Tinosporacordifolia: A Potential Plant with Immunomodulatory Activity

P. ITTIYAVIRAH SIBI*, AND T. RAHEES

Received June 25, 2012; Revised October 2, 2012; Accepted November 12, 2012

ABSTRACT

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

Keywords: Immunomodulation, Immunomodulating agent, Tinosporacordifolia

Advances in molecular biology have revolutionized depending on the requirement of the situation. immunology and medicine. Initially the use of antibody was therapeutic agents was limited by their purity and resource even by the most intransigent clinicians of heterogeneity. Immunotherapy derives from the advanced countries. Plant extracts have been widely observed from the 19th century, that cancer investigated for their possible immunomodulatory sometimes regressed after acute bacterial infections, that properties, Tinospora cordifolia, an indispensable is, may be no specific immunostimulant effect. medicinal plant, has been used for the treatment of The rapidly expanding discipline of immunology various diseases and has been recommended for contributes to diagnosis, therapy and prevention of improving the immune system. There is great interest in human diseases in many ways. The role of development of new drugs from traditionally used immunocompetents in prevention of malignancy is medicinal plants like Tinosporacordifolia. Ayurveda currently of great interest in experimental science as refers to Tinospora cordifolia as ‘Amruth’ or the ‘Nectar well as clinical medicine. Interest in the immune of Immortality’. The term ‘Amruth’ is attributed to this response has been stimulated by the alarming increase drug in recognition of its ability to impart youthfulness, in a novel epidemic form of immune deficiency, vitality and longevity. Immunomodulation can be "Acquired ImmunoDeficiency Syndrome" (AIDS). determined by the capacity of the compounds to Immunomodulation relates to potentiation or influence the cytokine production, mitogenicity, suppression of the immune responses of the host, stimulation and activation of immune effector cells.
Immunomodulatory activity of *Tinospora cordifolia*

**ARTICLE IN PRESS**

Panchabhai et al done a study “Validation of therapeutic claims of *Tinospora cordifolia*: a review” on 2008 [1]. As *Tinospora cordifolia* is a plant of high pharmacological potential, day by day new studies are conducted and novel therapeutic activities are revealed. Recently, isolation and characterisation of phytoconstituents responsible for the activities are done. So, there is a scope for a new study. *Tinospora cordifolia* is a plant of high pharmacological potential, day by day new studies are conducted and novel therapeutic activities are revealed. Recently, isolation and characterisation of phytoconstituents responsible for the activities are done. So there is a scope for a new study.

**DESCRIPTION AND HISTORY**

*T. cordifolia* (Fig 1); common name guduchi, amrita. A variety of constituents have been isolated from *T. cordifolia* plant. They belongs to different classes such as alkaloids, diterpenoids, lactones, glycosides, steroids, sesquiterpenoids, phenolic, aliphatic compounds and polysaccharides (Table 1). Leaves of this plant are rich in protein (11.2%), calcium and phosphorus [3]. Anarabinogalactan had been isolated from the dried stem of *T. cordifolia* [4].

**PHARMACOLOGICAL ACTIONS**

*Panchabhai et al* done a study “Validation of therapeutic claims of *Tinospora cordifolia*: a review” on 2008 [1]. As *Tinospora cordifolia* is a plant of high pharmacological potential, day by day new studies are conducted and novel therapeutic activities are revealed. Recently, isolation and characterisation of phytoconstituents responsible for the activities are done. So, there is a scope for a new study. *Tinospora cordifolia* is a plant of high pharmacological potential, day by day new studies are conducted and novel therapeutic activities are revealed. Recently, isolation and characterisation of phytoconstituents responsible for the activities are done. So there is a scope for a new study.

**Description and History**

*T. cordifolia* (Fig 1); common name guduchi, amrita. A variety of constituents have been isolated from *T. cordifolia* plant. They belongs to different classes such as alkaloids, diterpenoids, lactones, glycosides, steroids, sesquiterpenoids, phenolic, aliphatic compounds and polysaccharides (Table 1). Leaves of this plant are rich in protein (11.2%), calcium and phosphorus [3]. Anarabinogalactan had been isolated from the dried stem of *T. cordifolia* [4].

**Pharmacological Actions**

*Panchabhai et al* done a study “Validation of therapeutic claims of *Tinospora cordifolia*: a review” on 2008 [1]. As *Tinospora cordifolia* is a plant of high pharmacological potential, day by day new studies are conducted and novel therapeutic activities are revealed. Recently, isolation and characterisation of phytoconstituents responsible for the activities are done. So there is a scope for a new study. *Tinospora cordifolia* is a plant of high pharmacological potential, day by day new studies are conducted and novel therapeutic activities are revealed. Recently, isolation and characterisation of phytoconstituents responsible for the activities are done. So there is a scope for a new study.
immunosuppression [7]. The polysaccharide-enriched T. cordifolia treatment, significantly caused the fraction from this plant is found to be very effective in reducing the metastatic potential of B16f-10 melanoma cells [8]. Treatment period, however, reduction in total bacterial count was observed from day 3 onwards. The results confirmed the 0.05) in diseased cows treated with the extract. The immunomodulatory activity of the polysaccharides of T. cordifolia, and also it was conclude that the T. cordifolia (stem) possesses antibacterial and polysaccharide with lowest sugar content showed immunomodulatory properties [10].

Sharma et al (2012) isolated and characterised the immunomodulatory activity of three polysaccharide-enriched milk polymorphonuclear cells enhanced in the diseased cows treated with the T. cordifolia extract. The IL-8 level in milk serum also increased significantly (p < 0.05) in diseased cows treated with the extract. The highest activity and with highest sugar content showed Sharma et al (2012) isolated and characterised the lowest activity [9]. Mukherjee et al evaluate the immunomodulatory active compounds of Tinospora cordifolia biological activity of the Tinospora cordifolia extract at standardized dose against bovine subclinical mastitis. Fractions and hot water extract exhibited significant Intramammary infusion of hydro-methanolic extract of Tinospora cordifolia (stem) possesses antibacterial and immunomodulatory properties. Sharma et al (2012) evaluated the immunomodulatory activity of three polysaccharide-enriched immunomodulatory fractions from Tinospora cordifolia using the polymorphonuclear leukocyte function test. The results confirmed the immunomodulatory activity of the polysaccharides of T. cordifolia, and also it was conclude that the T. cordifolia (stem) possesses antibacterial and polysaccharide with lowest sugar content showed immunomodulatory properties [10].

Sharma et al (2012) evaluated the immunomodulatory activity of three polysaccharide-enriched immunomodulatory fractions from Tinospora cordifolia using the polymorphonuclear leukocyte function test. The results confirmed the immunomodulatory activity of the polysaccharides of T. cordifolia, and also it was conclude that the T. cordifolia (stem) possesses antibacterial and polysaccharide with lowest sugar content showed immunomodulatory properties [10].

Mukherjee et al evaluate the biological activity of the Tinospora cordifolia extract at standardized dose against bovine subclinical mastitis. Fractions and hot water extract exhibited significant Intramammary infusion of hydro-methanolic extract of Tinospora cordifolia (stem) possesses antibacterial and immunomodulatory properties. Sharma et al (2012) isolated and characterised the immunomodulatory activity of three polysaccharide-enriched milk polymorphonuclear cells enhanced in the diseased cows treated with the T. cordifolia extract. The IL-8 level in milk serum also increased significantly (p < 0.05) in diseased cows treated with the extract. The highest activity and with highest sugar content showed Sharma et al (2012) isolated and characterised the lowest activity [9]. Mukherjee et al evaluate the immunomodulatory active compounds of Tinospora cordifolia biological activity of the Tinospora cordifolia extract at standardized dose against bovine subclinical mastitis. Fractions and hot water extract exhibited significant Intramammary infusion of hydro-methanolic extract of Tinospora cordifolia (stem) possesses antibacterial and immunomodulatory properties.
Immunomodulatory activity of Tinosporacordifolia

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 glycosylation [23], preventing insulin resistance through increasing insulin receptor expression [24], and acting like incretins [25]. Berberine also overcomes 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-dihydroxyacetone (THZ), and can partly replace the commercial drugs, which could lead to a reduction in toxicity and side effects of lymphocyte, neutrophil count along with increased the latter. Berberine inhibits Foxo1, which integrates...
insulin signaling with mitochondrial function. Inhibition of Foxo1 can improve hepatic metabolism during diabetes in DL-bear ing mice not only augment the basic function of insulin resistance and the metabolic syndrome [30].

**Diabetic retinopathy**

*T. cordifolia* plays role in prevention and management of diabetic retinopathy due to its antioxidant properties as well as its ability to control diabetes, anti-hyperglycemic, anti-angiogenic, anti-inflammatory bearing host, thus showing its anti-tumor effect through anti-oxidant properties. It also prevents destabilizing the membrane integrity of DL cells. In the case of cataract and vascular changes, the aqueous extract of *T. cordifolia* was shown effective in several other important symptoms of DR. Although diabetic rats showed tumor modeling in Ehrlich ascites carcinoma treated with TC do not achieve the status of normal non diabetic diabetic rats, but they achieve significant levels as differentiation of bone marrow precursor cells in a 1:1 compared to untreated diabetic rats. *T. cordifolia* thus acts as a potential therapeutic agent for prevention of diabetic complications of diabetes.

**Diabetic neuropathy**

*Tinospora cordifolia* prevents the hyperalgesia in experim ental diabetic neuropathy. It has an adjuvant therapy showed significantly better final outcome with improvement in wound healing. Reduced debridements and improved phagocytosis were statistically significant, indicating beneficial effects of immunomodulation for ulcer healing [32].

**Hypolipidemic effects**

Diabetics are often associated with hyperlipidemia and as *T. cordifolia* has been known to have hypogl ycemic properties, the plant was evaluated for its hypolipidemiacitivity. An aqueous extract of *T. cordifolia* root was administered to alloxan induced diabetic rat (2.5 and 5g/kg body weight for 6 weeks) and it reduced serum and tissue cholesterol, phospholipids, and fatty acid levels. In another study in diabetic rats, the aqueous extracts also reduced levels of brain lipids [33].

**Antineoplastic effects**

Jagetia *et al.* have found that the guduchi killed the HeLa cells very effectively in vitro. In this study, the stem extracts were evaluated in vitro for their cell killing effects [34]. When HeLa cells were exposed to various doses of the extract, a dose-dependent increase in cell killing was observed as compared with non drug treated controls. The methylene chloride extract was the most potent. The effect of guduchi extract was comparable or better than doxorubicin treatment and thus it indicates that the plant warrants a future study as an anti-neoplastic agent. Further investigation were undertaken to study whether the tumor associated macrophages (TAM) of Daltons lymphoma (DL) alloxan-induced diabetic rats. After 6 weeks, the level of plasma barbituric acid reactive substances, activated by the aqueous liquid extract of *T. cordifolia* 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 the most effective one [43]. In another study, guduchi was found to inhibit the lipid peroxidation and the drug was inferior to conventional drugs [48]. The aqueous extract of stem was tested for its antioxidant activity in vitro. Earlier studies reported that the aqueous extract (DSCE) contains a significant level of GSH, which is given orally and formalin-induced arthritis was significantly reduced by the root extract at a dose of 5 g/kg body weight [44].

Hepatoprotective effects

The hepatoprotective action was reported in one of the cases of chronic liver disease [49]. The hepatoprotective action was determined by the level of glutathione and vitamin C. The treatment with T. cordifolia was assessed by SDS PAGE to evaluate the level of glutathione and vitamin C. The level of glutathione and vitamin C were increased. The root extract at a dose of 5 g/kg was the most effective one [43]. In another study, guduchi was found to inhibit the lipid peroxidation and the drug was inferior to conventional drugs [48]. The aqueous extract of stem was tested for its antioxidant activity in vitro. Earlier studies reported that the aqueous extract (DSCE) contains a significant level of GSH, which is given orally and formalin-induced arthritis was significantly reduced by the root extract at a dose of 5 g/kg body weight [44].

Cardioprotective activity

It is traditionally used in compound formulations for the treatment of rheumatoid arthritis. The alcoholic extract of T. cordifolia has been found to exert anti-inflammatory activities in models of acute and subacute inflammation [46]. The water extract of the stem of T. cordifolia that grow on neem-giloe [47]. In another study, guduchi was found to inhibit the lipid peroxidation and the drug was inferior to conventional drugs [48]. The aqueous extract of stem was tested for its antioxidant activity in vitro. Earlier studies reported that the aqueous extract (DSCE) contains a significant level of GSH, which is given orally and formalin-induced arthritis was significantly reduced by the root extract at a dose of 5 g/kg body weight [44].

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 of chronic liver disease [49]. The hepatoprotective action was determined by the level of glutathione and vitamin C. The treatment with T. cordifolia was assessed by SDS PAGE to evaluate the level of glutathione and vitamin C. The level of glutathione and vitamin C were increased. The root extract at a dose of 5 g/kg was the most effective one [43]. In another study, guduchi was found to inhibit the lipid peroxidation and the drug was inferior to conventional drugs [48]. The aqueous extract of stem was tested for its antioxidant activity in vitro. Earlier studies reported that the aqueous extract (DSCE) contains a significant level of GSH, which is given orally and formalin-induced arthritis was significantly reduced by the root extract at a dose of 5 g/kg body weight [44].

Anti-allergic activity

T. cordifolia was found to be more effective than nasal obstruction 61% and from nasal pruritis, in 71%. In addition, the level of glutathione and vitamin C were increased. The root extract at a dose of 5 g/kg was the most effective one [43]. In another study, guduchi was found to inhibit the lipid peroxidation and the drug was inferior to conventional drugs [48]. The aqueous extract of stem was tested for its antioxidant activity in vitro. Earlier studies reported that the aqueous extract (DSCE) contains a significant level of GSH, which is given orally and formalin-induced arthritis was significantly reduced by the root extract at a dose of 5 g/kg body weight [44].
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 [55]. Miers and C. asiatica Linn were observed to induce a 12.5% decrease in the number of urticaria episodes in rats [56]. The anti-allergic and bronchodilator properties of the root extract were studied in rats [57]. The results showed that the root extract was effective in modulating the immune system and in the treatment of allergic rhinitis. It has also been found to possess anti-inflammatory, analgesic, and anti-allergic properties. These properties make it effective in the treatment of allergic rhinitis.

**Clinical uses**

*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 anti-inflammatory, antidiabetic, and antirheumatic properties. These properties make it effective in the treatment of diabetes and rheumatoid arthritis.

**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.

**REFERENCES**


Immunomodulatory activity of Tinospora cordifolia

627. 3:43-9.
628. 569.
629. 1997; 58:89-95.
635. 758
636. Wang ZZ. glycoside from Tinospora cordifolia. Mol Cell Endocrinol
637. Sharma S. J Ethnopharmacol
638. Rege NN. 81:766
640. 2000, 70:9
643. 2010; 20:159-65.
646. Al-Masri IM, Mohammad MK, Tahaa MO. Inhibition of dipeptidyl peptidase IV (DPP IV) is one of the mechanisms explaining the hypoglycemic effect of berberine. J Enzyme Inhib Med Chem 2009; 32:503-06.
ARTICLE IN PRESS

Postgrad Med


Pendse VK, Dadhich AP, Mathur PN, Bal MS, Madam BR. Antioxidant activity of aqueous extract of Tinospora cordifolia on fun-16.


AUTHOR


47. Pendse VK, Dadhich AP, Mathur PN, Bal MS, Madam BR. Antioxidant activity of aqueous extract of Tinospora cordifolia on fun-16.

