

## Heartleaf Moonseed: A phytopharmacological review

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### Abstract

Medicinal herbs play commanding role in disease control across the globe. There is an increasing demand for plant-based drugs, food products, pharmaceuticals, etc. *T. cordifolia* is a versatile herb, well known for its immense applications in the treatment of dysentery, diarrhea, leprosy, jaundice, fever, dyspepsia, skin diseases, and urinary problems. Current study is performed to explore the plant chemistry along with traditional and pharmacological uses. Major phytoconstituents include alkaloids, terpenoids, glycosides, and steroids. The notable pharmacological properties are anti-diabetic, anti-microbial, immunomodulatory, anti-oxidant, anti-osteoporotic, anti-cancer, memory enhancing, and anti-toxic activities.

**Key words:** phytoconstituents, *T. cordifolia*, pharmacological activities, immunomodulatory

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### 1. Botany

#### 1.1. Introduction

Heartleaf Moonseed (*Tinospora cordifolia* L.) is a deciduous shrub belonging to the family *Menispermaceae* which consists of about seventy genera and 450 species [1-2]. The genus *Tinospora* contains about sixty species. Among them *Tinospora crispa*, *Tinospora smilacina*, *Tinospora sagittate*, *Tinospora sinensis*, *Tinospora bakis*, and *Tinospora cordifolia* are more common which are widely distributed in world's tropical and subtropical areas [3-4]. *Tinospora Cordifolia* L. is listed in Ayurvedic as "Rasayana" and it is used to treat various immunity related diseases. Plant has different vernacular names in different languages. It is commonly known as Heartleaf moonseed (English), Guduchi (Sanskrit), Giloy (Hindi), Gulancha (Bengali), Galac (Gujrati), Thippateega (Telgu), Giloi (Kashmiri), Guluchi (Oriya), Gilo (Punjabi) and Guruch (Urdu) [5-6].

#### 1.2. Demography/Location

*T. cordifolia* is primarily found in rainforests. It thrives in a wide variety of soils (acidic to alkaline), having appropriate moisture content [7]. It is a perennial herb and attains great height by climbing on host tree in a circular pattern. This plant is native to Sri-Lanka, South-Africa, Malaysia, Thailand, China, Borneo, Bangladesh, Philippines, Myanmar, Vietnam, and India [8-11].

#### 1.3. Botany, Morphology

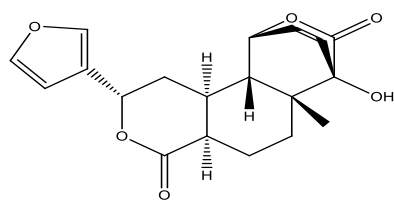
*Tinospora cordifolia* is a large deciduous, extensively spreading climbing shrub with a number of

coiling branches. This plant can grow 1 meter (3.3 feet) high and 0.5 meters (1.65 feet) wide. Seeds are curved and pea shaped. Wood is porous soft and white in color [12]. Stem of this plant is rather succulent with fleshy filiform, and climbing in nature. Aerial roots arise from the branches are characterized by tetra to penta arch primary structure. However, cortex of root is divided into outer thick walled and inner parenchymatous zone. Leaves of this plant are simple, alternate, exstipulate, long petiole approximately 15 cm, round, pulvinate, heart shaped, twisted partially and half way round. Lamina is ovate, 10-20 cm long. Flowers are unisexual, racemes, greenish yellow in color. Male flowers are clustered and female flowers exist in solitary inflorescence. Sepals are six in number, arranged in two series of 3 each. Outer ones are smaller than the inner sepals. Petals are also 6, smaller than sepals, free and membranous [13]. Flowering occurs during March to June. Fruit is orange red in color. The plant is very rigid in nature and it can be grown in almost all climates but prefers warm climate. It requires 18°C to grow. Rainy season is best for plantation of this plant. Well drained soils having sufficient moisture contents and rich in organic matter are best for the growth of *T. cordiflora*.

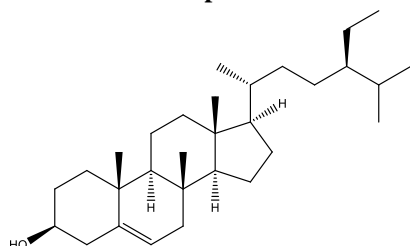
### 2. Chemistry

Plant is mainly composed of steroids, glycosides, sesquiterpenes, polysaccharides, fats, essential oil, and aliphatic compounds. The essential are generally characterized by GCMS analysis [14-20]. The key active phytoconstituents include tinosporaside, tinosporine,

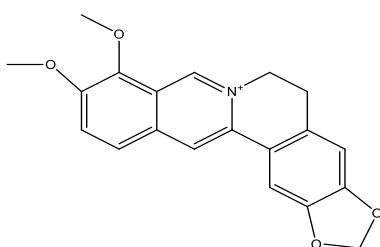
cordifolide, heptacosanol, columbin, choline, tinosporide, clerodane furano diterpene, tembertarine, palmatine, magniflorine,  $\beta$ -sitosterol, cordifol, diterpenoid furano lactone, and Berberine. Phytochemical investigation of water extract of *T. cordifolia* led to the isolation of Tinocordiside (a sesquiterpene having tricyclic skeleton with cyclobutane ring). Recent investigations resulted in isolation of four new compounds from methanolic extracts of *T. cordifolia*. These include alkaloids (tinoscorside A and tinoscorside B), a clerodane diterpene (tinoscorside C), and a phenylpropanoid (tinoscorside D) [13]. Nutritional value of plant is very high as it is rich in dietary fibers and proteins. In addition to this, appreciable amounts of essential minerals (Co, Sr, Zn, Cl, K, Ca, Fe, Br, Ni, Ti, and Cr) are also present. Plant stem provides low fat (2-3%), enough carbohydrates (55-60%), and 0.29Kcalories energy per 100g [21].



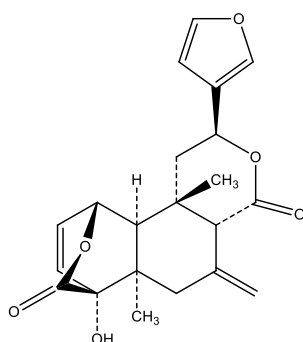
**Tinosporine**



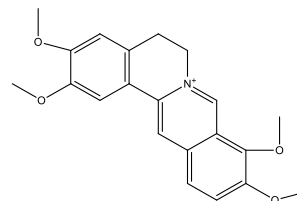
**$\beta$ -sitosterol**



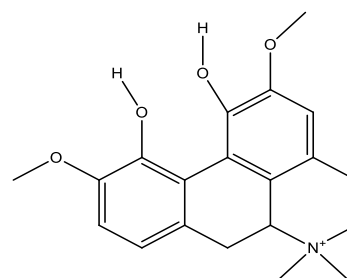
**Berberine**



**Columbin**



**Palmatine**



**Magniflorine**

**Figure 1. Structures of important chemicals present in heartleaf moonseed**

### 3. Postharvest technology

Conventionally, the mature plants are collected. They are then cut into small pieces and then dried. There are two ways of drying, sun drying and mechanical drying. In sun drying method, pieces of stem are spread in the aluminum trays uniformly. They are kept open to sun from 8 am to 5 pm [22]. The temperature during drying ranges from 29 to 34°C. During night time samples are kept in plastic covers to prevent the re-absorption of moisture. While during mechanical method the stem bites are kept in hot air oven uniformly. Temperature ranges from 40 to 60°C [23]. The dried stem pieces are packed in different bags like jute gunny bags, polythene lined gunny bags, ventilated polythene lined gunny bags and are stored at ambient conditions. Through these ways alkaloid contents of *Tinospora cordifolia* can be saved.

### 4. Processing

*Tinospora cordifolia* like other herbal plants is consumed in a variety of ways and for various purposes. In addition to its fresh leaves, other common processed forms of Heart Leaved Moonseed include dry leaves, powdered leaves and medicines. Whole plants, Stems and leaves can be used. Traditional methods are available to preserve this plant for longer time period. Through drying at temperature not exceeding 60°C alkaloid contents can be saved. This plant is cultivated in India mostly for medicines. Processed forms are less common despite the popularity of this plant. Yield is approximately 8-10 q/h per year in India.

### 5. General uses

*T. cordifolia* has been used in folk medicine in different regions of world. Some important uses are discussed in this article. The pills made from *Tinospora cordifolia* are used in the treatment of fever from ancient times. *T. cordifolia* was used as drug for the treatment of fever, dysentery, diarrhoea and jaundice in many countries. Stem, bark and powdered roots of *T. cordifolia* are used to cure cancer; decoction of stem is used to cure fever; decoction of roots is used in the treatment of diarrhoea and dysentery. Leaf paste of *T. cordifolia* is used to cure burn injury. *T. cordifolia* when combined with other herbs can be used to cure rheumatoid arthritis and gout. It is used to cure gastrointestinal ailments such as gastritis, jaundice, haemorrhoids and diarrhea. It plays important role in the treatment of various metabolic disorders including kidney diseases and diabetes. It is also used to cure urinary disorders, skin diseases and eye infections.

## 6. Pharmacological uses

*T. cordifolia* has been documented as potential medicinal plant in the history of traditional medicines due to its pharmacological properties. *T. cordifolia* has significantly improved immune system. This plant has many useful features. Its roots have anti-malarial and stress relieving activities. Stem is used to cure jaundice as it stimulates the secretion of bile. The main pharmacological properties of *T. cordifolia* include the following.

### 6.1. Anti-diabetic activity

*T. cordifolia* has been extensively used to cure diabetes as it regulates glucose level of blood. In an experiment, *T. cordifolia* leaf extracts were orally administered in streptozotocin induced diabetic rats to examine antidiabetic activities. Glucose transport and storage of glycogen was enhanced. In another study, the anti-hyperglycemic effect of *T. cordifolia* root extract was examined in the alloxan induced diabetic rats. Level of glucose in blood and urine of diabetic rats was decreased [24]. *T. cordifolia* stem extract also have strong antidiabetic potential as it enhances the efficiency of insulin by increasing its secretion of from  $\beta$ -pancreatic cell. It also inhibits the glucose formation by enhancing the process of glycogenesis [25].

### 6.2. Anti-cancer activity

Cancer is one of the main reasons for death among women all around the world. In a study, HCl extract of *T. cordifolia* roots was exposed to liver and extra hepatic organs of rats, at concentration levels of 50 and 100mg/kg of body weight. A significant increase in Glutathione and other metabolizing enzymes levels was observed. Furthermore, malonaldehyde (MLD) level was decreased. In another study, the effect of *T. cordifolia* hexane extract on rats having Ehrlich ascites tumor was examined. Inhibition of proliferation of tumor cell (G1 phase) was observed and at the same time the 'Bax' gene expression was enhanced. The anticancer properties of secondary metabolites including yangambin,

palmatine and magnoflorine extracted from *T. cordifolia* were tested in different types of tumor cells. Palmatine and yangambin were highly effective against oral cancerous cells, while others were effective against colon cancer cells. Synthetic chemotherapeutic agents have adverse effects on health, which is not the case with *T. cordifolia*. Therefore, it can be used as a safe drug to cure cancer disease [26].

### 6.3. Antioxidant activity

*T. cordifolia* extracts have strong antioxidant potential as they destroy free radicals and other reactive species [27]. In a clinical study, *T. cordifolia* extracts showed potent antioxidant activity by increasing the concentration of Glutathione (GSH) and decreasing the expression of nitric oxide synthase gene. *T. cordifolia* extracts also inhibit the enzyme aldol reductase and are therefore useful for the treatment of cataract [28]. Another investigation suggests that ethanolic extracts of *T. cordifolia* bark have high phenolics contents than methanolic extracts and show better free radical scavenging properties [29].

### 6.4. Anti-microbial activity

In a study, silver nanoparticles (synthesized using *T. cordifolia* stem) showed strong antimicrobial activity against *Pseudomonas aeruginosa* (a bacterium present in patients of burn injury) [30]. *T. cordifolia* extracts were tested against several strains of bacteria including *Salmonella typhi*, *Klebsiella pneumonia* and *Escherichia coli* and showed strong anti-microbial activity either by inhibiting the growth of bacteria or by extenuating the existence of these bacterial strains [31]. Leaf and stem of *T. cordifolia* exhibited maximum inhibitory action against various urinary bacteria (*Pseudomonas aeruginosa* and *Klebsiella pneumonia*) causing infections in urinary tract [32].

### 6.5. Anti-osteoporotic activity

One of the *in vitro* studies suggests that *T. cordifolia* extract (alcoholic) enhances the degree of differentiation and proliferation of osteoblast cells of mice and humans. Beta-Ecdysone (20-hydroxyecdysone) a steroid extracted from *T. cordifolia* is found to prevent the incidence of osteoporosis by promoting the formation of muscle tissues in mesenchymal stem cells of mouse [33].

### 6.6. Immuno-modulatory activity

Bioactive compounds (synergic and cordifolioside) isolated from *T. cordifolia* stem are reported as immune-modulating agents [34]. Plant stem stimulates lymphocytes by altering levels of enzyme catalase and strengthens immune system [35]. A clinical investigation reported that, *T. cordifolia* lotion decreases the levels of IL-1 and IL-6 (interleukin) in scabies animals by inhibiting hyperkeratosis and penetration of inflammatory cells into scabiatic wound. Aqueous extracts of plant induce cellular mitosis, enhance cytokine production and activation, and stimulate lymphocytes to enhance immunity. A

polysaccharide (G1-4A) isolated from *T. cordifolia* enhances the production and differentiation process of lymphocytes (B-cells and T-cells) [36].

### 6.7. Memory enhancing activity

Studies have shown that *T. cordifolia* helps in cognitive enhancement by immune-stimulation and synthesis of acetylcholine. Thus, contributing in increased choline level indicates its memory enhancing potential in memory deficit animals [37].

### 6.8. Anti-toxic activity

*T. cordifolia* has free radicals scavenging ability, thus, it shows anti-toxic effect. In an experiment, *T. cordifolia* extract inhibited the aflatoxin induced toxicity in kidneys of Swiss albino rats, by elevating the level of Glutathione (GSH) hormone and activities of certain enzymes including catalase and glutathione reductase. Antitoxic effect of plant was due to presence of alkaloids [38]. Lead nitrate toxicity decreased the number of erythrocytes and leukocytes in blood serum of Swiss albino rats. Oral administration of plant extract reversed the toxic effects of lead nitrate in rats. It decreased the levels of glutamic pyruvic transaminase and aspartate aminotransferase, and elevated the levels of free radical scavenging enzymes such as catalase [39].

### 6.9. Cardioprotective effect

*T. cordifolia* have been reported to show cardioprotective activities in a dose dependent manner. Plant root extract was administered in alloxan induced diabetic mice at dose levels of 2.5 and 5g/kg for six weeks to examine cardioprotective effect. A significant decrease in phospholipids, free fatty acids (FFA), and cholesterol level (tissue and serum) was observed. Administration of stem extract of *T. cordifolia* in streptozotocin diabetic mice normalized diabetes mellitus caused alterations in metabolism of lipids and showed indirect heart benefiting effect [40-41].

### 8. Toxicity and safety

Proper research or clinical evidence with reference to undesirable effects *T.cordifolia* extracts has not been reported yet. A little information is available and animal trials on toxic aspects of plant extracts are still being conducted. It is observed that higher doses (1g/kg) of plant extract are required to show any adverse effect in healthy animals (rabbit and mice). However, in humans, its usage is not recommended for lactating mothers and patients of autoimmune ailments, without prescription from physician.

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