albino rats. *Indian journal of pharmacology*, 31(3), 232.
26. Chavali, S. R. and Forse, R. A. (1997). *U.S. Patent No. 5,683,698*. Washington, DC: U.S. Patent and Trademark Office.
27. Dhuley, J. N. (1997). Effect of some Indian herbs on macrophage functions in ochratoxin A treated mice. *J. Ethnopharmacol.,* 58: 15-20.

28. Thatte, U. M., Rao, S. G. and Dahanukar, S. A. (1994). *Tinospora cordifolia* induces colony stimulating activity in serum. *J. Postgrad. Med*., 40: 202-3.
29. Sengupta, S., Mukherjee, A., Goswami, R. and Basu, S. (2009). Hypoglycemic activity of the antioxidant saponarin, characterized as alpha-glucosidase inhibitor present in *Tinospora cordifolia*. *J Enzyme Inhib Med Chem,* 24:684-690.
30. Narayanan, A.S., Raja, S.S., Ponmurugan, K., Kandekar, S.C., Natarajaseenivasan, K., Maripandi, A. and Mandeel, Q.A. (2011). Antibacterial activity of selected medicinal plants against multiple antibiotic resistant uropathogens: a study from Kolli Hills, Tamil Nadu, India. *Benef Microbes*, 2(3), 235-43.
31. Jayachandran, R., Xavier, T.F. and Anand, S.P. (2003). Antibacterial activity of stem extracts of *Tinospora cordifolia* (willd.) Hook. F. and Thoms. *Anc Sci Life,* 22:40-43.
32. Ambekar, D.H., Khante, B.S., Chandak, B.R., Titare, A.S., Baralkar, S.S., Aghadte, S.N. (2009). Screening of antibacterial potential of some medicinal plants from Melghat forest in India. *Afr J Trad Comp Altern Med,* 6:228-232.
33. Shanthi, V. and Nelson, R. (2013). Anitbacterial activity of *Tinospora cordifolia* (Willd) Hook.F.Thoms on urinary tract pathogens. *Int J Curr Microbiol App Sci,* 2(6), 190-194.
34. Singh, K., Panghal, M., Kadyan, S., Chaudhary, U. and Yadav, J. P. (2014). Antibacterial activity of synthesized silver nanoparticles from *Tinospora cordifolia* against multi drug resistant strains of Pseudomonas aeruginosa isolated from burn patients. *Journal of Nanomedicine & Nanotechnology*, 5(2), 1-6.
35. Duraipandiyan, V., Ignacimuthu, S., Balakrishna, K. (2012). Antimicrobial activity of *Tinospora cordifolia*: an ethnomedicinal plant. *Asian Journal of Traditional Medicines,* 7(2), 59-65.
36. Bonvicini, F., Mandrone, M., Antognoni, F., Poli, F., and Angela Gentilomi, G. (2014). Ethanolic extracts of Tinospora cordifolia and Alstonia scholaris show antimicrobial activity towards clinical isolates of methicillin-resistant and carbapenemase-producing bacteria. *Natural product research*, 28(18), 1438-1445.
37. Bhawya, D. and Anilakumar, K.R. (2010). In Vitro Antioxidant Potency of *Tinospora cordifolia* (gulancha) in Sequential Extracts. *International Journal of Pharmaceutical & Biological Archives,* 1(5), 448-456.
38. Stanely, M., Prince, P. and Menon, V. P. (2003). Hypoglycaemic and hypolipidaemic action of alcohol extract of *Tinospora cordifolia* roots in chemical induced diabetes in rats. *Phytotherapy Research*, 17(4), 410-413.
39. Sivakumar, V. and Rajan, M. D. (2010). Antioxidant effect of *Tinospora cordifolia* extract in alloxan-induced diabetic rats. *Indian journal of pharmaceutical sciences*, 72(6), 795-8.
40. Rawal, A., Muddeshwar, M. and Biswas S. (2004). Effects of *R. cordifolia, F. creticalinn., T. cordifolia*on free radical generation and lipid peroxidation during oxygen glucose deprivation in rat hippocampal slices. *Biochem Biophy Res Com,* 324:588-596.
41. Diwanay, S., Chitre, D. and Patwardhan, B. (2004). Immunoprotection by botanical drug on experimental metastasis. *J ethanopharmacol,* 90:223-237.
42. Dattatraya, N., Chitra, D. and Shobha, R. (2014). Determination of Chemical Composition and Evaluation of Antioxidant Activity of Essential Oil from *Tinospora cordifolia* (Willd.) Leaf. *Journal of Essential Oil Bearing Plants,* 17(2), 228-236.
43. Jayaprakash, R., Ramesh, V. and Sasikala, C. (2015). Antioxidant activity of ethanolic extract of *Tinospora cordifolia* on N-nitrosodiethylamine (diethylnitrosamine) induced liver cancer in male Wister albino rats. *J Pharm Bioall Sci,* 7:S40-5.
44. Gupta, R. and Sharma, V. (2011). Ameliorative effects of *Tinospora cordifolia* root extract on histopathological and biochemical changes induced by aflatoxin-b(1) in mice kidney. *Toxicol Int,* 18(2), 94-8.
45. Antony, S., DebRoy, P., Vadivelan, R., Jaysankar, K., Vikram, M., Nandini, S. and Suresh, B. (2010). Amelioration of CNS Toxicities of L-Dopa in Experimental Models of Parkinson's disease by Concurrent Treatment with Tinospora cordifolia. *Hygeia: Journal for Drugs and Medicines*, 2(1), 28-37.
46. Rege, N. N., Bapat, R. D., Koti, R., Desai, N. K. and Dahanukar, S. (1993). Immunotherapy with *Tinospora cordifolia*: A new lead in the management of obstructive jaundice. *Indian J Gastroenterol*; 12:5-8.
47. Nagarkatti, D. S., Rege, N. N., Desai, N. K. and Dahanukar, S. A. (1994). Modulation of Kupffer cell activity by *Tinospora cordifolia* in liver damage. *J. Postgrad. Med*., 40: 65-7.
48. Rege, N. N., Thatte, U. M. and Dahanukar, S. A. (1999). Adaptogenic properties of six rasayana herbs used in Ayurvedic medicine. *Phytother. Res*., 13: 275-91.
49. Manjrekar, P. N., Jolly, C.I., Narayanan, S. (2000). Comparative studies of the immunomodulatory activity of *Tinospora cordifolia* and Tinospora sinensis. *Fitoterapia.,* 71: 254-7.
50. Dikshit, V., Damre, A. S., Kulkarni, K. R., Gokhale, A. and Saraf, M. N. (2000). Preliminary screening of imunocin for immunomodulatory activity. *Indian. J. Pharm .Sci.,* 62: 257.
51. Aher, V. D. and Wahi, A. (2010). Pharmacological study of Tinospora cordifolia as an immunomodulator. *Int J Curr Pharm Res*, 2(4), 52-54.
52. Sharma, U., Bala, M., Kumar, N., Singh, B., Munshi, R.K. and Bhalerao S. (2012). Immunomodulatory active compounds from *Tinospora cordifolia*. *J Ethnopharmacol,* 141(3), 918-26.
53. Upadhyay, P.R., Sharma, V. and Anita, K.V. (2011). Assessment of the multifaceted immunomodulatory potential of the aqueous extract of *Tinospora cordifolia*. *Res J Chem Sci,* 1:71-79.
54. Aher, V. and Wahi, A. K. (2012). Biotechnological approach to evaluate the immunomodulatory activity of ethanolic extract of Tinospora cordifolia stem (mango plant climber). *Iranian journal of pharmaceutical research: IJPR*, 11(3), 863.

55. Salkar, K., Suthar, A. and Chotalia, C. (2014). Study of Immunomodulatory activity of Tinospora cordifolia extract. *International Journal of Advances in Pharmacy, Biology and Chemistry*, 3(4), 880-883.
56. Castillo, A. L., Ramos, J. D. A., De Francia, J. L., Quilala, P. F. and Dujunco, M. U. (2014). Immunomodulatory effects of tinospora cordifolia lotion on interleukin-1, interleukin-6 and interleukin-8 levels in scabies-infected pediatric patients: a single blind, randomized trial. *International Journal of Pharmaceutical Sciences and Drug Research*, 6(3), 204-210.
57. Ikram, M., Khattak, S. G. and Gilani, S. N. (1987). Antipyretic studies on some indigenous Pakistani medicinal plants: II. *J. Ethnopharmacol.,* 19: 185-92.
58. Vedavathy, S. and Rao, K. N. (1991). Antipyretic activity of six indigenous medicinal plants of Tirumala Hills, Andhra Pradesh, India. *J. Ethnopharmacol.,* 33: 193-6.
59. Ashok, B. K., Ravishankar, B., Prajapati, P. K. and Bhat, S. D. (2010). Antipyretic activity of *Guduchi Ghrita* formulations in albino rats. *Ayu*, 31(3), 367–370.
60. Chaudhari, S. and Shaikh, N. (2013).Gaduchi-The Best Ayurvedic Herb. *The Pharma Inn J,* 2 (4), 97-102.
61. Shanbhag, T., Shenoy, S. and Rao, M.C. (2005). Wound healing profile of *Tinospora cordifolia. Indian Drugs.* 42. 217-221.
62. Singh, C. S., Singh, A. K., Khandelwal, S. and Vishwkarma, R. (2013). Anti-Diabetic Activity of Ethanolic Extract of *Tinospora Cordifolia* Leaves. *International Journal Of Drug Discovery And Herbal Research*, 3(1), 601-604.
63. Girish, M. and Priyadarshini, K. (2012). The influence of tinospora cordifolia on wound healing in albino rats. *Int J Pharma Biosciences*, 3(2), 379-384.
64. Hashilkar, N. K., Patil, P. A., Bagi, J. G., Patil, S. Y. and Angadi N. B. (2016). Influence of *Tinospora cordifolia* on wound healing in wistar rats International Journal of Basic & Clinical Pharmacology, 5(3), 923-928.
65. Bishayi, B., Roychowdhury, S. and Ghosh, S. (2002). Hepatoprotective and immune modulatory properties of Tinospora cordifolia in CCl4 intoxicated mature albino rats*. J. Toxicol. Sci*. 27: 139-46.
66. Mehrotra, R., Katiyar, C. K. and Gupta, A. P. (2000). Hepatoprotective compositions and composition for treatment of conditions related to hepatitis B and E infection. *U.S. Patent.* 749296.
67. Sharma, V. and Pandey, D. (2010). Beneficial effects of *Tinospora cordifolia* on blood profiles in male mice exposed to lead. *Toxicology international*, 17(1), 8.
68. Pingale, S.S. (2010). Hepatosuppression Study by *Tinospora cordifolia.* Der Pharma Chemica, 2 (3), 83-9.
69. Chopra, A., Saluja, M., Tillu, G., Venugopalan, A., Narsimulu, G., Handa, R., Lata B., Raut, A., Sanjeev, S. and Patwardhan, B. (2012). Comparable efficacy of standardized Ayurveda formulation and hydroxychloroquine sulfate (HCQS) in the treatment of rheumatoid arthritis (RA): a randomized investigator-blind controlled study. *Clinical rheumatology*, 31(2), 259-269.
70. Abiramasundari, G., Sumalatha, K. R., and Sreepriya, M. (2012). Effects of Tinospora cordifolia (Menispermaceae) on the proliferation, osteogenic differentiation and mineralization of osteoblast model systems in vitro. *Journal of ethnopharmacology*, 141(1), 474-480.
71. Gao, L., Cai, G. and Shi, X. (2008). β-Ecdysterone induces osteogenic differentiation in mouse mesenchymal stem cells and relieves osteoporosis. *Biological and Pharmaceutical Bulletin*, 31(12), 2245-2249.
72. Singh, N., Singh, S. M. and Shrivastava, P. (2005). Effect of *Tinospora cordifolia* on the antitumor activity of tumor-associated macrophages derived dendritic cells. *Immunopharmacol Immunotoxicol.* 27: 1-14.
73. Jagetia, G.C., Nayak, V. and Vidyasagar, M.S. (1998). Evaluation of the antineoplastic activity of guduchi (*Tinospora cordifolia*) in cultured HeLa cells. *Cancer Lett,* 127:71‑82.
74. Ali H. and Dixit S. (2013). Extraction optimization of *Tinospora cordifolia* and assessment of the anticancer activity of its alkaloid palmatine. *Scientific World Journal,* 28:376216.
75. Verma, R., Chaudhary, H. S. and Agrawal, R. C. (2011). Evaluation of anticarcinogenic and antimutagenic effect of *Tinospora cordifolia* in experimental animals. *J Chem Pharm Res*, 3(6), 877-81.
76. Mishra, R. and Kaur, G. (2013). Aqueous ethanolic extract of Tinospora cordifolia as a potential candidate for differentiation based therapy of glioblastomas. *PLoS One*, 8(10), 78764.
77. Shilpa, P., Yashaswini, B. and Bharathi, P. S. (2015). Antimetastatic Activity of *Tinospora cordifolia* Involves Inhibition of Cell Migration and Invasion Regulated By Twist and Snail Genes. *Journal of Pharmacy and Biological Sciences,* 10(2), 44-49.
78. Bala M., Pratap K., Verma P.K., Singh B. and Padwad Y. (2015). Validation of ethnomedicinal potential of *Tinospora cordifolia* for anticancer and immunomodulatory activities and quantification of bioactive molecules by HPTLC. *J Ethnopharmacol,* 175(4), 131–137.
79. Nayampalli, S. S., Ainapure, S. S., Samant, B. D., Kudtarkar, R. G., Desai, N. K. and Gupta, K. C. (1988). A comparative study of diuretic effects of *Tinospora cordifolia* and hydrochloro-thiazide in rats and a preliminary phase I study in human volunteers. *J. Postgrad. Med*., 34:233-6.
80. Rai, M. and Gupta, S.S. ((1967). Experimental Evaluation of *Tinospora cordifolia* (Guduchi) for dissolution of Urinary Calculi, *J Res Ind Med*, 2(1), 115.
81. Nagaraja, P.K., Kammar, K.F. and Devi, S. (2007). Modulation of morphology and some gluconeogenic enzymes activity by ***Tinospora cordifolia*** (Willd.) in diabetic rat kidney. *Biomed Res.,* 18:179–83.
82. Stanely, M., Prince, P., Menon, V. P. and Gunasekaran, G. (1999). Hypolipidaemic action of *Tinospora cordifolia* roots in alloxan diabetic rats. *J. Ethnopharmacol*., 64: 53-7.
83. Nayampalli, S. S., Desai, N. K. and Ainapure, S. S. (1986). Anti-allergic properties of *Tinospora cordifolia* in animal models. *Indian. J. Pharm.,* 18: 250-2.

84. Badar, V. A., Thawani, V. R., Wakode, P. T., Shrivastava, M. P., Gharpure, K. J., Hingorani, L. L. and Khiyani, R. M. (2005). Efficacy of Tinospora cordifolia in allergic rhinitis. *Journal of ethnopharmacology*, 96(3), 445-449.
85. Lannert, H. and Hoyer, S. (1998). Intracerebroventricular administration of streptozotocin causes long-term diminutions in learning and memory abilities and in cerebral energy metabolism in adult rats. *Behavioral Neuroscience,* 112(5), 1199-208.
86. Anonymous (1976). Wealth of India: Raw materials, Vol X. New Delhi: CSIR.
87. Kalikae, M.V., Thawani, V.R., Varadpande, U.K., Santakke, S.D., Singh, R.P. and Khiyani, R.K. (2008). Immunomodulatory effect of *T. cordifolia* extract in HIV positive patients. *Ind J pharmacol,* 40:107-110.
88. Akhtar, S. (2010). Use of *T. cordifolia* in HIV infection. *Ind J pharmacol.,* 42:57-63.
89. Aiyer, K. N. and Kolammal, M. (1963). Pharmacognosy of Ayurvedic Drugs, Series 1. *Trivendram: The Central Research Institute*.
90. Raghunathan, K., Mittra, R., editors. (1982). New Delhi: Central Council for Research In Ayurveda & Siddha. *Pharmacognosy of Indigenous Drugs.*
91. Zhao, T., Wang, X., Rimando, A. M. and Che, C. T. (1991). Folkloric medicinal plants: *Tinospora sagittata* var. cravaniana and Mahonia bealei. *Planta Medica*, 57(05), 505-505.
92. Asthana, J. G., Jain, S., Ashutosh, M. and Vijay Kanth, M. S. (2001). Evaluation of antileprosy herbal drug combinations and their combinations with dapsone. *INDIAN DRUGS-BOMBAY-*, 38(2), 82-86.
93. Kapur, P., Wuttke, W. and Jarry, H. (2010). Beneficial effects of beta-ecdysone on the joint epiphyseal cartilage tissue and trabecular bone in ovariectomized rats. *Phytomedecine,* 17:350-355.
94. Kirtikar, K. R., Basu, B. D. editors. (1975). Indian Medicinal Plants, Vol 1. 2nd ed. New Connaught Place, Dehra Dun: M/S Bishen Singh, Mahendra Pal Singh.
95. Nadkarni, K. M., Nadkarni, A. K., editors. (1976). *Indian Materia Medica*, Vol 1. 3rd ed. Mumbai: M/S Popular Prakasan Pvt. Ltd
96. Sharma, A., Gupta, A., Singh, S. and Batra, A. (2010). *Tinospora cordifolia* (Willd.) Hook. F. & Thomson - A plant with immense economic potential. *J. Chem. Pharm. Res.,* 2(5), 327-333.
97. Nayampalli, S., Ainapure, SS. and Nadkarni, PM. (1982). Study of antiallergic acid Bronchodilator effects of *Tinospora cordifolia*. *Indian J Pharm.,* 14:64-6.
98. Murthy, J. R., Meera, R., Venkataraman, S., Satpute, B.T., Chidambaranathan, N. and Devi, P. (2010). Phytochemical investigation and anticonvulsant activity of leaves of *Tinospora cordifolia* Miers. *Int J Pharm Sci,* 2(2), 522-7.
1. Ethiopia). Ph.D. Dissertation, Wageningen University, The Netherlands.