

## The Amazing Pharmacological Properties of *Tinosporacordifolia*- A Short Review

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### Abstract

*Tinospora cordifolia* is a glabrous, perennial, deciduous, climbing shrub of weak and fleshy stem spread across Tropical India and Andmans. *T. cordifolia* is commonly called as 'Guduchi' and is well known for its immense application in the treatment of various diseases in the ancient and traditional ayurvedic literature. The chemical constituents reported from the stem include alkaloids, glycosides, diterpenoid lactones, sesquiterpenoid, steroids, phenolics and polysaccharides. Various properties of *T. cordifolia*, are described in ancient classical texts of Ayurveda, like *Rasayana*, *Balya*, *Medhya*, *Tridoshshamaka*, *Jwarhara*, *Kasa-swasahara*, *Sothhara*, *Pandunashaka*, *Kamla-Kushta-Vataraktanashaka*, *Krimihara*, *Prameha*, *Arshnashaka*, *Agnideepana*, *Dahnashaka*, *Hridroganashak*, etc. Potential therapeutic properties reported by modern scientific research include antipyretic, anti-inflammatory, antioxidant, anti-allergic, antispasmodic, adaptogenic, hypoglycemic, anti-stress, anti-leprotic, anti-rheumatic, antimalarial, hepato-protective, immuno-modulatory and anticancerous activities. This article briefly reviews the pharmacological and various therapeutic aspect of *T. cordifolia*.

### Keywords

*Ayurveda*, *Tinospora cordifolia*, *Guduchi*



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## INTRODUCTION

*Tinospora cordifolia* commonly named as “Guduchi” in Sanskrit belonging to family Menispermaceae is a genetically diverse, large, glabrous, deciduous climbing shrub. It is distributed throughout the tropical Indian subcontinent and China, ascending to an altitude of 300 m. In Hindi, the plant is commonly known as Giloe<sup>1</sup>, Guduchi, the Sanskrit name, means one which protects the entire body. The term amrita is attributed to its ability to impart youthfulness, vitality and longevity. It is considered one of the best rasayanas (adaptogens) and is unusual in its potent versatility. In recent years, significant progress has been attained regarding its biological activity and medicinal applications.

## MORPHOLOGY

Guduchi typically grows in deciduous and dry forests at elevations up to 1000 ft. Its

flowers bloom in summer. The male flower is small, yellow or green in color, and occurs in clusters. Female flowers are usually solitary and are green. The drupes are ovoid, glossy, succulent, red and pea sized. The leaves are heart shaped (giving the name cordifolia to the plant) and mucilaginous. Its stems, when fresh, have a green succulent bark covered by a thin brown bark and are studded with warty lenticels. When dry, the stem shrinks and the bark separate from the wood. The roots are long narrow aerial roots. The stems, leaves, and roots are used in medicine. All three parts should be collected in the summer when the bitter qualities are most abundant and, if not used fresh, dried in the shade. It is easy to recognize and can be propagated by cuttings<sup>2, 3, 4</sup>. Figure 1 *Tinospora cordifolia* (a) Plant, (b) Stem cuttings

## VERNACULAR NAMES -Table 1

**Table 1** Vernacular Names of *T. Cordifolia* (*Guduchi*)

<b>Sanskrit Name</b>	Guduchi, Amrita, Amritavalli, Madhuparni, Guduchika, Vatsadani, Tantrika, Kundalini, Chakralakshanika
<b>Hindi Name</b>	Gurcha Giloe,
<b>Telugu Name</b>	Thippateega
<b>English Name</b>	Heartleaf Moonseed, <i>Tinospora</i> <sup>5</sup>
<b>Tamil Name</b>	Seendil Kodi
<b>Kannada Name</b>	Amrutavalli
<b>Malayalam</b>	Chittamrutu

<b>Oriya</b>	Guluchi
<b>Bengali name</b>	Gulanha
<b>Gujarati name</b>	Garo, Galac
<b>Marathi name</b>	Gulvel
<b>Assamese name</b>	<i>Seendal, Siddhilata, Amarlata</i>
<b>Binomial name</b>	<i>Tinospora cordifolia</i>
<b>Family</b>	<i>Menispermaceae</i>
<b>Genus</b>	<i>Tinospora</i>
<b>Species</b>	<i>T. cordifolia</i>

**Fig 1** *Tinospora cordifolia* (

(a) Plant



(b) Stem cuttings



### Ayurvedic Pharmacology (Dravya-guna) of *T. Cordifolia* (Guduchi)<sup>5,6</sup>

Rasa (Taste)- Tikta (Bitter); Kashaya (Astringent)

Guna (Characteristics)- Guru (Heavy); Snigdha (Unctuous)

Veerya (Potency)- Ushna (Warm)

Vipaka (Post digestion effect)- Madhura (Sweet)

#### Effect on Tridosha

Pacifies all the three Doshas and maintain their balance with each other i.e. why it is said to be having Rasayana character. When taken with Ghruta (Ghee) it balances Vata, with Guda (Jaggery) Pitta and with honey the Kapha.

#### Parts Used:

The whole plant is used medicinally; however, the stem is approved for use in medicine by the Ayurvedic Pharmacopoeia of India<sup>5</sup>. This is due to higher alkaloid content in the stems than in the leaves. The fresh plant is said to be more effective than the dry one. However, it is traditionally dried and made into a starchy extract called Guduchi Sattva. It is a traditional belief that

*Guduchi satva* obtained from the *Guduchi* plant growing on *neem* tree (*Azadirachta indica*) is more efficacious and incorporates the medicinal values of *neem*<sup>6</sup>.

## CHEMICAL CONSTITUENTS

A large number of chemicals have been isolated from *T. cordifolia*, belonging to different classes such as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides. Leaves of this plant are rich in protein (11.2%), calcium and phosphorus<sup>7</sup>. Detailed chemical constitution of *T. cordifolia* is given in Table 2<sup>8</sup>.

## Karma (Pharmacodynamics) and Prayoga (uses) of *T. Cordifolia*<sup>9-15</sup>.

### Actions according to Ayurveda:

Vaya sthapana- *Guduchi* increases longevity

Rasayan- Rejuvenator

Balya- *Guduchi* increases strength

Agni deepani- *Guduchi* ignites digestive fire  
Medhya- Enhances grasping power, memory and recollection ability.

Triptighna- *Guduchi* alleviates anorexia making a person to feel hungry

Daha prashamana- *Guduchi* alleviates burning sensation

Trishna nigravana- *Guduchi* alleviates excessive thirst

Stanya shodhana- *Guduchi* purifies the breast milk

Samgrahini- Means it has the tendency to absorb the liquid content from the Malas (Gastric waste) giving it normal consistency

Valee palita nashini- *Guduchi* delays the signs of aging

In the classical texts of Ayurveda, namely, *T. cordifolia* is claimed to be useful in treating leprosy, fever, asthma, anorexia, jaundice, gout, skin infections, diabetes, chronic diarrhea, dysentery, etc.<sup>9-15</sup>.

**Table 2** Chemical Constituents of *T. cordifolia* (*Guduchi*)<sup>8</sup>

Type of chemical	Active principles	Part in which present
Alkaloids ( <i>Tikta</i> -Bitter Principle)	Berberine, Palmatine,	Stem
	Tembetarine, Magnofl orine, Choline, Tinosporin, Isocolumbin, Palmatine, Tetrahydropalmatine, Magnoflorine	Root
Glycosides	18-norclerodane glucoside, Furanoid diterpene glucoside, Tinocordiside, Tinocordifolioside, Cordioside, Cordifolioside A, Cordifolioside B, Syringin, Syringin-apiosylglycoside, Palmatosides C, Palmatosides F, Cordifolioside A, Cordifolioside B, Cordifolioside C, Cordifolioside D, Cordifolioside E	Stem

Diterpenoid lactones	Furanolactone, Clerodane derivatives and [(5R,10R)-4R-8R-dihydroxy-2S-3R:15,16-diepoxy-cleroda-13 (16), 14-dieno-17,12S:18,1S-dilactone] and Tinosporon, Tinosporides, and, Jateorine, Columbin	Whole plant
Steroids	$\beta$ -sitosterol, $\delta$ -sitosterol, 20 $\beta$ -Hydroxy ecdysone.	Aerial part
	Ecdysterone, Makisterone A, Giloinsterol.	Stem
Sesquiterpenoid	Tinocordifolin.	Stem
Aliphatic compound	Octacosanol, Heptacosanol,	Whole plant
Miscellaneous	Nonacosan-15-one3,( $\alpha$ ,4-dihydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxy-benzyl)-tetrahydrofuran.	Root
	Jatrorrhizine.	
	Tinosporidine, Cordifol, Cordifellone, N-trans-feruloyl tyramine as diacetate, Giloin, Giloinin, Tinosporic acid.	Whole plant

## RESEARCHES AND STUDIES

### ANTIOXIDANT ACTIVITY

*T. cordifolia* is described as *amapachak* and *rasayana* in Ayurveda. *T. cordifolia* has been reported to elevate GSH levels, expression of the gamma-glutamylcysteine ligase and Cu-Zn SOD genes. The herb also exhibited strong free radical-scavenging properties against reactive oxygen and nitrogen species as studied by electron paramagnetic resonance spectroscopy<sup>16</sup>. *Tinospora cordifolia* Willd.(Menispermaceae) extracts possess possible inhibitors of aldose reductase and anti-oxidant agents<sup>17</sup> thereby reducing chemotoxicity induced by free radicals<sup>18</sup>. In various studies, *T.cordifolia* was found effective in amelioration of

cyclophosphamide-induced toxicity<sup>19</sup>, and free radical generation and lipid peroxidation during oxygen-glucose deprivation<sup>20</sup>,The extract of *T. cordifolia* has demonstrated antioxidant action in the alloxan induced diabetes model as well<sup>21</sup>. (5R, 10R)-4R, 8R-dihydroxy-2S, 3R: 15, 16-diepoxycleroda-13 (16), 17, 12S: 18,1S-dilactone (ECD), a diterpenoid from *Tinospora cordifolia* has been shown to possess chemo-preventive potential in DEN induced HCC rats. Treatment of ECD in both preventive and curative DEN induced animals increased the level of antioxidants and detoxification enzymes<sup>22</sup>.The arabinogalactan polysaccharide (TSP) isolated from *Tinospora cordifolia* showed good protection against iron-mediated lipid

peroxidation of rat brain homogenate as revealed by the TBARS and lipid hydroperoxide (LOOH) assays<sup>23</sup>. The effect of a hydroalcoholic (80% ethanol: 20% distilled water) extract of aerial roots of *Tinospora cordifolia* on carcinogen/drug metabolizing phase-I and phase-II enzymes, anti-oxidant enzymes, GSH content, LDH and lipid peroxidation has been shown in liver of Swiss albino mice. The enhanced GSH level and enzyme activities involved in xenobiotic metabolism and maintaining anti-oxidant status of cells are suggestive of a chemo-preventive efficacy of *Tinospora cordifolia*<sup>24</sup>. *Tinospora cordifolia* has been reported to contain an alpha-glucosidase inhibitor, characterized as saponarin (apigenin-6-C-glucosyl-7-O-glucoside). The leaf extract had appreciable anti-oxidant and hydroxyl radical scavenging activities<sup>25</sup>. Pepticare, a herbomineral formulation of the Ayurveda medicine consisting of the herbal drugs: *Glycyrrhiza glabra*, *Embolia officinalis* and *Tinospora cordifolia*, has anti-ulcer and anti-oxidant activity in rats<sup>26</sup>.

#### **ANTI-INFLAMMATORY, ANTIPYRETIC AND ANTI- MICROBIAL ACTIVITY**

*T. cordifolia* is known for its *jwarahara* activity (antipyretic activity),

in Ayurveda. The water-soluble fraction of 95% ethanolic extract of *T. cordifolia* plant has shown significant antipyretic activity<sup>27</sup>. The anti-bacterial activity of *Tinospora cordifolia* extracts has been assayed against *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Salmonella typhi*, *Shigella flexneri*, *Salmonella paratyphi*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Enterobacter aerogene*, and *Serratia marcescens* (Gram-positive bacteria)<sup>28-30</sup>. In another experimental study, antipyretic effects have been reported in the hexane- and chloroform-soluble portions of *T. cordifolia* stems<sup>31</sup>. The alcoholic extract of *T. cordifolia* has been found to exert anti-inflammatory actions in models of acute and subacute inflammation<sup>32</sup>. Various studies show remarkable anti-infective and antipyretic properties of *T. cordifolia*.<sup>33,34</sup> The methanol extracts of *Tinospora cordifolia* have been reported to have potential against microbial infections<sup>28</sup>. Intra-mammary infusion of hydro-methanolic extracts of *Tinospora cordifolia* treatment showed enhanced phagocytic activity of polymorphonuclear cells in bovine subclinical mastitis<sup>35,36</sup>. Pre-

treatment with *T. cordifolia* was shown to impart protection against mortality induced by intra-abdominal sepsis following coecal ligation in rats and significantly reduced mortality from induced by *E. coli*-induced peritonitis in mice<sup>37</sup>. In mice models, TCE has been reported to function in bacterial clearance and improved phagocytic and intracellular bactericidal capacities of neutrophils<sup>38</sup>. TCE has been reported of immunostimulant properties on macrophages<sup>39</sup>.

### IMMUNOMODULATORY ACTIVITY

In Ayurveda *T. cordifolia* is believed to have *rasayana* (rejuvenating), *vayahsthapana* (anti-aging), *ayushya* (increases the lifespan) and *vrishya* (aphrodisiac), *chakshusya* (useful in eye disorders) properties. The immunomodulatory property of *Tinospora cordifolia* is well documented. Active compounds 11-hydroxymustakone, N-methyl-2-pyrrolidone, N-formylannonain, cordifolioside A, magnoflorine, tinocordiside and syringin<sup>40</sup> has been reported to have potential immunomodulatory effects<sup>41,42</sup>. They have been reported to function by boosting the phagocytic activity of macrophages, production of reactive oxygen species

(ROS) in human neutrophil cells<sup>43</sup>, enhancement in nitric oxide (NO) production by stimulation of splenocytes and macrophages indicative of anti-tumor effects. In mice, *Tinospora cordifolia* extracts has been shown to result in up-regulation of IL-6 cytokine, resulting in acute reactions to injury, inflammation, activation of cytotoxic T cells, and B cell differentiation<sup>44</sup>.

Aqueous *Tinospora* extracts has been also reported to influence the cytokine production, mitogenicity, stimulation and activation of immune effector cells<sup>45</sup>. Active compounds in aqueous extracts like alkaloids, di-terpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds or polysaccharides<sup>46</sup> in experimental rat model have been reported for their cytotoxic action. Dry stem crude extracts of *Tinospora cordifolia* with a polyclonal B cell mitogen, G1-4A on binding to macrophages have been reported to enhance immune response in mice by inducing secretion of IL-1, together with activation of macrophages. Reports on *Tinospora cordifolia* in prevention of oxidative damage also exist<sup>47</sup>. The (1,4)-alpha-d-glucan (alpha-d-glucan), derived *Tinospora cordifolia* have been

shown to activate human lymphocytes with downstream synthesis of the pro- and anti-inflammatory cytokines, *in vitro*<sup>48</sup>. Synergistic effects of compounds in the immunomodulatory activity of *Tinospora cordifolia* are reported<sup>49</sup>. The alcoholic and aqueous extracts of *T. cordifolia* are reported to have beneficial effects on the immune system<sup>50</sup> and have been tested successfully for their immunomodulatory activity<sup>51</sup>. *Tinosporacordifolia* differentially regulate elevation of cytokines as evidenced by the increased production of antiangiogenic agents IL-2 and tissue inhibitor of metalloprotease-1 (TIMP-1) in the B16F10-injected, extract-treated animals. The observed antiangiogenic activity of the plant *T. cordifolia* is related to the regulation of the levels of cytokines and growth factors in the blood<sup>52</sup>. *T. cordifolia* extract (TCE) treatment caused significant reduction in eosinophil count and improved hemoglobin in HIV patients. Sixty percent patients receiving TCE and 20% on placebo reported decrease in the incidence of various symptoms associated with disease<sup>53</sup>. Ten days of treatment with *T. cordifolia* (100 mg/kg/d) induced a significant ( $P < 0.01$ ) increase in the number of (Colony Forming Units of granulocyte-

macrophage series (CFU-GM;  $255 \pm 49.32$  vs.  $38.51 \pm 9.98$ ). This suggests that activation of macrophages by *T. cordifolia* leads to increase in GM-CSF, which leads to leukocytosis and improved neutrophil function<sup>54</sup>. The aqueous extract of *T. cordifolia* was found to enhance phagocytosis *in vitro*. The aqueous and ethanolic extracts also induced an increase in antibody production *in vivo*<sup>55</sup>. Diabetic patients with foot ulcers on *T. cordifolia* as an adjuvant therapy showed significantly better final outcome with improvement in wound healing<sup>56</sup>. The degradation of proteins due to photosensitization as assessed by Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was effectively reduced by simultaneous treatment with G1-4A/PPI (partially purified immunomodulator) from *Tinospora cordifolia* during photosensitization<sup>57</sup>. The novel (1,4)- $\alpha$ -D-glucan derived from the plant activates the immune system through the activation of macrophages via TLR6 signaling, NF $\kappa$ B translocation and cytokine production<sup>58,59</sup>.

#### ANTI-ALLERGIC ACTIVITY

*T. cordifolia* is used in Ayurveda for the treatment of *kasa* (cough) and *swasa* (asthma). The anti-allergic and



bronchodilator properties of an aqueous extract of the stem evaluated on histamine-induced bronchospasm in guinea pigs.<sup>60</sup> 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<sup>61</sup>. In a clinical study, 100% relief was reported from sneezing in 83% of the patients on treatment with *T. cordifolia*. Similarly, there was relief from nasal discharge was reported in 69%; from nasal obstructions 61% and from nasal pruritus, in 71%. In placebo group, there was relief from sneezing only in 21% patients; from nasal discharge, in 16.2%; from nasal obstruction, in 17%; and from nasal pruritus, in 12%. Thus, *T. cordifolia* significantly decreased all symptoms of allergic rhinitis and was well tolerated<sup>62</sup>.

#### **ANTINEOPLASTIC AND RADIO-PROTECTIVE ACTIVITY**

Intraperitoneal injection of the alcoholic extract of *T. cordifolia* has been shown to Dalton's lymphoma (DL) bearing mice e stimulated macrophage functions likephagocytosis, antigen-presenting ability and secretion of Interleukin-1 (IL-1), tumour

necrosis factor (TNF) and Reference Nutrient Intake (RNI) as well as slowed tumor growth and increased lifespan of the tumor-bearing host<sup>63</sup>. Aqueous extract of *Tinospora cordifolia* inhibited radiation mediated 2-deoxyribose degradation by inhibiting the formation of (Fe<sup>2+</sup>)-bipyridyl complex formation to confer radio-protective effects. The results showed various amounts of protection against the radiation through increased survival time and signs and symptoms of radiation sickness<sup>64</sup>. *T. cordifolia* has been shown effective in several other tumour models including Ehrlich ascites carcinoma (EAC) in mice<sup>65</sup>. It induces proliferation and myeloid differentiation of bone marrow precursor cells in a tumor-bearing host<sup>66</sup>. *T. cordifolia* is effective against various cancers<sup>67</sup>, activates tumor-associated macrophages-derived dendritic cells<sup>68</sup>, and inhibits experimental metastasis<sup>69</sup>. *Tinospora* supplies protection against gamma irradiation in mice. An aqueous extract of *Tinospora cordifolia* has a radio-protective enhancing the survival of mice against a sub-lethal dose of gamma radiation.<sup>70</sup> The effect of Guduchi extracts was comparable or better than doxorubicin treatment.<sup>71</sup> The effect of a hydroalcoholic

extract of aerial roots of *Tinospora cordifolia* on Swiss albino mice<sup>72</sup> revealed a significant increase in acid-soluble sulfhydryl (-SH), cytochrome *P* (450) contents, and enzyme activities of cytochrome *P* (450) reductase, cytochrome b5 reductase, GST, DT-diaphorase (DTD), SOD, catalase, GPX, and GR activity in the liver highlighting the chemopreventive role of *Tinospora cordifolia* against carcinogenicity<sup>72</sup>.

### HEPATO-PROTECTIVE ACTIVITY

*T. cordifolia* are indicated in and *kamla* (jaundice) in Ayurveda. The antihepatotoxic activity of *T. cordifolia* has been demonstrated in CCl<sub>4</sub> induced liver damage, normalising liver function as assessed by morphological, biochemical (SGPT, SGOT, serum alkaline phosphatase, serum bilirubin) and functional (pentobarbitone sleep time) tests. *T. cordifolia* revealed hepatoprotective action in goats<sup>73</sup>. A clinical study has shown that *Guduchi* plays an important role in normalization of altered liver functions (ALT, AST)<sup>74</sup>. A significant increment in the functional capacities of rat peritoneal macrophages was observed following *T. cordifolia* treatment<sup>75</sup>. The extract has also exhibited *in vitro* inactivating property

against hepatitis B and E surface antigens in 48 to 72 hours<sup>76</sup>. *T. cordifolia* also prevents obstructive jaundice<sup>77</sup>. and antitubercular drugs-induced hepatic damage<sup>78</sup>.

### ANTI-HYPERGLYCEMIC ACTIVITY

The stem of *Tinospora cordifolia* is widely used in the therapy of diabetes by regulating the blood glucose. *Guduchi* has been studied for its hypoglycemic actions. It has been reported to mediate its anti-diabetic potential through mitigating oxidative stress (OS), promoting insulin secretion and also by inhibiting gluconeogenesis and glycogenolysis, thereby regulating blood glucose<sup>78</sup>. Alkaloids, tannins, cardiac glycosides, flavonoids, saponins, and steroids as the major phytoconstituents<sup>79</sup> of *Tinospora cordifolia* have been reported to play an anti-diabetic role. Various studies demonstrate amelioration of experimental diabetic neuropathy and gastropathy in rats<sup>80</sup>, reduction of blood sugar in alloxan-induced hyperglycemic rats and rabbits<sup>81</sup>, significant reduction in blood glucose and brain lipids<sup>82</sup>, increase in glucose tolerance in rodents<sup>83</sup>, increase in glucose metabolism<sup>84</sup>, inhibitory effect on adrenaline-induced hyperglycemia by pyrrolidine derivative<sup>85,86</sup>, and significant

hypoglycemic effect in normal and alloxan diabetic rabbits<sup>87</sup> following administration of *T. cordifolia*. The isoquinoline alkaloid rich fraction from stem, including, palmatine, jatrorrhizine, and magnoflorine have been reported for insulin-mimicking and insulin-releasing effect both *in vitro* and *in vivo*. The root extract has been reported to decrease the levels of glycosylated hemoglobin, plasma thiobarbituric acid reactive substances, hydroperoxides, ceruloplasmin and vitamin E diabetic rats<sup>89</sup>. Decreased concentration of GSH, GPx, and SOD, catalase activity is reported in heart and brain of diabetic rats<sup>90</sup>.

#### CARDIOPROTECTIVE ACTIVITY

*T. cordifolia* have *hrudya* (cardioprotective) properties and is useful in *hridroga* (cardiac disorders). Administration of the extract of *T. cordifolia* roots (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>91</sup>. A dose-dependent reduction in infarct size and in serum and heart lipid peroxide levels were observed with prior treatment with *T. cordifolia* in ischemia-reperfusion-induced myocardial infarction in rats<sup>92</sup>.

#### ANTI-TOXIC EFFECTS

*Tinospora cordifolia* stem and leaves extract has shown hepatoprotective effect in Swiss albino male mice against lead nitrate induced toxicity effects on the hematological values<sup>93</sup>. *Tinospora cordifolia* extracts have been reported to scavenge free radicals generated during aflatoxicosis. Alkaloids such as a choline, tinosporin, isocolumbin, palmatine, tetrahydropalmatine, and magnoflorine from *Tinospora cordifolia* showed protection against aflatoxin-induced nephrotoxicity<sup>94</sup>. Cyclophosphamide (CP) an anti-cancer drug has been reported to reduce the GSH content in both bladder and liver and lowered levels of cytokines Interferon- $\gamma$  and IL-2 an increased levels of pro-inflammatory cytokine TNF- $\alpha$ . This effect could be reversed on *Tinospora cordifolia* treatment indicating the role of *Tinospora cordifolia* in overcoming CP induced toxicities in cancer treatment<sup>95</sup>. Oral administration of plant extracts prevented the occurrence of lead nitrate induced liver damage. Decreased level of SOD, CAT and increased level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), ALP, and ACP were observed in mice suffering from lead toxicity<sup>96</sup>.

## ANTI-HIV EFFECTS

Anti-HIV effects of TCE was revealed by reduction in eosinophil count, stimulation of B lymphocytes, macrophages and polymorphonuclear leucocytes and hemoglobin percentage thus, revealing its promising role of application in management of the disease<sup>97</sup>. TCE has been shown to demonstrate a decrease in the recurrent resistance of HIV virus thus improving the therapeutic outcome<sup>98</sup>. *Tinospora cordifolia* also has the components that decrease the recurrent resistance of HIV virus to antiretroviral therapy (ART) and improve the outcome of the therapy<sup>99</sup>.

## OSTEOPROTECTIVE ACTIVITY

*Tinospora cordifolia* have been reported to affect the proliferation, differentiation and mineralization of bone like matrix on osteoblast model systems *in vitro* and hence finds potential application as an anti-osteoporotic agent. Alcoholic extract of *Tinospora cordifolia* have been shown to stimulate the growth of osteoblasts, increasing the differentiation of cells into osteoblastic lineage and also increasing the mineralization of bone like matrix<sup>100</sup>. Rats treated with *T. cordifolia* (10 mg/kg body weight) showed an osteoprotective effect, as

the bone loss in tibiae was slower than that in controls. Serum osteocalcin and cross-laps levels were significantly reduced. This study demonstrates that extract of *T. cordifolia* has the potential for being used as antiosteoporotic agent<sup>101</sup>. Beta-Ecdysone (Ecd) from *Tinospora cordifolia* extracts have been reported to induce a significant increase in the thickness of joint cartilage, induce the osteogenic differentiation in mouse mesenchymal stem cells<sup>102</sup> and to relieve osteoporosis in osteoporotic animal models<sup>102</sup>. Further 20-OH- $\beta$ -Ecd isolated from *Tinospora cordifolia* has been reported of its anti-osteoporotic effects<sup>100</sup>.

## ANTI-ARTHRITIC ACTIVITIES

*T. cordifolia* is mentioned to treat *vatarakta* (gouty arthritis) and *amavata* (rheumatoid arthritis) in various Ayurvedic texts. The aqueous extract of stem was reported to exert a significant anti-inflammatory effect in formalin-induced arthritis (1 mg/kg given orally) rat models<sup>103, 104</sup>. In another study aqueous extract of *T. cordifolia* showed a significant anti-inflammatory effect in the cotton pellet granuloma and formalin induced arthritis model, its effect was comparable with indomethacin and its mode of action appeared to resemble that of nonsteroidal

antiinflammatory agent<sup>105</sup>. A significant inhibition of primary and secondary phases of inflammation was observed in a model of adjuvant-induced arthritis. It also significantly inhibited antibody formation by typhoid "H" antigen. A mild analgesic effect of its own as well as potentiation of morphine analgesia has been reported<sup>106</sup>.

## EFFECTS

### ONSTRESSANDCOGNITIVE

#### FUNCTIONS

*T. cordifolia* is well known as a *medhya rasayana* (intellect promoting and memory enhancer) in Ayurveda. The usefulness of *Tinospora cordifolia* as a cognitive enhancer has been substantiated by modern research. In a 21-day randomized, double-blind placebo-controlled study, the pure aqueous extract of the root was found to enhance verbal learning and logical memory<sup>107</sup>. *T. cordifolia* has also been shown to enhance cognition (learning and memory) in normal rats and reverse cyclosporine-induced memory deficit. The histopathological examination of hippocampus in cyclosporine-treated rats showed neurodegenerative changes, which were protected by *T. cordifolia*<sup>108</sup>. Significant response has been found in children with moderate degree of behavior

disorders and mental deficit, along with improvement in IQ levels<sup>109</sup>. Various extracts of the *T. cordifolia* exhibited comparable anti-stress activity in mice<sup>110, 111</sup>.

## DRUG SAFETY

In a clinical study, *T. cordifolia* has been shown to be at a dose of 500 mg/d for a period of 21 days in healthy individuals. It has not shown any remarkable adverse effects<sup>112</sup>. No adverse effect is found on the gastrointestinal system<sup>113,114</sup>, central nervous system<sup>107,108,115</sup>, renal system<sup>116,117</sup>, and cardiovascular system<sup>115,117</sup>.

## CONCLUSION

*Tinospora cordifolia* is a promising plant as a versatile resource for life. As already discussed the plant extracts have active compounds in the form of alkaloids, glycosides, lactones and steroids. All these active compounds have immunomodulatory, antipyretic, anti-inflammatory, antioxidant, anti-allergic, antispasmodic, adaptogenic, hypoglycemic, anti-stress, anti-rheumatic, antimalarial, hepato-protective, immunomodulatory and anticancerous activities thereby demonstrating the diverse versatility of the plant. With so much to offer to the scientific world of medicine, the plant

Tinosporia truly acts as an incredible source. In a nutshell, the present review is indicative of multiple uses of *T. cordifolia* in clinical conditions, however the exact mechanism of drug action and adverse reactions needs to be evaluated further.

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