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A Detail Review on Heart-Leaved Moonseed (*Tinospora cordifolia*) Medicinal Plant

Vinotha Sanmugarajah[1,*], Gowri Rajkumar[2], P.A.H.R. Panambara[2]

[1]Unit of Siddha Medicine, University of Jaffna, Sri Lanka
[2]Department of Botany, Faculty of Science, University of Jaffna, Sri Lanka
*Corresponding author: vsanmuga@univ.jfn.ac.lk

Abstract

Worldwide, a usage of herbal medicine is gradually increasing for the safety and maintains the health due to its lower side effects. Numerous medicinal plants are using by the healers and traditional physicians to control the disease conditions. *Tinospora cordifolia* (Willd.) Miers (Menispermaceae Family) is distinguished as Heart-Leaved Moonseed herb of the Siddha Medicine which is practicing by Tamil speaking people in Sri Lanka. This present study emphases the detailed review of the pharmacological activities of the *Tinospora cordifolia* (*T. cordifolia*) based on the previous scientific studies and textbooks. Data were collected from all existing sources such as ancient and current indigenous text books, websites, proceedings, research and review articles and other related documents based on prepared data entry form. According to this study, *T. cordifolia* is an important traditional plant which has a variety of pharmacological activities and medicinal usage due to the numerous chemical constituents are present in the various part of this plant. As such, this review paper can serve as evidence for researchers to conduct future scientific research as well as clinical studies in Siddha Medicine.

Keywords: Heart-leaved moonseed, Pharmacology, Review, Seenthil, *Tinospora cordifolia*

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1 Introduction

The World Health Organization informed that, 80% of the world's population are using traditionally plant-based remedies to live with healthy. Plants with nutritive and therapeutic capabilities are the gems in nature's crown, and

for obvious reasons, these therapeutic plants have been the maximum utilized and relied upon sources for human being. Therapeutic plants have curative and therapeutic characteristics in the usage of naturally active substances, which can be found incorporated in plant components such as leaves, flowers, seeds, or bark [1].

Tinospora cordifolia (Willd.) Miers is categorized under the Menispermaceae family, which comprises roughly 70 genera and 450 species found in tropical coastal areas [2] and it is recognized "*Guduchi*"; Heart-Leaved Moonseed and "*Seenthil kodi*" in the Siddha Medicine. It is woody climbing plant which is inherent to India and moreover originates in Burma and Sri Lanka [3]. It has innumerable therapeutic benefits and is widely used in indigenous medicine [4, 5] in the management of the jaundice, rheumatic, urinary, skin, diabetic, anaemia, inflammatory, allergic, and anti-periodic conditions etc. [6, 7].

Most people nowadays are aware of the benefits of *Tinospora cordifolia* (*T. cordifolia*), but many are unaware of how to consume this plant. *T. cordifolia* can be found in three different forms: extracts, juice, and powder. Extract and juice are widely available on the market nowadays. The present study overviews the current state of findings related to the therapeutic and pharmacological effects of *T. cordifolia* based on researchers' interest and experience in the field of study.

2 Methodology

It is a descriptive review related study and data were collected from all existing sources such as ancient and current indigenous text books, electronic databases as Google Scholar, Research gate, Academia, DOAJ, Science Direct, PubMed, Scopus and other websites and reputed scientific databases including proceedings, research articles and other related documents during the period from January 2021 to April 2022 at Jaffna District, Sri Lanka. Detail information was taken from the literatures based on prepared data entry form by the Researchers. The search for review was limited to publications and or studies in the English language only.

3 Results and Discussion

3.1 Scientific Classification [2]

Clasification

Kingdom	: - Plantae
Sub kingdom	: - Tracheophyta
Super-division	: - Spermatophyta
Division	: - Magnoliophyta
Class	: - Magnoliopsida
Sub class	: - Polypetalae
Series	: - Thalamiflorae
Order	: - Ranunculales
Family	: - Menispermaceae
Genus	: - *Tinospora*
Species	: - *Tinospora cordifolia*

Synonyms

Menispermum crispum	: Linnaeus
Tinospora gibbericaulis	: Handel-Mazzetti
Tinospora mastersii	: Diels
Tinospora rumphii	: Boerlage
Tinospora thorelii	: Gagnepain.

Vernacular Names [2, 8]

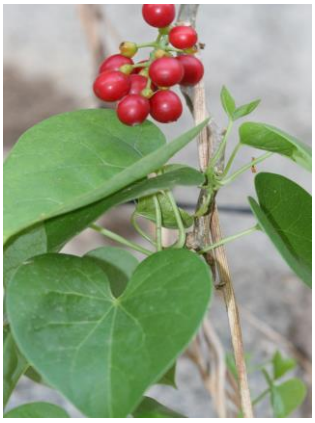
Tamil name	:	*Shindilakodi, Amridavalli, Niraidarudian*
Sinhala name	:	*Rasakinda*
Sanskrit name	:	*Amritavalli, Amrita, Guduchi*
Malayalam	:	*Amruthu, Chittamruthu*
English name	:	Tinospora
Telugu	:	*Tippa-teega*
Kannada	:	*Amrutha balli*
Hindi	:	*Gurcha Giloe, Gulbel*
Gujarati	:	*Gado, Galo, Gulo*
Marathi	:	*Guduchi*
Oriya	:	*Guluchi*
Urdu	:	*Guruch*

3.2 Botanical Description

It is a huge climber (Figure 1) which raises over the uppermost trees in the jungles and throws out aerial roots which range the length of 10 meters, however not thicker than pack-thread. The stem is smooth white, spirally and longitudinally split, and dabbed with enormous rosette-like lenticels nearby between. Its wood remains delicate, white plus permeable, also when presented to air, the newly cut surface promptly becomes yellow. Simple, alternate, long petiolate leaves have chordate-molded with multicoated reticulate venation. The

branches have elongated threadlike aeronautical roots. Blossoms are little and unisexual. Male blossoms sprout in gatherings, though female blossoms blossom alone. Three sepals are arranged in two whorls. Six obovate and membranous petals are gathered in two whorls. The total natural product is red, succulent, and has a few drupelets on a solid tail with red hued sub terminal style scars [3]. The leaves provide excellent livestock feed and flowers and fruits bloom in the summer and winter [2].

a) Leaves



b) Fruits

c) Flowers

Figure 1. Different Parts of the Tinospora cordifolia

3.3 Medicinal Usage

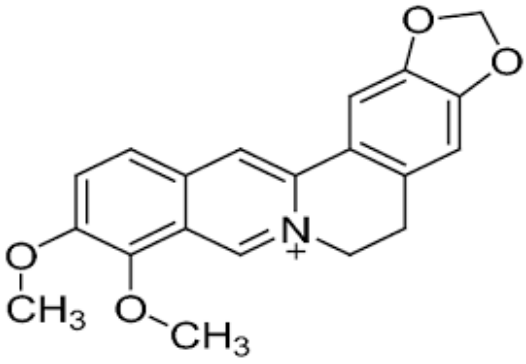
T. cordifolia is a revered therapeutic plant whose utilizations and applications for human advantage have been praised to unfathomable statures in Ayurveda and Vedic works and practices. *T. cordifolia* may be a familiar therapeutic plant in traditional medicine, and up to date scientific research have emphasized *T. cordifolia's* potential application in modern medicine. *T. cordifolia* is unique of the utmost commonly utilized plants in Indian's oldest medical traditions. When taken orally, the leaves, stems, and roots of *T. cordifolia* have no harmful effects on the human body [9]. Further, it is classified as a *Rasayana* medicine in traditional Ayurveda due to its various pharmacological effects [10].

The root of this plant is utilized as powerful emetic and for intestinal obstruction. The starch of the stem is extremely nutritious and digestive, and it's wanted to treat a spread of disorders [11] and it serves a helpful traditional preparation for persistent burning sensation, fever, builds energy and hunger. This plant also helpful to the management of helminthiasis, cardiac problems, Hansen's disease, arthritis, immuno-deficiency, protection from infections, upholds WBC construction, capacity, and altitudes [11]. It likewise supports in gastrointestinal related illnesses like hyperacidity, colonic inflammation, larva invasions, stomach pain, extreme thirst, vomiting, and hepatic problems [12, 13]. *T. cordifolia* is noted for its usage in tribal or traditional medicine in several locations of the USA. In ethnobotanic reviews found that, most portions of the plant are shown to be helpful [14,15].

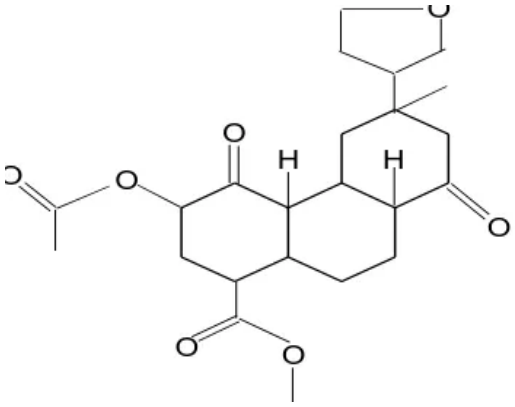
This plant portions are commonly used in the managing of several ailments in folk and tribal medicine such as febrile condition, jaundice, dysentery, debility, cough, asthma, leucorrhea, dermatological disorders, ophthalmic diseases, insect or snake bites, etc. [16,17]. *T. cordifolia* juice is effective to the treatments of leucorrhea when combined with cow's milk and Pitta-related burning sensations when combined with cumin seeds. The juice of this plant is extremely effective in menorrhagia. *T. cordifolia's* starch (Sattva) is used to treat chronic fever, as well as to lessen the burning feeling and boost hunger and vitality [18].

3.4 Chemical Constituents

The occurrence of chemical composites is extremely determined in the stem, leaves and roots a part of the plant [19]. The utmost compounds are berberine and furanolactone (Figure 2) and moreover composites (Figure 3) similar tinosporone, tinosporic acid, cordifolisides A to E, giloin, gilenin, crude giloininand, arabinogalactan polysaccharide, picrotene, bergenin, gilosterol, tinosporol, tinosporidine, sitosterol, cordifol, heptacosanol, octacosonal, tinosporide, columbin, chasmanthin, palmarin, palmatosides C and F, amritosides, cordioside, tinosponone, ecdysterone, makisterone A, hydroxyecdysone, magnoflorine, tembetarine, syringine, glucan polysaccharide, syringine apiosylglycoside, isocolumbin, palmatine, tetrahydropalmaitine, jatrorrhizine are the composites those are isolated. The therapeutic benefits of the plant have been related to the presence of proteins and other substances [5,20].

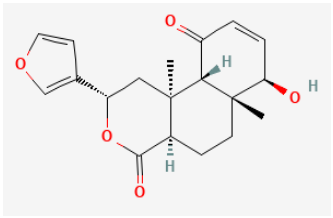


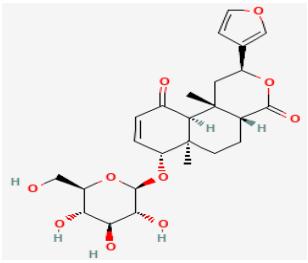
Berberine

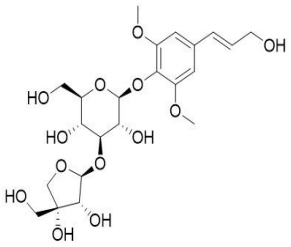


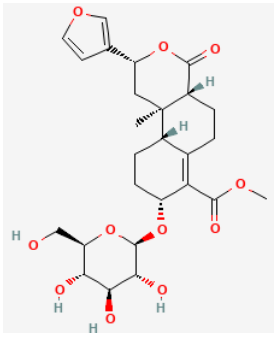
Furanolactone

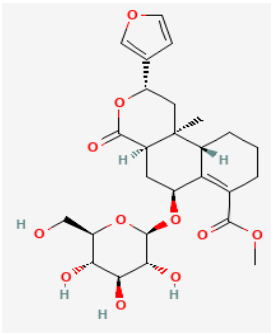
Figure 2. Structure of Berberine and Furanolactone

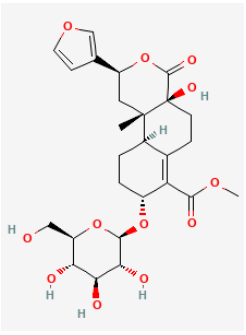

Tinosporone

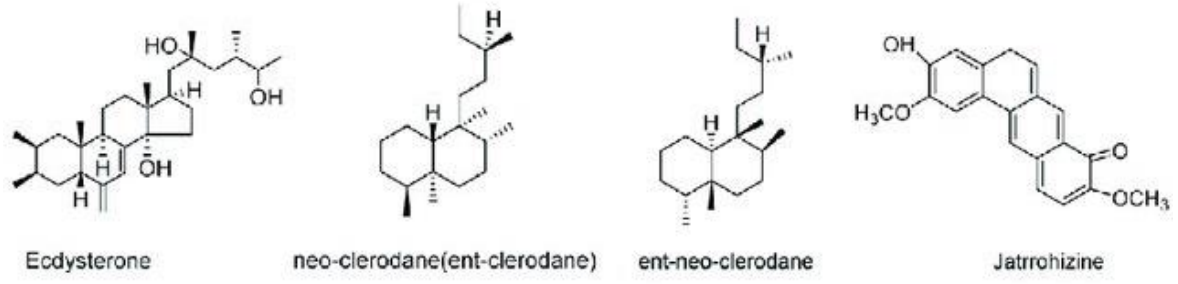

Tinosporaside


Cordifolisides A


Cordifolisides B


Cordifolisides C


Cordifolisides D



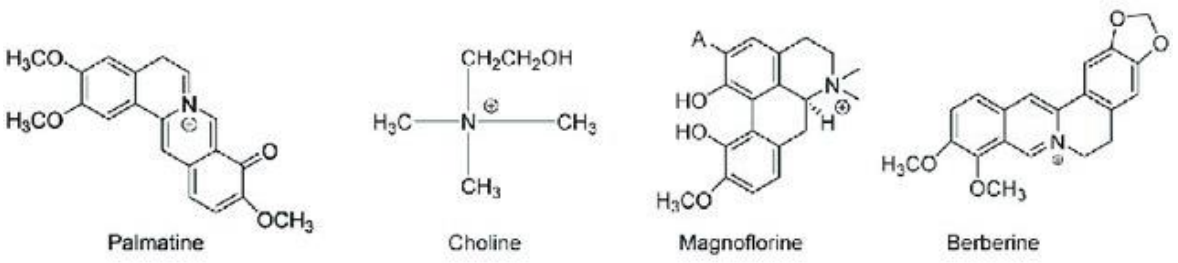


Figure 3. Structure of the chemical constituent of T. cordifolia

3.5 Pharmacological Activities

The pharmacological actions of this climber (Table 1) are owing to its substances like alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic mixtures, essential oils, a combination of unsaturated fats, plus polysaccharides are available in root, stem, and or entire part of the plant [10, 21].

Table 1. Summary of different Pharmacological Studies of *T. cordifolia*

Preparation / extract	Effects
***In vitro* Studies**	
Methanolic extract of stem	Antimicrobial [22]
Aqueous extract	Antifungal [27]
Ethanol leaves extracts	Antioxidant [74]
In vivo Studies	
Aqueous, ethanol and acetone extracts of leaves and stem	Antimicrobial [24]
Silver nanoparticles from the stem	Antimicrobial [25]
Ethanol extract of stem	Antibacterial and antifungal [26] & Immuno-modulatory [41]
Leaf extract	Antibacterial [28, 29]
Ethyl acetate, water fractions and hot water extracts	Immuno-modulatory [29]
Different extracts	Hypoglycaemic, Immuno-modulatory [43] & Anti-Cancer [62]
Alcohol extract	Hypoglycaemic [33, 34]
Root extract	Reduce diabetes-related oxidative stress [35] & Anti-hyperglycaemic [36]
Ethanol extract	Anti-stress [37] & Anti-Cancer [61]
Methanol extract	Anti-Cancer [60] & Antioxidant [71]
Aqueous extract	Immuno-modulatory [40, 41], Parkinson's disease [57], Regularized liver function [58], Anti-toxic [63] & Analgesic and anti-inflammatory [76]
Methanolic stem extract	Anti-fertility [76]
hexane and chloroform soluble fractions from stem	Anti-pyretic [46]
Aqueous extract of root	Hypolipidemic [47]
Root extract	Anti-HIV [48]
Sem extract	Anti-viral [49, 50, 51, 52]
leaf and stem extract	Hepatoprotective [64] & Anti-toxic [2]
Alcoholic extract	Wound healing [53] Anti-osteoporotic [54-56]
Methanolic, ethanolic and water extracts	Antioxidant [67]
Ethanol root extract	Anti-Ulcer [75]
Clinical Studies	
Sedimental extract	Anti-diabetic & anti-obese [32]
T. cordifolia lotion	Anti-scabies [44]

3.5.1 Anti-Microbial Activity

A study reported that *in-vitro* antimicrobial action of methanolic extract of stem compared to both gram-positive and gram-negative bacteria and also exhibited respectable beneficial action against the infections [22]. *T. cordifolia* extracts were confirmed for antimicrobial activity compared to around eleven Gram-positive bacteria [23]. Aqueous, ethanol and acetone extracts of leaves and stem of this plant exhibited supreme inhibitory action compared to an experimental separates of urinary pathogens *K. pneumoniae* and *P. aeruginosa* [24]. Silver nanoparticles made from the stem had superb antimicrobial effectiveness beside multidrug-resistant *Pseudomonas aeruginosa* strains improved from burn victims [25]. The ethanol extract of stem of this plant revealed antibacterial and antifungal activities. The constituents from *T. cordifolia* showed an upper inhibitory activity compared to reference

microbial strains and clinical isolates of methicillin-resistant *S. aureus* and carbapenemase generating *K. pneumoniae* [26]. The aqueous extract of this plant exhibited powerful activity beside *A. fumigatus*, *A. flavus,* and *A. nigar* when using agar well plate diffusion method [27]. Its leaf extract has antibacterial action against gram-positive and gram-negative bacteria, clinically important fungal infections, and malarial parasites, according to studies [28, 29] due to its phytoconstituents such as furanolactone, and tinosporon [29].

3.5.2 Anti-Diabetic Activity

Different extracts of this plant have been revealed to possess hypoglycemic activity *in vivo* in pharmacological tests. This plant has facilitated its anti-diabetic potential through myriad of naturally active phytoconstituents isolated from various parts of this plant, with alkaloids, tannins, cardiac glycosides, flavanoids, saponins and steroids [30]. Alkaloids of this plant exhibited insulin-mediated actions due to insulin hormone [31]. A study stated that the sedimental extract of this plant (1000mg/kg/p.o -30 day's treatment) on diabetic subjects was confirmed for its effectiveness and undoubtedly founds the anti-diabetic and anti-obese actions [32]. The alcohol extract (oral administration) has shown a significant drop of glucose in blood and urine and proven for the hypoglycaemic activity in alloxan diabetic rats after 6 weeks [33]. *T. cordifolia* has been presented to have strong anti-diabetic action in diabetic mice, with an effectiveness of 50% to 70% when associated to insulin [34]. Its root extract was proved to effectively diminish diabetes-related oxidative stress in the maternal liver by increasing glutathione and total thiol levels while lowering malondialdehyde and reactive oxygen species [35]. *T. cordifolia* root extract has an anti-hyperglycemic effect in an alloxan-induced diabetes mouse, dropping the additional glucose level in urine and blood [36].

3.5.3 Anti-stress activity

A study found that a 100 mg/kg ethanolic extract has significant anti-stress effect in all parameters when associated to the conventional medication diazepam (dosage of 2.5 mg/kg) [37]. A moderate degree of behavior deviations and mental diminishing response is formed by the plant extract. Patients' I. Q levels enhanced as a result of the clinical examination. It functions as a brain tonic, by enlightening mental capabilities such as memory and recall [38]. *T. cordifolia* has been established in studies to aid cognitive enhancement through immune-stimulation and acetylcholine production. As a result, choline levels have increased, indicating that it possesses memory-enhancing possessions in both normal and memory-deficient animals [39].

3.5.4 Immuno-modulatory Activities

Aqueous extracts have also been exposed to alter cytokine synthesis, mitogenicity, immune effector cell stimulation, and activation [40]. Ethanolic stem extract (100 mg/Kg/p.o.) was confirmed by changing the concentration of antioxidant enzymes, increasing T and B cells and antibody, improving the concentration of melatonin in the pineal gland, and increasing the level of cytokines like IL-2, IL-10, and TNF-, which are play a key role in immunity [41]. Ethyl acetate, water fractions and hot water extracts of *T. cordifolia* shown good immunomodulatory activity with a rise in percentage phagocytosis [29]. A concentrated form of aqueous extract made traditionally was found to have strong immune-stimulatory action on the immune system [42]. Its extracts were capable to activate polymorphonuclear leucocytes to phagocytose additional Candida cells [43]. A randomized, controlled, parallel pilot clinical trial demonstrated the consequence of the prepared *T. cordifolia* lotion for Interleukin-1, 6, and 8 which levels are reduced in scabies infestations, inhibiting hyperkeratosis and inflammatory cell infiltration into the scabietic lesion. *Tinospora* lotion's anti-scabies efficacy is bolstered by its regulation of interleukin levels [44]. The active phytoconstituents, Tinocordioside, Cordifolioside A, Magnoflorine, and Syringinare known for its immunomodulatory effect [45].

3.5.5 Antipyretic activity

The hexane and chloroform soluble fractions from stem have been established to have significant antipyretic properties [46].

3.5.6 Hypolipidemic effect

Its aqueous extract of root was exhibited the hypolipidemic impact (decreased tissue

cholesterol, serum, phospholipids, and free fatty acid) in alloxan diabetic rats weighing 2.5 and 5.0 g/kg body weight on the 6th week [47].

3.5.7 Anti-HIV potential and Anti-viral effect

Root extract has been demonstrated to diminish HIV viral recurrent resistance, resulting in a better therapeutic effect [48] in HIV positive patient. *T. cordifolia* stem extract lowers eosinophil count, B lymphocyte stimulation, macrophage stimulation, haemoglobin level, and polymorphonuclear leucocytes [49]. Silver nanoparticles from *T. cordifolia* have been revealed to be effective against the chikungunya virus [50]. In view of the positive reports of antiviral activity of selected natural compounds found in *Tinospora cordifolia* extracts, in silco pharmacology was used to screen them against three SARS-CoV-2 targets (surface glycoproteins (6VSB, 6M0J); RNA dependent RNA polymerase (6M71); and Main Protease (6Y84) [51]. A review study stated that the *T. cordifolia* can be considered an indispensable herb plant for COVID-19 in terms of the worldwide pandemic due to its biological activities along with ethnobotanical uses [52].

3.5.8 Wound healing

Its potential of *T. cordifolia* alcoholic extract was investigated via incision, excision, and dead space wound models. The higher tensile strength extract might be due to the enhancement of collagen formation [53].

3.5.9 Anti-osteoporotic effects

T. cordifolia alcoholic extract has been established to increase the proliferation of osteoblasts, enhancing cell variation into the osteoblastic lineage as well as the mineralization of bone-like matrix [54]. This plant can be used in the management of osteoporosis and osteoarthritis [55]. In mammals, ecdysteroids extracted from the plant revealed to have protein anabolic and anti-osteoporotic properties. Beta-Ecdysone derived from this plant has been shown to improve joint cartilage thickness, promote osteogenic difference in mouse mesenchymal stem cells [56], and alleviate osteoporosis in osteoporotic animal models [22, 56].

3.5.10 Parkinson's disease

The aqueous extract was discovered in a Parkinsonian mice model intoxicated with 1-methyl-4-phenyl-1, 2, 3, 6-tetra hydropyridine (MPTP). The extract upturned the behaviour of the target MPTP-intoxicated mice and it's recommended that this extract protected dopaminergic neurons by suppressing neuro-inflammation in MPTP-induced Parkinsonian mouse model [57].

3.5.11 Hepatic disorder

The aqueous extract of *T. cordifolia* on hepatic and gastrointestinal toxicity was stated, a significant rise in the levels of gamma-glutamyl transferase, aspartate transaminase, alanine transaminase, triglyceride, cholesterol, HDL and LDL in alcoholic sample whereas their level descend controlled later TCE intervention, patients exhibited the regularized liver function [58].

3.5.12 Anti-Cancer Activity

T. cordifolia has anti-cancer properties, which have largely been demonstrated in animal models. The anticancer potential of the alkaloid palmatine extracted from this plant utilizing response surface methodology was demonstrated in a 7,12-dimethylbenz(a) anthracene DMBA generated skin cancer model in mice [59]. A single application of this plant extract at doses of 200, 400, and 600 mg/kg dry weight, given 24 hours before the i.p. administration of cyclophosphamide (at 50 mg/kg), dramatically reduced the production of micronuclei in the bone marrow of mice. The 50% methanolic extract at a dose 750 mg/kg b.wt (30 days) displayed increase in life span and tumour size was suggestively reduced as related with control [60]. Using C6 glioma cells, a study evaluated the anti-brain cancer potential of a 50% ethanolic extract of this plant and it inhibited cell proliferation and encouraged differentiation in C6 glioma cells in a dose-dependent manner [61]. A study evaluated eight phytoconstituents from this plant against four different human cancer cell lines, KB (human oral squamous carcinoma), CHOK-1 (hamster ovary), HT- 29 (human colon cancer) and SiHa (human cervical cancer) and murine primary cells correspondingly. All extracts and fractions were active compared to

KB and CHOK-1 cells whereas among the pure molecules palmatine was found to be energetic against KB and HT-29; tinocordiside contrary to KB and CHOK-1; yangambin contrary to KB cells [62].

3.5.13 Anti-toxic Activities

The occurrence of antioxidants in the aqueous extract has already been stated to have scavenging ability against free radicals generated during aflatoxicosis. Choline, tinosporine, isocolumbin, palmetine, tetrahydropalmatine, and magnoflorine are different alkaloids from *T. cordifolia* were found to protect against aflatoxin-induced nephrotoxicity [63]. *T. cordifolia* leaf and stem extract was found to have a hepato-protective consequence in male albino mice when exposed to lead nitrate poisoning. Likewise, an oral dosage of plant extract prevented liver damage caused by lead nitrate [64]. It has shown no toxicity or negative effects [2].

3.5.14 Antioxidant activity

In a study, prepared the formulation and used the DPPH activity to test its antioxidant properties. The total flavanol and phenolic contents were estimated. When compared to the reference medication ascorbic acid, the formulation presented high antioxidant action and inhibitory concentration (IC50) at 5 g/ml [65]. In alloxan-induced diabetic rats, a study investigated the antioxidant activity of methanolic, ethanolic and water extracts, finding that the stemic ethanol extract increased erythrocyte membrane lipid peroxide, catalase activity, and decreased superoxide dismutase, glutathione peroxidase. The methanol extract of leaves, partitioned in water with ethyl acetate and butanol at 250 mg/ml, and exhibited antioxidant action; extracts of methanol phosphomolybdenum and metal chelating action were high followed by ethyl acetate, butanol, and aqueous extract [66]. It similarly declines level of free radical species of diabetic rat and up-regulate the antioxidant enzyme [67-70], free radical of methanol extract was great scavenging activity associated with phenol extract [71]. By controlling the lipid peroxidation process and glutathione level, this plant alters the various enzymatic systems that control the formation of these sensitive species and preserves the oxidative load [72, 73]. The chloroform, methanol, ethanol, hexane, and aqueous leave extracts of this plant exhibited other solvent extracts was low, whereas the ethanol extract was high *in vitro* antioxidant action. The results showed that ethanol extract has more antioxidant components with a clear association among total polyphenols and anti-oxidant effect [74].

3.5.15 Anti-Ulcer activity

Its root ethanol extract was established a significant protecting effect contrary to stress-induced ulceration and this effect was equivalent to that of diazepam [75].

3.5.16 Analgesic and Anti-inflammatory activity

Its aqueous extract had analgesic and anti-inflammatory properties in rodents [76]. 100mg of this plant established significantly higher anti-inflammatory effect which was identical [77].

3.5.17 Anti-fertility activity

The 70% methanolic extract of stem (Oral administration - 100mg/rat/day) was exhibited antifertility effects in male rats for 60 days [78].

4 Conclusions

Tinospora cordifolia (Menispermaceae Family) is distinguished as Heart-Leaved Moonseed herb of the Siddha Medicine. This plant has a variety of pharmacological effects and using the management of the different disease conditions from many years in the Indigenous Medicine which is practicing by Tamil speaking people in Sri Lanka. This present review highlighted that the overview of the medicinal uses and pharmacological activities of the *T. cordifolia*. As such, this review paper can serve as evidence for researchers to conduct future scientific research as well as clinical studies in Siddha Medicine.

5 Author Contribution

V. Sanmugarajah: collected data, conceived and process, writing of the paper. G. Rajkumar: contributed data, conceived and support the process. P.A.H.R. Panambara: collected data, conceived and writing of the paper.

6 Conflicts of Interest

The authors declare no conflict of interest.

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