

TAXONOMY, PHYTOCHEMISTRY AND PHARMACOLOGICAL SIGNIFICANCE OF *TINOSPORA CORDIFOLIA* PLANT - A COMPREHENSIVE REVIEW

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ABSTRACT

80% of the global population, reported by the World Health Organization, generally uses traditional treatments, which may involve the consumption of plant extracts or active ingredients. The use of a broad variety of plants in healthcare in general and the treatment of common ailments has a strong basis thanks to India's mega-biodiversity as well as its rich historical traditional medical systems. China and the Indian subcontinent are home to the Ayurvedic medicinal herb *Tinospora cordifolia*. In folk medicine and the Ayurvedic system, the whole plant is utilized, both alone and in conjunction with other herbs. The isolation of a wide range of compounds, including alkaloids, sesquiterpenoids, diterpenoids, phenolics, steroids, aliphatic compounds, and polysaccharides, as well as the discovery of a wide range of medicinal properties like immunomodulation, anticancer, hepatoprotective and treatment of cardiac disease, dysentery, helmenthiasis, skin diseases, leprosy, and many more diseases, have made *T. cordifolia* a subject of intense research interest over the last forty years due to its commercial significance. While *T. cordifolia* extracts and compounds have been researched for their pharmacological properties in vitro and in vivo, very few of their modes of action have been studied and require more work. The taxonomy, phytochemistry, and medicinal importance of the *Tinospora cordifolia* plant have all been covered in this paper.

KEYWORDS: *Tinospora cordifolia*, Alkaloids, Berberine, Tinocordifolin, Phytochemistry.

INTRODUCTION

Asian nations are home to a vast array of flora, including a high floristic diversity of medicinal plants. Many diverse plant families have an enormous variety of plants with medicinal properties that are used in medicine to treat a wide range of illnesses. Medicinal plants constitute a significant natural resource and are essential to a healthy society, particularly in India. Numerous widely-used indigenous systems, including Ayurveda, Yoga, Siddha, Homeopathy, Unani, and Naturopathy, have its roots in India and other Asian nations, as well as Africa, Australia, and other places. In the most

sophisticated literature written in Sanskrit, Hindi, and other regional languages, Ayurveda, The Science of Life, discusses a variety of therapeutic herbs.^[1]

T. cordifolia, also called Guduchi/Amrita, is a member of the Menispermaceae family.^[2] The plant has several medicinal qualities, including the ability to treat jaundice, rheumatism, urinary disorders, skin conditions, diabetes, anemia, inflammation, allergic conditions, anti-periodic, and radioprotective qualities. It is also frequently employed in traditional ayurveda medicine.^[3,4,5,6] Giloya (*T. cordifolia*) root is used as a strong emetic and for

intestinal blockage. Together with cow's milk, powdered leaves and their decoction are said to help cure gout, ulcers, jaundice, fever, wounds, and blood sugar.^[7] Stem starch, or satva, is used as a tonic; the extract of stems alone or in combination with honey is beneficial as a tonic for fever, skin conditions, and jaundice.^[7,8] A mixture of roots & stem is recommended as a countermeasure for scorpion stings and snake bites.^[9] The plant's stem bark and roots are used in North Gujarat (India) in conjunction with milk to cure cancer.^[8] Fruits are used to cure rheumatism and jaundice.^[9] Roots are employed as a mild emetic for diarrhea, dysentery, leprosy, and visceral blockages.^[10,11] This plant's starch acts as a good at-home treatment for persistent fever, reduces burning, and boosts appetite and vitality. Giloya

boosts the immune system, increasing resistance to infections, and normal white blood cell structure, function, and levels. It is helpful in the management of helminthiasis, heart disease, leprosy, rheumatoid arthritis, and other conditions.^[12] Additionally, it aids in the treatment of liver diseases like hepatitis as well as digestive issues including hyperacidity, colitis, worm infestations, appetite loss, stomach discomfort, and excessive thirst.^[13,14] The chemical components of the plant, which are found in the root, stem, and entire portion of the plant, include diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds, essential oils, and a mixture of fatty acids. These constituents are what give the plant its pharmacological activity.^[15]

VERNACULAR NAMES^[16,22]

Table 1: Vernacular names of *Tinospora cordifolia*.

| | |
|-------------------|---|
| Latin | <i>Tinospora cordifolia</i> |
| English | Gulantha/ Indian Tinospora |
| Sanskrit | Guduchi, Madhuparni, Amrita, Chinnaruha, Vatsadaani, Tantrika, Kundalini & chakralakshanika. |
| Hindi | Giloya, Guduchi |
| Bengali | Gulantha |
| Telugu | Thippateega |
| Tamil | Shindilakodi |
| Marathi | Shindilakodi |
| Gujarathi | Galo |
| China | Da ye ruan jin teng, Bo ye qing, Niu dan, Ye qing niu dan, Fa leng teng |
| Philippines | Makabuhay, Panyawan, Meliburigan, Manunggal |
| Thailand | Boraphet, Ho-Boraphet, Khrua khao, Pae jae, Wan kab hoi yai, Chung ching, Kuakhohoo, Ching cha li |
| Indonesia | Bratawali, Brotowali, Antawali, Andawali, Putrawali, Daun gade |
| Cambodia | Banndol Pech |
| Vietnam | Day coc |
| Laos | Hmab Iab, Kheuah khao, Ho |
| Brunei | Ratnawali, Akar nawali, Nawali |
| Guyana | Liane amere |
| Martinique Island | Lyann span, Zeb kayenn |
| Indochina | Day than thong, Bandaul pich, Day ki nin, Thuoc sot ret |
| Java | Brotowali, Andawali, Putrowali, Akar pahat |

TAXONOMIC CLASSIFICATION^[23]

Table 2: Taxonomic classification of *Tinospora cordifolia*.

| | |
|-----------------|--|
| Kingdom | Plantae – Plants ; |
| Subkingdom | Tracheophyta –Vascular Plants; |
| Super- division | Spermatophyta-Seed bearing plants; |
| Division | Magnoliophyta-Flowering; |
| Class | Magnoliopsia-Dicotyledons |
| Subclass | Polypeptalae-Petals are free; |
| Series | Thalamiflorae-Many stamens and flower hypogynous |
| Order | Ranunculales |
| Family | Menispermaceae-The Moonsee family |
| Tribe | Tinosporeace |
| Genus | Tinospora |
| Species | cordifolia |

MORPHOLOGICAL DESCRIPTION

Tinospora cordifolia is a broad, glabrous, deciduous shrub that grows quickly. It has numerous coiling branches that are about one foot long and three to four feet tall.^[24] The stem of *T. cordifolia* is very tasty, with long, filiform, juicy aerial branch roots.^[25] The plant stem is cylindrical, dry, softly woody, bitter, and ranges in circumference from 5 to 25 mm. Its color is grayish brown-black.^[26] The leaves are spherical, chordate, simple, 5–10 cm long, alternating, exstipulated, and have a multicoated, reticulated midrib. Long aerial roots that resemble tentacles emerge from the branches.^[27] When the bark is exposed to a carefully peeled stem, it is thin,

grayish, or creamy in texture.^[28] Tiny yellow or yellow-greenish blooms are present. While the female flowers are often solitary, the male flowers are clustered in accessory and terminal racemes or racemose panicles.^[29] The composite fruit has a crimson, juicy body and large, scarlet-colored drupelets on a stout stalk with a border sub-terminal shape.^[30] For this plant, the bent seed has been reported. This family is hence also known as the Moonseed family. Given the curved nature of seeds, the embryo likewise naturally assumed a curved form. On the other hand, the endocarp is embellished in a variety of settings and given significant taxonomic traits.^[31]



Figure 1: Different parts (stem, fruit, leaves and flower) of *Tinospora cordifolia*.

GEOGRAPHICAL DISTRIBUTION^[32]

Tinospora cordifolia is found in India, Bangladesh, Sri Lanka, Myanmar. Its native to India and is found in different states of India including

Andhra Pradesh: Anantapur district, Chittoor district, Kadapa district, East Godavari district, Guntur district, Krishna district, Kurnool district, Nellore district, Prakasam district, Srikakulam district, Vishakapatnam district, Vizianagaram district, West Godavari district.

Telangana: Nalgonda district, Khammam district, Mehboobnagar district.

Karnataka: Ballari district, Chamarajanagar district, Kolar district.

Kerala: All districts of Kerala.

Maharashtra: Akola district, Nagpur district; also planted.

Odisha: Angul district, Balasore district, Bargarh district, Bolangir district, Boudh district, Cuttack district,

Deogarh district, Dhenkanal district, Gajapati district, Ganjam district, Kalhandi district, Kandhamal district, Kendrapara district, Keonjhar district, Khurda district, Koraput district, Malkangiri district, Mayurbhanj district, Puri district, Rayagada district, Sambalpur district, Sundergarh district.

Tamil Nadu: Coimbatore district, Dindigul district, Dharmapuri district, Kanchipuram (Changalpattu-CGP) district, Karur district, Krishnagiri district, Madurai district, Namakkal district, Pudukkottai district, Sivaganga district, Salem district, Tiruchirapalli district, Tiruvannamalai district, Villipuram district, Vellore district.

PHYTOCHEMISTRY

Numerous chemical compounds have been isolated from this plant, and their structures have been determined. The active components include aliphatic chemicals, sesquiterpenoids, phenolics, glycosides, hormones, polysaccharides, and diterpenoid lactones.

1. Alkaloids

Berberine, Tembeterine, Choline, Aporphine alkaloids, Jatrorrhizine, Magnoflorine, Tetrahydropalmatine, Tinosporin, Palmetine, Isocolumbin.^[33,38]

2. Terpenoids

Tinosporide Furanolactone diterpene, Furanolactone clerodane diterpene, phenylpropene disaccharides cordifolioside A, B and C, cordifolioside D and E, Tinocordioside, cordioside, palmatosides C and F, furanoid diterpene, Tinosporaside, ecdysterone makisterone and several glucosides isolated as poly acetate.^[39,42]

3. Glycosides

norclerodane glucoside, furanoid diterpene glucoside, cordifolioside A, cordifolioside B, palmatosides C, palmatosides P1, cordifolioside C, cordifolioside D, cordifolioside E.^[43,46]

4. Sesquiterpene

Tinocordifolin.^[47,48]

5. Steroids

β -sitosterol, δ -sitosterol, 20 β -hydroxyecdysone, Ecdysterone, Makisterone A, Giloinsterol.^[49,51]

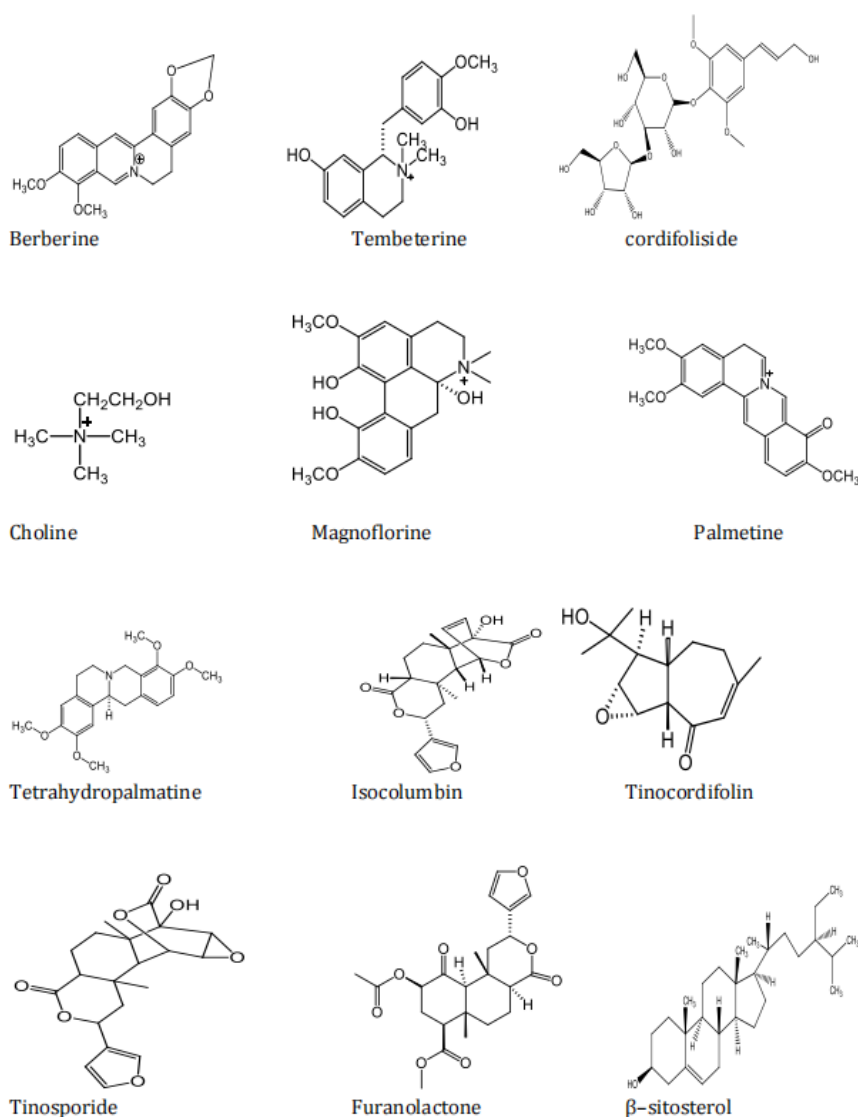


Figure 2: Major phytochemicals present in *Tinospora cordifolia*.

PHARMACOLOGICAL SIGNIFICANCE

1. Antimicrobial Activity

Tinospora cordifolia extracts have been tested for their antibacterial activity against Gram-positive bacteria, including *Salmonella typhi*, *Shigella flexneri*, *Salmonella paratyphi*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Enterobacter aerogene*, and *Serratia*

marcescens. Maximum inhibitory action was demonstrated by aqueous, ethanolic, and acetone extracts of the leaves and stem of *Tinospora cordifolia* Hook. F. Thoms against clinical isolates of urinary pathogens, *Klebsiella pneumonia* and *Pseudomonas aeruginosa*. The stem of *Tinospora cordifolia* is used to create silver nanoparticles, which have excellent antibacterial action

against strains of *Pseudomonas aeruginosa* that are resistant to many drugs and have been identified from burn victims. *Tinospora cordifolia* stem ethanol extract contained the active component [(5R, 10R)-4R, 8R-Dihydroxy-2S, 3R:15, 16-diepoxycleroda-13(16), 17, 12S, 18, 1S-dilactone], which had antibacterial and antifungal properties.^[52]

2. Antidiabetic activity

The antidiabetic effects of *T. cordifolia* stems are likely due to a combination of flavonoids, alkaloids, tannins, and saponins.^[53] Dichloromethane, ethyl acetate, chloroform, and hexane were used to examine the crude extract of the stem when the enzyme blocked action in hypoglycemic diabetic animals and normal animals. The aqueous extract tested in rats raised sugar by 21.3%, insulin by 51.5%, triglycerides by 54.12%, and the glucose-insulin index by 59.8% in the absence of *T. cordifolia* extract.^[54]

3. Anti-HIV Activity

Research has assessed the use of *T. cordifolia* in the treatment of HIV-positive individuals by reducing the patients' resistance to the retroviral regimen. Because *T. cordifolia* has anti-HIV properties, it can help manage HIV-positive individuals by raising their CD4 T-cell count and lowering their eosinophil (a kind of WBC) concentration. Significantly increased phagocytic and intracellular bactericidal activity was demonstrated by *T. cordifolia* extract. Peritoneal macrophages were similarly activated by *T. cordifolia*. *T. cordifolia* also enhances the ability to destroy cells inside cells and to perform phagocytosis. *T. cordifolia* greatly increases the activity of macrophages, polymorph nuclear leucocytes, and B lymphocytes.

4. Anti-Cancer activity

Mouse macrophages were used to test the anticancer effects of a formulation of *Tinospora cordifolia*, *Asparagus racemosus*, *Withania somnifera*, and *Picrorrhiza kurroo*. Impacts on the chemotaxis, interleukin-1 (IL-1), and tumor necrosis factor in macrophages exposed with ochratoxin. HeLa cells were more deadly to Gulvel's aqueous, methanolic, and dichloromethane extracts in a dose-dependent manner (highest activity with dichloromethane extract). The majority of the effects were linked to immunomodulatory processes. The reduction of cyclophosphamide toxicity is also correlated with antioxidant properties.^[55,57]

5. Antipyretic activity

Traditional knowledge attributes *T. cordifolia*'s jwarahara effect (antipyretic activity) to it. The water-soluble component of a 95% ethanolic *T. cordifolia* extract was shown to have antipyretic effectiveness. In a different experiment, it was discovered that the hexane- and chloroform-soluble portions of *T. cordifolia* stems have antipyretic qualities. Numerous studies have shown that *T. cordifolia* possesses anti-infective and antipyretic

properties. Pre-treating rats with *T. cordifolia* prevented them from dying from intra-abdominal sepsis following coecal ligation, and it significantly decreased the death rate in mice from *E. coli*-induced peritonitis.^[58]

6. Anti-Parkinson's activity

T. cordifolia extract has been shown by Birla et al. to be very effective against parkinsonism. In a Parkinsonian animal model that was intoxicated with 1-methyl-4-phenyl-1,2,3,6-tetra hydroxy pyridine (MPTP), they looked at the anti-inflammatory properties of the aqueous extract. The MPTP-intoxicated mice's behavior was reversed by the extract, indicating that *T. cordifolia* preserved dopaminergic neurons in the MPTP-induced Parkinsonian mouse model via reducing neuroinflammation.^[59]

7. Anti-Anxiety activity

Sarma et al. found that a 100 mg/kg ethanolic extract of *T. cordifolia* demonstrates a significant anti-anxiety effect when compared to standard diazepam (2.5 mg/kg).^[60] The patients' improved I.Q. level was consistent with the findings of the clinical examination. In Ayurveda, preparation of *T. cordifolia* is used as a brain tonic. It is said to work by improving mental abilities such as memory and recall.^[61] Effect of Hypolipidemia Rats weighing 2.5 and 5.0 g/kg body weight were used in Stanely et al.'s investigation of the hypolipidemic responses to an aqueous extract of the root on the sixth week. The results showed decreased levels of free fatty acid, serum, phospholipids, and tissue cholesterol. These rats have diabetes caused by alloxan. At a dosage of 5.0 g/kg of body weight, the root extract had the most notable hypolipidemic impact. There has never been any prior research on *T. cordifolia* root extract's capacity to lower tissue lipid levels or serum in diabetic rats.^[62]

8. Antioxidant activity

This is caused by the aromatic glycoside secoisolaricresinol and the alkaloidal components (choline, palmatine, tetrahydropalmatine, and magnoflorine), as well as (-)- epicatechin. Because of its strong sensitivity towards DPPH, superoxide radicals, and hydroxyl radicals, an arabinogalactan polysaccharide from *T. cordifolia* demonstrated protection against iron-mediated lipid peroxidation of rat brain homogenate utilizing lipid hydroperoxide (LOOH).^[63] In the DPPH inhibition experiment, our research demonstrated that, in a dose-dependent manner, the alkaloidal fraction (mostly palmatine, jatrorrhizine, and magnoflorine) exhibited superior antioxidant activity compared to columbin.^[64]

9. Immunomodulatory Activity

The immunomodulatory effects of *Tinospora cordifolia* are widely recognized. The active ingredients 11-hydroxymustakone, N-methyl-2-pyrrolidone, N-formylannonain, cordifolioside A, magnoflorine, tinocordiside, and syringin have been shown to have immunomodulatory and cytotoxic properties.^[65] The

stem claims that the ethanolic extract of *Tinospora cordifolia* (100 mg/kg/p.o.) has immunomodulatory activity, which is supported by an increase in antioxidant enzymes, the activation of T and B cells, the production of antibodies, and an increase in melatonin concentrations in the pineal gland and cytokine levels, including TNF, IL-2, and IL-10. Additionally, it has been shown that aqueous *Tinospora* extracts influence the production of cytokines, mitogenicity, and the stimulation and activation of immune effector cells.^[66] Polymorphonuclear leucocytes, or PMN cells, are a crucial component of the host defense mechanism. Activating PMN cells with extracts from *Tinospora cordifolia* facilitates the phagocytosis of extra *Candida* cells by the use of an in vitro slide phagocytosis technique.^[67] An obvious increase in foot pad thickness and a significant increase in WBC counts and bone marrow cells were the results of oral therapy with *T. cordifolia* alcoholic extract (100 mg/kg, p. o), suggesting a stimulatory effect on the hemopoetic system.^[68]

10. Cardioprotective activity

T. cordifolia has been shown in several animal experiments to have a preventive effect against heart disease. In Streptozotocin (STZ) diabetic rats, a high dosage (200 mg/kg) of *T. cordifolia* root extract significantly protects against isoprenaline-induced cardiotoxicity.^[69] In rats with ischemia-reperfusion-induced myocardial infarction, an alcoholic extract of *T. cordifolia* demonstrated dose-dependent cardioprotective action as evidenced by a decrease in the size of the infarct and blood lipid peroxide level.^[70] Its free radical scavenging action, protection of the Mg²⁺-dependent Ca²⁺-ATPase enzyme, suppression of sarcolemmal Na⁺-K⁺-ATPase activity by free radicals, and Ca²⁺ channel blocking activity might all be contributing factors to its cardioprotective effect. Rats with calcium chloride-induced cardiac arrhythmia in another investigation showed that an alcoholic extract of *T. cordifolia* had cardioprotective effects.^[71]

11. Wound healing activity

T Shanbhag et al. The purpose of this study was to assess the impact of *T. cordifolia* alcoholic extract on dexamethasone-suppressed healing as well as the extract's profile of wound healing. The wound models' incision, excision, and dead space were used to examine the plant's capacity to heal wounds. *T. cordifolia*'s extract has a higher tensile strength, which may be related to its ability to stimulate collagen formation. The inhibition of wound healing by dexamethasone was not restored by *T. cordifolia* extract.^[72]

12. Anti-allergic activity

The juice of *T. cordifolia* is used to treat persistent coughs and asthma in addition to other conditions.^[73] Through its anti-histaminic properties, *T. cordifolia* aqueous extract lessens mast-mediated allergy responses in rats. Additionally, there have been reports of less allergic rhinitis symptoms, including sneezing, nasal

discharge, nasal blockage, and nasal pruritus.^[74] Both in vitro and in vivo allergic responses were mediated by the aqueous extract of *T. cordifolia* stem on mast cells. *T. cordifolia* considerably reduced both the histamine-induced constriction of the guinea-pig ileum and the cutaneous anaphylactic reaction in a rat model.^[75] It also greatly reduced the intracellular calcium levels of activated mast cells and blocked the release of TNF- α in rat peritoneal mast cells triggered with antidinitrophenyl (DNP) IgE. These findings collectively suggested that *T. cordifolia* could be helpful in the management of both acute and long-term allergic reactions. Compared to commercially available anti-allergens, the current evaluation found that *T. cordifolia* extract offers a unique chance to treat allergic illnesses with minimal to no adverse effects.^[76]

13. Anti-osteoporotic activity

The effects of an alcoholic *T. cordifolia* extract on bone remodeling (including osteoblastic and osteoclastic activities) in vitro and protection against ovariectomy-induced bone loss in vivo were studied by Abiramasundari et al. (2017). The results of treating osteoblastogenesis with *T. cordifolia* extract included increased collagen deposition, elevated osteocalcin levels, and increased expression of the osteogenic gene. Nevertheless, there was no discernible effect of its extract treatment on osteoclast growth. In vivo ovariectomy-induced bone loss was prevented by pretreatment with *T. cordifolia* extract at a dosage of 50 mg/kg body weight/day orally for 21 days, followed by therapy for 12 weeks post-ovariectomy. *In-vitro* studies showed that the ethanolic extract of *T. cordifolia* stimulated the proliferation of osteoblasts, but the aqueous extract of *T. cordifolia* showed no influence on cell proliferation. Study results revealed that ethanolic extract of *T. cordifolia* treatment on osteoblasts elicits pro-stimulatory effects. On the other hand, no such effect has been seen on osteoclast cells, thereby indicating that it has no effect on resorption in bone tissue.^[77,78]

14. Hypolipidemic activity

Stanely et al. investigated the hypolipidemic impact of an aqueous extract of the root on rats weighing 2.5 and 5.0 g/kg body weight in the sixth week of life. The results showed that the rats with alloxan diabetes had lower tissue cholesterol, blood phospholipids, and free fatty acid. The maximum amount of root extract that had a hypolipidemic effect was 5.0 g/kg of body weight. Reduced serum lipid levels lowered the risk of vascular illness, but elevated serum lipid levels in diabetes were indicative of coronary heart disease. Up until then, no research had been done on *T. cordifolia* root extract's capacity to lower blood or tissue lipid levels in diabetic mice.^[79]

15. Hepatoprotective activity

T. cordifolia has been shown in several trials to have a preventive effect against liver damage. Rats' liver damage caused by carbon tetrachloride was prevented by

ethanolic preparations of *T. cordifolia*'s whole plant.^[80] In CCl₄, ethanol, and paracetamol-induced hepatotoxicity in Wister rats, a prior investigation on a polyherbal formulation comprising *T. cordifolia* extract demonstrated hepatoprotective efficacy. Another study showed that *T. cordifolia* aqueous extracts from Ayurveda Swaras and Hima greatly decreased the harmful effects of paracetamol and considerably enhanced the antioxidant and hepatoprotective properties of the plant in albino mice.^[81]

CONCLUSION AND FUTURE PROSPECTS

T. cordifolia has been used extensively in traditional medicine, especially Ayurveda, and is receiving more and more attention in contemporary studies. Its usage in treating a wide range of illnesses, like fever, diabetes, skin conditions, digestive problems, and many more, is documented in ancient scriptures like the Sushruta Samhita and Charaka Samhita. It is also utilized in various conventional medical systems, including Indian Siddha and Unani medicine. Because of its therapeutic qualities, it is a mainstay in the conventional pharmacopeia of Southeast and South Asian civilizations. *T. cordifolia* is used medicinally, but it also has ceremonial and cultural value in many different cultures. It is frequently linked to longevity and is regarded in Ayurveda as an adaptogen, or Rasayana, which is said to promote vigor and longevity. Furthermore, there has been an increase in *T. cordifolia* pharmaceutical research. Numerous traditional applications have been confirmed by scientific research, which has also identified the plant's active ingredients, which include polysaccharides, diterpenoids, and alkaloids. Herbal medicine is frequently thought to be less harmful, have less side effects, be able to treat a number of serious illnesses, and be a superior option than allopathic treatment. Herbal medicine's primary flaw is that it has no known mechanism of action. It would be hard to embrace the herbal formulation as a target drug in the current therapeutic application system without a mechanism of action. Future research should concentrate on *T. cordifolia*'s medicinal use for a range of illnesses. *T. cordifolia* needs further clinical trials and research investigations to support its safety, effectiveness, and dose recommendations. The personal care and cosmetics industries may use *T. cordifolia*'s anti-aging and antioxidant qualities in their skin care products. turn become a crucial component of nutraceuticals and dietary supplements meant to improve overall health, treat chronic illnesses, and strengthen the immune system. Furthermore, because of its flexibility and hardiness, it could be used in horticulture and agriculture to increase crop output and resilience. Wider adoption within the context of evidence-based medicine would need this. The current assessment points to the need for more investigation into the creation of innovative plant-based medications for the treatment of illnesses for which there is now no effective treatment.

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