

## ***Tinospora cordifolia* (Guduchi), a reservoir plant for therapeutic applications: A Review**

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*Tinospora cordifolia* (Guduchi or Amrita) is an important drug of Ayurvedic System of Medicine and found mention in various classical texts for the treatment of diseases such as jaundice, fever, diabetes and skin disease etc. In present times, this drug has been subjected for numerous chemical, pharmacological, pre-clinical and clinical investigations and many new therapeutic applications have been indicated. This paper presents a critical review in areas of chemical constituents, proved pre-clinical and clinical trials along with its medicinal uses in different streams of medical sciences.

**Keywords:** *Tinospora cordifolia*, Guduchi, Tinosporosides, Immunomodulator.

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*Tinospora cordifolia* (Willd.) Miers ex Hook. F. & Thoms. (Family: Menispermaceae) commonly known, as “Amrita” or “Guduchi” is an important drug of Indian Systems of Medicine (ISM) and used in medicines since times immemorial. The drug is well known Indian bitter and prescribed in fevers, diabetes, dyspepsia, jaundice, urinary problems, skin diseases and chronic diarrhoea and dysentery<sup>1</sup>. It has been also indicated useful in the treatment of heart diseases, leprosy, helmenthiasis and rheumatoid arthritis<sup>1-4</sup>. The starch obtained from the stem known

as “Guduchi-satva” is highly nutritive and digestive and used in many diseases. During last two decades, the drug has been subjected to extensive phytochemical, pharmacological and clinical investigations and many interesting findings in the areas of immunomodulation, anticancer activity, liver disorders and hypoglycaemic are reported.

### **Botanical and phramacognostical descriptions**

#### **Botanical description**

It is a large, deciduous extensively spreading climbing shrub with several

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elongated twining branches. **Leaves** simple, alternate, exstipulate, long petioles up to 15cm long, roundish, pulvinate, both at the base and apex with the basal one longer and twisted partially and half way around. **Lamina** broadly ovate or ovate cordate, 10-20 cm long or 8- 15 cm broad, 7 nerved and deeply cordate at base, membranous, pubescent above, whitish tomentose with a prominent reticulum beneath. **Flowers** unisexual, small on separate plants and appearing when plant is leafless, greenish yellow on axillary and terminal racemes. Male flowers clustered, female usually solitary. **Sepals** 6, free in two series of three each, the outer ones are smaller than the inner. **Petals** 6 free smaller than sepals, obovate and membranous. **Fruits** aggregate of 1-3, ovoid smooth drupelets on thick stalk with sub terminal style scars, scarlet or orange coloured.

#### **Distribution**

The plant is distributed throughout the tropical region of India up to 1,200 m above sea level from Kumaon to Assam, in north extending through West Bengal, Bihar, Deccan, Konkan, Karnataka and Kerala. It is a fairly common plant of deciduous and dry forests, growing over hedges and small trees.

#### **Pharmacognostical Description**

The drug Guduchi or Amrita consists of dried pieces of mature stem of *Tinospora cordifolia*. Roots and leaves are also medicinal. The diagnostic pharmacognostical characteristics of medicinal parts are as follows:

#### **Stem**

Stem is characterized by the presence of bicollateral vascular bundles surrounded by pericycle fibres. The cork arises in the sub-epidermal layers and give rise to 2-3 layers of cork. Starch is present throughout the parenchyma of the stem<sup>5, 6</sup>.

#### **Root**

The aerial root is characterized by tetra- to penta-arch primary structure. The cortex is divided into outer thick walled zone representing the velamen and inner parenchymatous zone containing secretory canals. Starch is present throughout the parenchyma of the aerial root. The starch grains are oval or elliptical in shape, mostly simple but some times as compound grains of 2 to 5 components, with faintly marked concentric striation and central hilum appearing like a point<sup>5, 6</sup>.

#### **Leaf**

The petiole in transverse section is more or less circular in outline. No trichomes were found. The cross section shows a single layered epidermis and a wide zone of cortex composed of 3 to 4 layers of endodermis. The vascular bundles consist of radial rows of xylem on the inner side and a few rows of cambium cells on the outer side followed by phloem. The mid-rib is more or less circular in outline and palisade do not extend over the stellar tissue. The cross section of lamina shows a dorsiventral structure with its mesophyll differentiated into palisade and spongy tissue. The mesophyll is clearly differentiated into a palisade layer made up of one row of thin

walled columnar cells which occupy a little more than half of the width of mesophyll. Glandular hairs are present in lower surface only. They are unicellular and somewhat club shaped. The base is surrounded by 4 to 5 epidermal cells. Starch is present throughout the tissue<sup>7</sup>.

#### Substitutes and adulterants

*T. cordifolia* is substituted or adulterated with other species of *Tinospora*, viz. *T. sinensis* (Lour.) Merrill (syn. *T. malabarica* Miers ex Hook. f. and *T. crispa* (Linn.) Miers ex Hook. f. & Thoms.). Although, the microscopical characters of *T. sinensis* resemble that of *T. cordifolia*, there are few characters by which these two species can be differentiated. The distinguishing characters are:

In *T. cordifolia* the sclerenchymatous sheath becomes disintegrated into scattered irregular patches in the cortical regions whereas in *T. sinensis* it is broken into areas capping the vascular bundle and remains persistent even after further secondary growth. Crystals are absent in *T. cordifolia* while in *T. sinensis* a large crystal of calcium oxalate is present within the lumen of each cork cell. Mucilaginous cells are more in *T. cordifolia* as compared to *T. sinensis*. Vascular strands are fewer in *T. cordifolia* while greater in *T. sinensis*. Xylem is well developed in each strip of vascular strand in *T. cordifolia* while it is poorly developed in *T. sinensis*. Pith is very narrow and composed of thin walled cells in *T. cordifolia* while it is wide in *T. sinensis*. Starch content is more in *T. cordifolia* as compared to *T. sinensis*<sup>8</sup>.

#### Standards for identity and purity

##### Quantitative Standards

The following standards for identity and purity are reported<sup>9,10</sup>:

Foreign Matter not more than 2.0%; Total ash not more than 7.0%; Acid-soluble ash not less than 0.8%; Ethanol-soluble extractive not less than 6.0%; Loss on drying not more than 7.5%; Lead not more than 10 ppm; Arsenic not more than 2 ppm; Heavy metals not more than 20 ppm; Total bacterial count not more than 3000 CFU/gm; Yeasts and moulds not more than 100 CFU/gm; Bitters content on dry basis by Gravimetry /HPTLC not less than 3% w/w.

##### TLC pattern

On TLC identity test the drug showed 6 major molecules having Rf value and colour 0.24 (yellow); 0.35 (dark green) (tinosporoside); 0.42 (green); 0.44 (light yellow); 0.76 (dark green) and 0.79 (dark green) using chloroform and methanol (9:1) as a solvent system and anisaldehyde-sulphuric acid as spraying reagent<sup>9</sup>.

#### History and Traditional Uses

##### Uses in Indigenous Systems of Medicine

The Ayurvedic drug Guduchi or Amrita is mentioned in various classical texts of Ayurvedic System of Medicine, viz. *Charak*, *Sushrut* and *Ashtang Hridaya* and other treaties like *Bhava Prakash* and *Dhanvantari Nighantu* under other various names, viz. *Amara*, *Amritvalli*, *Chinnarruha*, *Chinnodebha* and *Vatsadani* etc<sup>8, 11-14</sup>. In *Sushurta Samhita*, it is mentioned under "Tikta-Saka Varga" and

claimed to be useful in treating Kustha (leprosy), Maha-jvara (a kind of fever), Svasa (asthma) and Aruchi (anorexia)<sup>13</sup>. In other treatises i.e. *Charak Samhita* and *Ashtang Hridaya*, it has been indicated in diseases like Kamala (jaundice), Jvara (fever) and Vat Rakta (gout), etc.<sup>12, 14</sup>. In *Bhava Prakash*, it is considered as a bitter tonic, astringent, diuretic and potent aphrodisiac and curative against skin infections, jaundice, diabetes and chronic diarrhoea and dysentery<sup>1</sup>. In *Dhanvantari Nighantu*, its medicinal properties are mentioned for cure of bleeding piles, promoting longevity, curing itching and erysipelas<sup>5</sup>. It is reported to be potent vegetable tonic. Being a rejuvenator, it is indicated in several diseases causing debility. The fecula is nutritious especially in diarrhoea, largely given in cold fevers, seminal weakness, in urinary affections, jaundice, skin disease, various forms of diabetes and irritability of stomach<sup>15</sup>. It is a traditional belief among the Ayurvedic practitioners that *Guduchi Satva* obtained from Guduchi plant growing on Neem tree (*Azadirachta indica*) is more bitter and more efficacious and is said to incorporate the medicinal virtue of Neem also<sup>8, 15</sup>. The drug also caught the attention of European physicians in India as a specific tonic, antiperiodic and for its diuretic properties and it was included in the Bengal Pharmacopoeia of 1868<sup>16</sup>.

*T. cordifolia* is mentioned in Ayurvedic literature as a constituent of several compound formulations used in general debility, dyspepsia, fever and urinary diseases. Some of the important formulations are:

Guduchyadi churna, Guduchi taila, Dashmoolarishttha, Sanjivani vati, Kantakari avaleha, Chyavanaprasha, Guduchi sattva, Brihat guduchi taila, Stanyashodhana kashaya churana, Punchedha churana, Guduchi ghrita, Amritaguggulu, Amritashtaka churna, etc.<sup>11</sup>.

In Unani System, mostly "Sat Giloe" is incorporated in the preparations. "Arq Giloe" prepared from the fresh plant is considered a febrifuge, while "Arq Maul Laham Mako-kashiwala" is a general tonic<sup>17</sup>.

#### Uses in folk and tribal medicine:

*T. cordifolia* finds a special mention for its use in tribal or folk medicine in different parts of the country. Some of the important uses mentioned are given below:

The tribals Baiga, living in the interior areas of Naugarh and Chakia Block of Varanasi district, Uttar Pradesh make the paste of stem of the Guduchi (*T. cordifolia*) and the roots of Bhatkatiaya (*Solanum surattense*). The pills are prepared and used in the treatment of fever for three days<sup>18</sup>.

The tribals of Bombay and its neighbouring areas and the fishermen along the sea coast use *T. cordifolia* as drug in the treatment of fever, jaundice, chronic diarrhoea and dysentery<sup>19</sup>.

The tribals of Khedbrahma region of North Gujarat use the plant in their day-to-day life as food or medicine. They use powdered root and stem bark of *T. cordifolia* with milk for the treatment of cancer; decoction of root is used for the cure

of dysentery and diarrhoea and decoction of old stems is preferred in the treatment of periodic fever<sup>20</sup>.

Decoction of stem is administered orally by the people of Jammu (J & K) and Bigwada (Rajasthan) for the treatment of fever<sup>21</sup>.

The inhabitants of Bhuvneshwar (Orissa) use the warm juice of root of *T. cordifolia* orally for the treatment of fever<sup>21</sup>.

Juice or decoction of leaves is administered orally with honey in fever by the local people of Patiyala (Punjab)<sup>21</sup>.

The Muslim tribals of Rajouri, Jammu (Tawi) comprising Gujjar and Backwals used the plant in bone fracture<sup>22</sup>.

In Dahanu forest division of Maharashtra, tribal races, viz. Agaris, Bhils, Dhodias, Dublas, Khakaris, Rimoshis, Thakurs, Vardaris, Vagharis and Varlis use the stem decoction with cold or hot water (about 3-4 gm) in morning in an empty stomach as a tonic in general debility<sup>23</sup>.

Shirt of child is dyed in juice of Guduchi and worn in *balashosha* (emaciation in children) by the inhabitants of Banka (Bihar)<sup>21</sup>.

Paste or juice of *Amrita* (*T. cordifolia*) leaves and *Sarsapa beeja churna* (seed powder of *Brassica campestris*) is applied locally in case of Daha (Burning sensation)<sup>21</sup>.

Powder of *Terminalia chebula* (Haritaki), *Tinospora cordifolia* (*Amrita*) and *Trachyspermum ammi* (*Ajwain*) in equal quantity is administered orally, once daily early morning with salt for the treatment of Kasa (cough). Decoction of these drugs is also to be taken in dose of 50 ml for the treatment of Kasa (cough) by the

people of Dhurala (Haryana)<sup>21</sup>.

Two drops of leaf juice of allied species of Guduchi (*T. sinensis*) is dropped in the ear for the treatment of Karna Shula (pain in ear) by the local people of Patiyala (Punjab)<sup>21</sup>.

Paste of Guduchi (*T. cordifolia*) and 5 seeds of Krishna marich (*Piper nigrum*) is administered orally once daily in morning in rakta pradar (leucorrhoea) by the local women of Arjunpura (Rajasthan)<sup>21</sup>.

The inhabitants of Badala (U.P.) take the juice of stem orally with honey for the treatment of swasa (Asthma)<sup>21</sup>.

Decoction of stem is administered orally in case of twak-roga (skin disease) by the people of Dehrabara Kolaras, Sivpuri District of M.P.<sup>21</sup>.

### Chemical Constituents

The plant *T. cordifolia* has been subjected to chemical investigations extensively and a number of chemical constituents belonging to the different groups, viz. terpenoids, alkaloids, lignans, steroids have been reported. Some of the important constituents reported so far are:

#### A. Terpenoids

Tinosporide<sup>24</sup>, Furanolactone diterpene<sup>25</sup>, Furanolactone clerodane diterpene<sup>26,27</sup>, furanoid diterpene<sup>28</sup>, Tinosporaside<sup>29</sup>, ecdysterone makisterone and several glucosides isolated as poly acetate<sup>30</sup>, phenylpropene disaccharides cordifolioside A, B and C<sup>30, 31</sup>, cordifolioside D and E<sup>32</sup>, Tinocordioside<sup>33</sup>, cordioside<sup>33</sup>, palmatosides C and F<sup>34</sup>, Sesquiterpene glucoside tinocordifolioside<sup>35</sup>, Sesquiterpene tinocordifolin<sup>35</sup>.

#### B. Alkaloids

Tinosporine, (S)<sup>24</sup>, Magnoflorine, (S)<sup>36</sup>, Tembetarine, (S)<sup>36</sup>, Berberine, (S)<sup>36</sup>, Choline, (S)<sup>37</sup>, Palmatine, (S)<sup>37</sup>, Jatrorrhizine, (S)<sup>37</sup>, 1,2-Substituted pyrrolidine, (S)<sup>38</sup>, Alkaloids, viz. jatrorrhizine, palmatine, beberine, tembetarine<sup>39</sup>, choline<sup>40</sup>.

#### C. Lignans

3( $\alpha$ , 4-dihydroxy-3-methoxybenzyl)-4-(4-hydroxy-3-methoxybenzyl), (S)<sup>41</sup>.

#### D. Steroids

Giloinsterol, (S)<sup>42</sup>,  $\beta$ -Sitosterol, (S)<sup>43</sup>,<sup>44</sup>, 20 $\alpha$ -Hydroxy ecdysone, (S)<sup>45</sup>.

#### F. Others

Giloin, (S)<sup>42</sup>, Giloinin, (S)<sup>42</sup>, Tinosporan acetate, (S)<sup>46</sup>, Tinosporic acid, (S)<sup>46</sup>, Tinosporal acetate, (S)<sup>46</sup>, Tinosporidine, (S)<sup>47</sup>, Heptacosanol, (S)<sup>47</sup>, Cordifolone, (S)<sup>47</sup>, Octacosanol, (S)<sup>44</sup>, Tinosponone<sup>48</sup>, Tinosporic acid, tinosporal, tinosporon, 20-hydroxyecdysone<sup>45</sup>, two phytoecdysones<sup>49</sup>, an immunologically active arabinogalactan<sup>50</sup>.

### Therapeutic Applications

#### Pre-Clinical Studies (Animal Model)

During last two decades, *T. cordifolia* has demonstrated various pre-clinical activities in animal models/*in vitro* testings. Some of such notable findings are reported here:

##### *I Anti-cancer/anti-tumour activity:*

Exposure of HeLa cells to 0, 5, 10, 25, 50 and 100 g/ml of extracts methanol, aqueous and methylene chloride resulted in a dose-dependent but significant increase in cell killing, when compared to

non-drug-treated controls. The results demonstrate that Guduchi killed the cells very effectively *in vitro* and deserves attention as an antineoplastic agent<sup>51</sup>. Administration of *T. cordifolia* stem methanolic extract to BALB/c mice (200 mg/kg, i.p. daily for 5 days) increased the total white blood cell count significantly (P<0.001). It also increased bone marrow cellularity (18.16 $\times$ 10<sup>6</sup>/femur) and  $\alpha$ -esterase positive cells (1423/4000 cells) in bone marrow indicating increased maturation of stem cells. Administration of the extract was also found to significantly increase humoral immune response, as seen from the increase in plaque-forming cells in the spleen (1575 PFC/10<sup>6</sup> spleen cells) and circulating antibody titre (256), and to produce an enhancement (129%) in macrophage activation. Tinospora extract reduced solid tumour growth and synergistically acted with cyclophosphamide in reducing (83%) the animal tumours<sup>52</sup>. The effect of *T. cordifolia*, on the functions of macrophages obtained from mice treated with the carcinogen ochratoxin A (OTA) was investigated. Treatment with plant significantly inhibited OTA-induced suppression of chemotactic activity and production of IL-1 and TNF- $\alpha$  by macrophages<sup>53</sup>. One of the compounds, NII-70, isolated from *T. cordifolia*, has been found to activate the macrophages and induced production of IL-12 and TNF- $\alpha$  and antigen specific Th<sub>1</sub> response; NII-70 also induces production of nitric oxide by macrophages and has shown therapeutic effect against Leishmania infection and tumour implant in experimental ani-

mals<sup>54</sup>.

### **II. Anti Diabetic and Hyperglycaemic activity:**

Alcoholic extracts of the stem showed activity against *E.coli*. The acute and chronic effect of oral feeding of the plant extracts affect rabbit and albino rats. Effect on fasting blood sugar, glucose tolerance and against equieprine induced hyperglycemia have been studied. The aqueous and alcoholic extract caused reduction in the fasting blood sugar, which have been interpreted as indicating some indirect action of the drug on carbohydrate metabolism. Similarly, glucose tolerance had increased in the beginning but the deterioration in tolerance occurred after one month. It has been suggested that the action of the drug is due to its favourable effects on the endogenous insulin secretion, glucose uptake inhibition of peripheral glucose release<sup>55</sup>. The aqueous, alcoholic, and chloroform extracts of the leaves of *T. cordifolia* in doses of 50, 100, 200 mg / kg body weight to normal and alloxan-diabetic induced rabbits exerted significant hypoglycaemic effect<sup>56</sup>. An Ayurvedic compound formulation Transina (TR) containing *T. cordifolia* and other drugs was studied for hyperglycaemia and superoxide dismutase (SOD) activity of pancreatic islet cells. The result indicates that the earlier reported antihyperglycaemia activity of streptozotocin (STZ) being the consequence of decrease in islet SOD activity leading to the accumulation of degenerative oxidative free radicals in islet beta-cells<sup>57</sup>. Oral administration of an aqueous *T. cordifolia* root extract (TCREt) to alloxan induced diabetic rats, cause a significant reduction

in blood glucose and brain lipids. The extract caused an increase in body weight, total haemoglobin and hepatic hexokinase. The root extract also lowers hepatic glucose-6-phosphatase and serum acid phosphatase, alkaline phosphatase, and lactate dehydrogenase in diabetic rats. Thus TCREt has hypoglycaemic and hypolipidaemic effect<sup>58</sup>. In a comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats the crude ethanolic extract of *T. cordifolia* has been found to exhibit hypoglycaemic activity in experimental model<sup>59</sup>. The effect of daily oral feeding of *T. cordifolia* extracts for 40 days on blood glucose concentrations and kidney functions in streptozotocin (STZ)-diabetic rats was studied. Plasma glucose concentration was reduced by 7.45% ( $P < 0.05$ ) and treatment with *T. cordifolia* prevented polyurea ( $P < 0.001$ ), but it failed to modify renal hypertrophy<sup>60</sup>. The effect of aqueous extract of *T. cordifolia* on alloxan induced hyperglycaemic rats and rabbits has been observed. The aqueous extract of *T. cordifolia* caused reduction of blood sugar in alloxan induced hyperglycaemic rats and rabbits in dose of 400 mg/kg body weight. Histological studies of pancreas did not reveal any evidence of regeneration of  $\beta$ -cells of islets of Langerhance. The possible mode of action of the drug has been discussed projecting a hypothesis related to control of glucose metabolism<sup>61</sup>.

### **III. Anti-inflammatory activity:**

The decoction of *T. cordifolia* showed anti-inflammatory activity on carrageenin-induced hind paw oedema in

rats<sup>62</sup>. The effect of extract of stem of *T. cordifolia* was studied on the contractile response due to various agonists (such as histamine, 5-HT, bradykinin, prostaglandin E<sub>1</sub> and F<sub>2α</sub>, cholinomimetics and KCl) on smooth muscles of rat in the dose of 100 to 600 µg/mg. The possible mechanism of antagonistic action of *T. cordifolia* has been discussed in the light of involvement of various autocooids in the pathophysiology of clinical joint inflammation. The mechanism of potentiating effects of *T. cordifolia* on NA induced responses is suggested to be due to an uptake blocking effect of *T. cordifolia* or to an inhibition of metabolism by COMT since MAO inhibition would also produce potentiation of 5-HT responses<sup>63</sup>.

#### IV. Antioxidant activity:

Antioxidant activity and amelioration of cyclophosphamide-induced toxicity has been reported<sup>64</sup>. It has an ameliorative effect in aflotoxicosis of duck<sup>65</sup>.

#### V. Anti-stress activity:

Ethanol extract of *T. cordifolia* at the dose of 100 mg/kg exhibited significant anti-stress activity in all the parameters studied, compared with diazepam at the dose of 2.5 mg/kg<sup>66</sup>.

#### VI. Anti Ulcer activity:

The ethanol extract of the root of *T. cordifolia* was observed to induce a marked protective action against restrain stress induced ulcerization. The activity was comparable to that of diazepam<sup>67</sup>.

#### VII. Digestive activity:

The antiamebic effect of a crude drug formulation containing *T. cordifolia* against *Entamoeba histolytica* was stud-

ied. There were varying degrees of inhibition of the enzymes, viz. DNase, RNase, aldolase, alkaline phosphatase, acid phosphatase, α-amylase and protease activities of crude extracts of axenically cultured amoebae<sup>68</sup>.

#### VIII. Hypolipidaemic activity:

The hypolipidaemic effect of an aqueous extract of roots was evaluated. Administration of the extract of 2.5 and 5.0 g/kg body weight for 6 weeks resulted in a significant reduction in serum and tissue cholesterol, phospholipids and free fatty acids in alloxan diabetic rats. The root extract at a dose of 5.0 g/kg body weight showed highest hypolipidaemic effect. The effect at the dose of roots at 2.5 and 5.0 g/kg body weight was better than glibenclamide. Insulin restored all the parameters to near normal values<sup>69</sup>. Aqueous extract of *T. cordifolia* roots when administered (2.5 and 5.0 g/kg body weight) for 6 weeks, resulted in a significant reduction in serum and tissue cholesterol, phospholipids and free fatty acids in alloxan diabetic rats<sup>70</sup>.

#### IX. Immunobiological activities:

The water and ethanol extracts of stem of *T. cordifolia* inhibit immunosuppression produced by cyclophosphamide. The ethanol extract of stem of the plants inhibits cyclophosphamide-induced anemia. The water extract of the plant is found to be more potent than the other extract<sup>71</sup>. An arabinogalactan of mean M<sub>r</sub> 2.2×10<sup>6</sup> has been isolated from the dried stems of *T. cordifolia* and examined by methylation analysis, partial hydrolysis and carboxyl reduction. Purified polysaccharide



showed polyclonal mitogenic activity against B-cells. Their proliferation did not require macrophages<sup>72</sup>. The immunobiological activity of ethanolic extract was investigated on delayed type hypersensitivity, humoral responses to sheep RBCs, skin allograft rejections and phagocytic activity of the reticuloendothelial system in mice. It appears that *T. cordifolia* improves the phagocytic function without effecting the humoral or cell mediated immune system<sup>73</sup>. The activity of a crude extract formulation containing *T. cordifolia* and other plant drugs was evaluated in experimental amoebic liver abscess in golden hamsters and in immunomodulation studies. The formulation had a maximum cure rate of 73% at a dose of 800 mg/kg/day in hepatic amoebiasis reducing the average degree of infection (ADI) to 1.3 as compared to 4.2 for sham-treated controls. In immunomodulation studies humoral immunity was enhanced as evidenced by the haemagglutination titre. The T-cell counts remained unaffected in the animals treated with the formulation but cell-mediated immune response was stimulated as observed in the leukocyte migration inhibition (LMI) tests<sup>74</sup>. The active principles of *T. cordifolia* were found to possess anticomplementary and immunomodulatory activities. Syringin (TC-4) and Cardiol (TC-7) inhibit the in-vitro immunohaemolysis of antibody coated sheep erythrocytes by guinea-pig serum. The reduced immunohaemolysis was found to be due to inhibition of C<sub>3</sub> convertase of the classical complement pathway. The compounds also give rise to significant increases in IgG antibodies in serum. Humoral and

cell-mediated immunity were also dose independently enhanced. Macrophage activation was more pronounced with increasing incubation times<sup>75</sup>. *T. cordifolia* has been studied for effect on intra-abdominal sepsis to elucidate host defense mechanism to counter infective stress. The results indicate that *T. cordifolia* has immunomodulating properties<sup>76</sup>.

#### X. Liver disorders:

The drug was also studied against the hepatic damage induced by a standard hepatotoxin – carbon tetra chloride (CCl<sub>4</sub>). Though acute damage was aggravated by *T. cordifolia*, it was proved to be effective in preventing fibrous changes and promoting regeneration by paranchymal tissue<sup>77</sup>. In another antihepatotoxic activity, the drug was studied in albino rats intoxicated with CCl<sub>4</sub>. Liver function was assessed based on morphological (liver weight to animal body weight ratio), biochemical (SGPT, SGOT, serum alkaline phosphatase, serum bilirubin and functional (Pentobarbitone sleep time) tests. A decrease in liver weight was observed in the group treated with alcoholic extract of *T. cordifolia*. However there was no effect on elevated serum level of SGPT, SGOT, SALP, serum bilirubin and pentobarbitone sleep time. The chloroform extract of *T. cordifolia* failed to reduce the liver toxicity in tested dose (200 mg/kg)<sup>78</sup>. An Ayurvedic preparation HPN-12 containing *T. cordifolia* was investigated for the hepatoprotective effect on CCl<sub>4</sub> induced hepatic dysfunction in male albino rats of Sprague Dawley strain. It was found that HPN-12 is an effective drug against CCl<sub>4</sub> induced

liver damage<sup>79</sup>.

#### **XI. Mental disorders:**

A herbal psychotropic preparation BR-16A containing *T. cordifolia* was investigated in short term memory paradigms in mice. The results suggest for possibly nootropic action of BR-16A involving cholinergic and GABAergic modulation<sup>80</sup>.

#### **XII. Urinary calculi:**

The water extract of the stem of *T. cordifolia* was experimentally evaluated for dissolution of urinary calculi<sup>81</sup>.

#### **XIII. Uraemia:**

Pharmacological and clinical study of *T. cordifolia* was undertaken and its role in uraemia elicited. The water extract produced marked but transient fall in B.P. along with bradycardia and increased force of ventricular contraction in dogs and diuresis in rats. It significantly decreases blood urea levels in uremic dogs and patients<sup>82</sup>.

### **Clinical Studies**

#### **I. Anti-Cancer activity:**

A prospective, randomized, double blind placebo controlled clinical trial was conducted on breast cancer patients. Consenting breast cancer patients, who were receiving adjuvant therapy (CMF regimen), were recruited, and randomized to drug and placebo group. From the results, it appears that the drug *T. cordifolia* provided some protection against the cancer chemotherapy induced leucopenia<sup>83</sup>.

#### **II. Immunomodulator activity:**

In clinical studies, it also showed immunosuppression on obstructive jaundice patients<sup>84, 85</sup>.

#### **III. Hepatic disorders:**

In clinical studies 20 patients of infective hepatitis were selected on the basis of clinical and biochemical findings. Four tablets (500mg each) thrice in a day, orally with fresh water were given to the patient for 4 weeks. Comparison between before and after treatment of those patients (N=20) were showed that drug *T. cordifolia* (*Guduchi*) played an important role in relieving the symptoms as well as normalization of altered liver function test<sup>86</sup>.

#### **IV. Post menopausal syndrome:**

Clinical evaluation of a non-hormonal drug minofil containing *T. cordifolia* along with other plant drugs was done in women of post-menopausal syndrome. Breast discomfort, nausea and fluid retention was observed in 22% (7 cases) with estriol and almost no side effect was observed with minofil. Minofil with short period of therapy and more sustained effect and without side effects is cost effective and may be an alternative to HRT, which is still in controversy. However, long term follow up is required before universal use in post menopausal syndrome<sup>87</sup>.

#### **Others**

A multi-ingredient herbal preparation containing *T. cordifolia* has demonstrated anabolic potential<sup>88</sup>. The study carried out so far on evaluation of adjuvant therapy of a multi-ingredient herbal preparation in

patients of tuberculosis on anti-tubercular therapy has also showed the benefit of the subjective (appetite, sense of well being) and objective (weight, serum proteins) parameters<sup>89</sup>.

#### Toxicity

No significant information on side effects is available so far<sup>9</sup>. Nothing conspicuous has been done as yet in this aspect although many experiments have already been conducted on this plant. According to Ayurveda, herbs are taken in combination with other herbs with the opposing effect of the other or to enhance the particular effect of one herb with the help of the other.

#### Safety Aspects

The drug is traditionally considered to be safe in the dosage mentioned<sup>9</sup>.

#### Conclusion

The therapeutic efficacy of *Tinospora cordifolia* extensively used in Indian System of Medicine (ISM) has been established through modern testing and evaluation (pre-clinical and clinical trials) in different disease conditions. These studies place this indigenous drug a novel candidate for bioprospection and drug development for the treatment of such diseases as cancer, liver disorders, ulcers, diabetes, heart diseases and postmenopausal syndrome, etc. where satisfactory cure managements are still not available.

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