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REVIEW ARTICLE

Therapeutic potential of Giloe, *Tinospora cordifolia* (Willd.) Hook. f. & Thomson (Menispermaceae): The Magical Herb of Ayurveda

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ABSTRACT

Since time immemorial our saints & sages prophesied the importance of medicinal plants in our life for combating diseases. The Sanskrit treatise 'Rig Veda', the world's oldest book, mentions the use of medicinal plants in the treatment of man and his animals. Even today in the world of modern medicines, *Tinospora cordifolia* (Willd.) Hook. f. & Thomson, is also called 'a magical herb' due to its property of curing a lot of maladies. Among many vernacular names, the most striking one is 'AMRITA', which is attributed to this wonder-drug for its ability to impart everlasting youthfulness, vitality and longevity to its patron. It improves body's defence mechanism as an immunomodulator. In today's world of expensive and highly-commercialized modern medicines, it is indeed the magical rejuvenator-herb. The plant has been demonstrated to possess multiple ethnomedicinal, pharmacological and medicinal activities, but systematic updated information lack on the therapeutic effectiveness of *T. cordifolia*, a popular herbal remedy in India, Southeast Asia and other parts of the world. This review highlights updated information that may provide incentive for proper evaluation of the plant as medicinal agent against many human diseases. It may offer immense opportunity for researchers engaged in validation of the traditional claims and development of safe and effective herbal medicine. The present review introduces a comprehensive update of more than 350 scientific reports to date on *Tinospora cordifolia* an indispensable herb in Indian system of medicine (ISM).

Key words: *Tinospora cordifolia*, Human diseases, medicinal value, bioactive constituents, Safety evaluation.

1. INTRODUCTION

As per the reports of World Health Organization (WHO) nearly 80% of the world's population relies mainly on plant-based-traditional-medicines to meet their primary healthcare needs [1]. It's quite interesting to note that a research paper entitled "A Neanderthal flower burial in northern Iraq" published in the renowned journal named 'Science' in the year 1975 revealed that fossil studies have confirmed the use of plants 'a means of therapy' in the Middle Paleolithic age some 60,000 years ago [2]. This plant, *T. cordifolia*, occupies the top of the list of 'Ayurvedic Materia Medica' because of its extraordinary power of healing [3]. Ayurveda, the traditional (ISM) is around 5000 years old healing tradition rooted in ancient Indian culture, designates this plant as a 'Rasayana'. This vast faculty-of-knowledge is often referred to as the'Mother of all healing'. Ayurveda recommends that *T. cordifolia* enhances general-body-resistance, promotes longevity, an anti-stress medicine and an adaptogen [4,5]. *T. cordifolia* i.e. GILOE or AMRITA is mentioned in the ancient Sanskrit classical-texts of Ayurveda such as Charak Samhita, Sushruta Samhita, Ashtanghridayam, Bhava Prakash Nighantu, Dhanvantari Nighantu, Dravya Guna Vigyan, Nighantu Adarsh as a potential healer of many diseases viz. Fever, leprosy, asthma, anorexia, jaundice, diabetes, chronic diarrhea & dysentery, gout, skin-infections, irritability of stomach [6-16]. All these aforementioned classical texts considered *T. cordifolia* as an astringent, a bitter-tonic, diuretic and a potent aphrodisiac [152] too. In 'Sushruta Samhita' it is considered under the "Tikta-saka-varga". The remarkable medicinal potentiality of *T. cordifolia* also caught the

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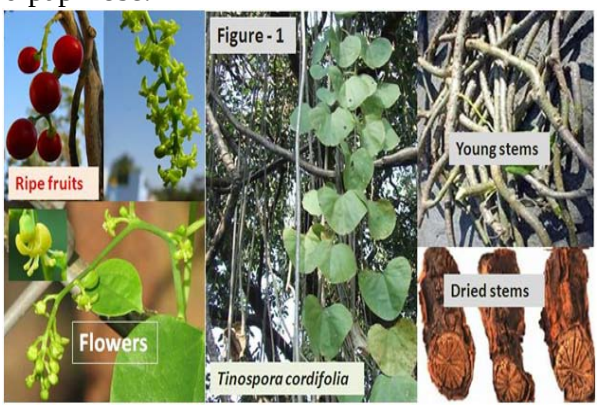
attention of botanists & physicians of Europe; the very fact is included in the Bengal Pharmacopoea [17]. Off late the attention of Western medical researchers is seeking novel therapeutic compounds due to the concerns over more invasive, expensive and sometimes even potentially-toxic compounds. Various pharmacological research-works confirmed that the extract of different parts of the plant is effective to cure variety of diseases [18-22] and some pharmacopoeias too mentioned its amazing healing properties [29,30]. Herbal remedies are an important resource for the discovery of modern drugs [4]. *T. cordifolia* is one of the most commercially exploited plants in pharmaceuticals. The estimated annual demand of this species used in the preparation of crude herbal drugs in the Indian system of medicines (ISM) is 10,000 tonnes [23]. The whole plant possesses diverse health benefits and has been used as traditional medicine for household remedy against various human ailments since the distant past [24,25]. *T. cordifolia* has been extensively used in Ayurveda, Unani and Homoeopathy. The health benefits observed may be due to the presence of the various notable phytochemicals like phenols, terpenes, anthocyanins, flavonoids, alkaloids and glycosides. The purpose of this review is to gather together the available published information on ethnomedicinal lores, pharmacological reports and phytochemical-analysis of the extracts and some of the isolated compounds of this plant as well as their toxic effects in a bid highlighting the importance of this untapped resource in the fight against the human diseases. *T. cordifolia* is mentioned in some of the renowned classic literature [31-40] as a constituent of several compound preparations and used to cure several diseases. It is also believed that the plant has effective properties against Swine flu H_1N_1 Virus [41].

2. *TINOSPORA CORDIFOLIA*, THE MAGICAL HERB

2.1. Botanical description

Botanically Giloe has the following synonyms:- (*Tinospora cordifolia* (Thunb.) Miers, *Menispermum cordifolium* Willd.; *Tinospora cordifolia* (Willd.) Miers.; *Cocculus cordifolius* (Willd.) DC.). The genus *Tinospora* Miers (Menispermaceae) has around thirty-two different species distributed in Tropical Africa, Madagascar, Asia to Australia and the Pacific Islands[27,28]. In India, this genus is represented by four species; two species, *T. cordifolia* and *T. sinensis* (syn. *T. malabarica* Miers ex Hook. f.) are known to occur in South India and the other two *T. crispa* and *T. glabra* are reported from Northeast India and the Andaman Islands[26]. *T. cordifolia* is quite large, extensively-spreading, glabrous, dioecious, perennial deciduous climber grows on wide range of hedges and trees, typically found growing in dry deciduous forests of tropical and subtropical regions up to an altitude of 1000m. It produces distinct male and female flowers. Its fresh stem has a green succulent bark covered by a thin brown-bark, which is studded with warty lenticels while the dry-stem shrinks and the bark separates from the wood. The grey-green branches turn brown with age. The branches are slender having pendulous fleshy & terete roots with parallel ridges & grooves and pale or shining glabrous bark. The underground roots are tubercled. Leaves 5 to 10 cm, membranous, seven to nine veins diverging from the base, somewhat roundish to 'cordate' i.e. 'heart-shaped' (that is why the species name of the plant is '*cordifolia*') with a petiole of 2.5 to 7 cm long. The unisexual flowers bloom in summer in conspicuous racemes often found longer than that of the leaves (**Figure-1**). Yellowish green male flowers are quite small, occur in few-flowered clusters in the axils of small subulate bracts while the female-flowers usually borne singly (i.e. solitary) along the axis. In both male and female flowers Sepals are 6 numbers, 3 outer ones very-small, ovate-oblong and acute while the inner 3 are larger, membranous, broadly elliptical, concave and yellowish. Staminodes are 6 numbers; carpels 3 and ellipsoid. The male and female Inflorescences are usually borne on leafless stems [31,37]. Fruits are fleshy small single-seeded orange-to-red-coloured drupes, tiny stony-seed within is broadly ellipsoid, curved, 6 to 7mm, rounded at both ends and papillose.



2.2. Distribution of *T. cordifolia*

Tinospora cordifolia is a climbing shrub widely distributed throughout India, China, North West

parts of South-Africa, Pakistan, Malaysia, Indonesia, Vietnam, Philippines, Thailand, Myanmar, Bangladesh, and Sri-Lanka.

2.3. Standards for identity, purity and validation of *T. cordifolia*

Pharmacognostical standardization of *T. cordifolia* revealed standardization profile for the drug, value in botanical identification and authentication of the plant-drug and may help us in preventing its adulteration [154]. The following Standards for identity and purity of the herbal-drug, *Tinospora cordifolia* (i.e. Giloe), were reported earlier [42,43]. The Pharmaceutical Standardization of this plant (Guduchi) *T.* cordifolia [44,154,189-193] as an 'Ayurvedic Rasayana' is well documented. There are many herbs and medicinal plants having immunopotentiating capacity and those are referred to as 'Rasayanas' in the Ayurveda. Being a rasayana drug, *T. cordifolia* is widely used in the Ayurvedic system of medicine (ISM). Various parts of the plant contain immense medicinal properties [41]. Pharmacognostical descriptions of *T. cordifolia* including microscopic anatomical details were studied meticulously and reported earlier [20,396]. There are research articles regarding the validation of the traditional claims and development of safe and effective herbal medicine through experimental and clinical studies [359]. It is parctically very difficult to avoid various organic and inorganic contaminants while collecting crude drugs and affect the purity of any crude drug which needs proper assessment & detection based on different pharmacognostic & phytochemical parameters [397].

2.4. Special identity

Taxonomic descriptions of *T. cordifolia* Include, Kingdom: Plantae-Plants; Subkingdom: Tracheophyta-Vascular plants; Superdivision: Spermatophyta-seed bearing plants; Division: Magnoliophyta-flowering plants; Class: Magnoliopsida-dicotyledons; Subclass: Polypetalae; Series: Thalamiflorae; Order: Ranales; Family: Menispermaceae-(The Moonseed Family; the Hindi vernacular-name of this family is called 'GILOE AUR KAKMARI KUL'); Genus: *Tinospora*; Species: T. *cordifolia* (Willd.) Hook f & Thomson. There are many vernacular names of this wonderful medicinal-plant, which include:- Arabic: SAT-GILO, Assamese: HOGUNI-LOT, AMARLOT, AMARLATA, AOR-LOTA, Bengali: GADANCHA, GULANCHA, GILOE, (in Bangladesh: PIPOLTI, GULUNCHI, PIPULTI, PADMA GULANCHA, PIPUL-MORICH, GULONCHO), Chinese: K'UAN CHU HSING, XIN YE QING NIU DAN, English: HEART-LEAF-MOONSEED, TINOSPORA, French: CULANCHA, TINOFOLIN, GUDUCHI, Gaddi tribe of Himachal Pradesh: GALOEIN, GULJYA, Garo tribe of Meghalaya, India & Bangladesh: PODDHO-GULONCHO, Gujarati: GADO, GALO, GADU-NA-VEL Hindi: GILOE, GULBEL, GULVEL, GURCHA, CHINNA, CHINNARHUHA, GILOY, GILOYA, GUDACH, GULANCHA, GULUNCHA, GURCH, AMARA, JIVANTI, JIVANTIKA, PITTAGNI, TIKTAPARVAN, VAJRA, AMRITVALLI, CHINNODEBHA, VATSADANI, Kannada: AGNIBALLI, AMRUTHABALLI, Kashmiri: GILO, Konkani: AMRITVEL, Malayalam : AMRYTU, SITTAMRYTU, Manipuri: NINGTHOU KHONGLI, Marathi: AMBARVEL, GIROLI, GULVEL, AMRITA, AMRITAVALLI, GUDOCHI, GUDUCHI, Mijo: THEISAWNTLUNG, Nepali: GARJO, GURJO, GURJU, Oriya: GULANCHA, Persian: GUL-BEL, Punjabi: GILO, Russian: Тиноспора сердцелистная, Sanskrit: AMRITA, GUDUCHI, CHINNA, GILOY, JIVANTI, JIVANTIKA, JVARA-ARIHI, VAJRA, VATSAHANI, SIKKIMESE: GURJO, Sri Lankan: RASAKINDA, Tamil: AMRIDAVALLI, NIRAIDARUDIAN, AKACA-K-KARUTAN, AKACA-VALLI, AKACI, ACANAMIRTA-TAILAM, AKAYA-VALLI, AMARAI, AMUDOM, AMIRTAI, AMIRTA-K-KOTI, AMIRTAVALLI, SHINDIL KODI, Tamang: GURJU, Telegu: TIPPA-TEEGA, TIPPATHEEGA, GUDAPAALA, GUDUCHI, IRULUCHI, Urdu: GURUCH, GILO and 'ABB-E-HYAT' meaning 'water of life'.

2.5. Commercial importance of the drug

Considering the distribution, growth-habit and commercial importance of *T. cordifolia*, it was pertinent to characterize the DNA fingerprinting for conservation and utilization of the plant genetic resources because it was helpful to know the genetic background of the medicinal plants having high commercial value, and also provides a major input into conservation biology [383]. Research confirmed the average body weight gain and increase in feed conversion efficiency in broiler chicks administered with different preparations of *Tinospora cordifolia* stem extracts orally mixed in their feed [361]. Due to indiscriminate collection and over-exploitation the natural stands of this plant is fast disappearing.

Since conventional vegetative propagation has limited potential for large scale cultivation of this plant, Micro-propagation technique can be most useful for its mass propagation as well as for its conservation [136]. Sustainable and profitable uses of 'non-timber-forest-produce' including medicinal-plants, if promoted and augmented well, it is certain to safeguard the existence of many forest areas around us [384]. *T. cordifolia* is a rich source of biologically active compounds, which would attract the attention of drug discovery groups to discover novel bioactive molecules for safer and effective treatment of various diseases and studies by HPTLC method has reported for the analysis of cordifolioside-A, both in 60% methanol extracts of *T. cordifolia* and in the available commercial formulations[161].

3. ETHNOBOTANY

Anthropologically, every Tribal group along the length & breadth of our vast country, is an 'ethnic group' having unique identity such as own tradition, festivals, folk culture, language (many of them do not have a written-script though), unique beliefs and knowledge about the use of natural resources, to be very specific they do have an intellectual-property-of-ethnomedicinal-plant-lore and the same is passed on from one generation to the other through oral tradition. India possesses the second largest concentration of tribal people anywhere in the world. Earlier these people lived in isolated hamlets. Today the prominent tribal areas constitute around 15 percent of the total geographical area of this vast country [45]. The associated tribal and folk indigenous-knowledge-systems are a proud possession of this sub-continent [20,46-72], here is an example:- the Baiga tribals from Naugarh and Chakia blocks of Varanasi district of Uttar Pradesh prepare a paste using the stem of *T. cordifolia* and roots of *Solanum surattense* and then make pills[46] for the treatment of fever. Here is another example:- Powder of *Terminalia chebula* (HARITAKI) *Tinospora cordifolia* (AMRITA) and *Trachyspermum amni* (AJWAIN) in equal quantity is taken orally once daily in the early morning with little salt for the treatment of cough; decoction of these herbal medicines is also taken in dose of 50ml for the treatment of cough by the people of Dhurala, Haryana [169].

3.1. Ethno-Medico-Botanical uses

Ethno-Medicinal-Plant-Lores from Various regions of India and the neighbouring countries were reported by many authors [20,46-133,169,230-233]. It is used as an ingredient of different compound-herbal-preparations. It is also used in the traditional medicinal system of Thailand for treatment of diarrhea and has been reported to inhibit the *in vitro* growth of the intestinal protozoan parasite, *Blastocystis hominis* [228]. *T. cordifolia* is highly valued in 'Sri Lankan' traditional medications too. There are a pretty good number of references cited in this article, one of these is, Shade-dried-leaves are ground into powder and mixed with hot water and the mixture is taken orally in the treatment of diabetes by the people living in sacred-groves in Cuddalore district of Tamilnadu, India [88]. Another interesting use is, the smashed leaf and root is added to brown sugar and taken orally at night after normal dinner as a potent aphrodisiac by the village-folk of Natore and Rajshahi districts of Bangladesh [89]. The entire summary of all these different Ethnobotanical & Pharmacological Uses of *Tinospora cordifolia* are shown in the (**Table 1)**.

Table 1: Different Ethnobotanical and Pharmacological Uses Of *Tinospora cordifolia*

S. No	Plant parts used as medicine	Ethnobotanical & Pharmacological uses	References cited
1	Leaf	Used in the treatment of gout and ulcer leaf extract showed inhibition of E. coli Extraction of leaves improves fertility & decoction of leaves cures malarial fever.	18,134 136 108
2	Stem	bitter stomachic, stimulates bile secretion, diuretic, enriches the blood, cures jaundice, useful in skin diseases-juice is useful in diabetes, vaginal and urethral discharges, fevers and enlarged spleen (Stem as an infusion used as vermifuge; to cure jaundice, intestinal worms) (Stem as decoction used for washing sore-eyes and syphilitic-sores, antipyretic & antimalarial) (Starch, statue extracted from stem used for chronic-diarrhoea & obstinate chronic-	37 37, 38
3	Root	A powerful emetic, visceral obstruction, water-extract is used in leprosy	24,138,137
4	Stem+Root	(combined with other drugs as an antidote to snake bite)	37, 38, 139, 140
5	Fruit	with ghee or honey used as tonic and in treatment of jaundice & rheumatism juice of ripe fruits with a little honey is given to children in cold	37 101
6	Whole plant (Not-specific part)	Beneficial in the treatment of :- urolithiasis General weakness/Debility Dyspepsia Dysentery Gonorrhea	 135, 126,267, 131,267, 49,50,53,131, 360

		Syphilis	360
		Urinary Diseases	126,267,268,
		Impotency	57,360,
		Gout	6,12,135-138,159,165
		Rheumatoid Arthritis	53,70,94,97,197,261,
		Viral Hepatitis	96
		Skin diseases	49,50,53,78,97,98,123, 132,161,207,261,269, 270,271,362,
		Anemia	20,41,137,138,174,176, 107,126,155,208,357
		Leprosy	100,
		Leucoderma	11,12,53,55,66,71,74,91,92,
		Fever	97, 104,108,115,131,132, 267
		Asthma,	20,132,135,138,159,160, 161,165,
		Anorexia,	12,20,160,255,327,
		Jaundice,	11,12,18,20,38,41,140,303, 318, 332,338
		Diabetes,	22,49,50,58,62,66,79, 83,88,89,95,116-to-122, 131,141,142,165,166, 240-263,292
		Chronic Diarrhea,	11,12,161,369,
		Allergy	19,63,141,142,165,200,206-to-208,357
		Malaria,	141-to-143, 145
		Menstrual problems	70,
		Helmenthiasis,	38,
		Heart diseases	93,155,250,347
		Aphrodisiac	13,89,140,152,272,368,382

4. DISEASES THAT HAVE BENEFICIAL EFFECTS

Allergic diseases, anemia, anorexia, asthma, cancer, chronic diarrhea & dysentery, diabetes mellitus, fever, gonorrhea, gout, heart diseases, helmenthiasis, impotency, irritability of stomach, jaundice, leprosy, malaria, rheumatoid arthritis, skin diseases, syphilis, tuberculosis, urinary diseases, viral hepatitis, Alzheimer's disease etc.

5. PHYTOCONSTITUENTS OF *T. CORDIFOLIA*.

Table 2: Different Phytoconstituents of *T. cordifolia*

Phytoconstituents	References cited in the article
Alkaloids	20,41,61,89,131,135-138,145-149,151-168,170, 177,179-184
Ascorbic acid	151,161,312,365,174,175,176,308,317,
Anthocyanins	161, 363,364,
Carotenoids	175,183,312,363,366,
Betalains	363,
Lycopene	161,363
Carotene	161, 363,
Carbohydrates Polysaccharides	41,135-to-138,145,148,151,152,155,171,158,165,166,168, 171-to-174, 176,235, 236,237
Lipopolysaccharides	168,
Fixed oils	176,227
Essential oils	137,165
Flavanoids	80,136,151,159,160,165,166,175,176
Glycosides	41,135-to-138,145,148,151-to-161,165-to-168,174,176,177,185,209-to-215,219,220,
Gums and mucilage	135,136,138,148,151,153,155,161,175,176,183
Phenols	135,136,148,151,153,154,159,176,160,165,175,183,226,227
Tannins	41,155,238
Phytosterols	41,136,137,138,145,148,152,154,155,159,161,165,166,167,178,187
Phytosteroids	136,148,152,154,176,166
Protein and amino acids	173,166
Peptides	136,148,151,152,153,154,159,176
Saponins	165,173,246,
Lectins	41,138,152,155,158,161,165,167,168,186,188,216,217,222-225
Diterpenoid lactons	41,137,138,152,155,161,165,194
Aliphatic compounds	137,138,152,155,161,165,167
Sesquiterpenoid	148,151,156,159,166
Triterpenoids	132,154,180,368,
Resins	151,154,165,
Quinones	165,
Coumarins	

While screening a number of medicinal plants, scientists discovered one of the most revered medicinal plants, i.e. Giloe, which exhibited a number of medicinal activities [41] because it contains a large number of different types of phyto-constituents. The Aqueous and alcoholic extract were taken for various qualitative chemical tests to determine the presence of various

phytoconstituents such as alkaloids, carbohydrates polysaccharides, lipopolysaccharides, fixed oils, essential oils, flavanoids, glycosides, gums and mucilage, phenols, tannins, phyto-sterols, Phyto-steroids, protein and amino acids, peptides, saponins, lectins, diterpenoid lactons, aliphatic compounds, tannins, sesquiterpenoid, Triterpenoids, Resins, Quinones, Coumarins etc., which are shown in (**Table 2)**. The phytoconstituents are diterpene, tinosporone, tinosporic acid, cordifolisides A to E, syringen, berberine, 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, berberine, ecdysterone, makisterone A, nonacosan-15-one, magnoflorine, tembetarine, syringine, glucan polysaccharide, syringine apiosylglycoside, isocolumbin, palmatine, tetrahydropalmaitine, jatrorrhizine, the alkaloids include berberine, a bitter glucoside giloin, non-glycoside gilonin[155], gilosterol etc[24]. The TLC analysis of *T. cordifolia* by Soni H et al. 2011 revealed the presence of Tinosporide [396].

6. ENVIRONMENT FRIENDLY PRODUCTS & SERVICES

6.1. Safe drinking water

Occurrence of high fluoride concentrations beyond permissible limit in groundwater is a problem faced by many countries of Asia and East-Africa. High fluoride concentration in the ground water as well as in surface water in many parts of the world is a cause of great concern. The biomass of the natural plants of *T.* cordifolia demonstrated a good capacity of fluoride biosorption, highlighting its potential for the drinking water treatment process to get safe potable water [239]. There are new possibilities of such interesting discoveries for the researchers who intended to do studies in this particular field using this wonderful plant.

6.2. Colouring agent & nutraceuticals

The green, yellow & red fruits of *T. cordifolia* can be a source of bioactive food colourants such as lycopene and berberine plus ripened fruits may contain other nutraceuticals as well, further research-work will be best suited for such commercial exploitation [363]. The stem of *T. cordifolia* has potential application in food systems as an antioxidant and as a biologically potent nutraceutical because it can reduce oxidative stress with consequent health benefits [175].

7. PHARMACOLOGICAL ACTIVITIES

Various pharmacological activities of *Tinospora cordifolia* (Willd.) Hook. f. & Thomson are shown in (**Table 3)**.

7.1. Antioxidant and free radical scavenging activity

The methanolic extract of *T. cordifolia* stem contains high amount of phenolics, flavonoids and alkaloids with moderate amount of tannins and carbohydrate, which exhibit good total antioxidant activity and moderate free radical scavenging activities [151]. It also has good DNA protective potential. *Tinospora cordifolia* exhibited excellent antioxidant activity in methanol, ethanol and water extracts. It possesses phytochemicals such as polyphenols, flavonoids and tannins which attribute to a strong free radical scavenging activity [175]. Research study confirmed that fresh plant aqueous extracts are more potent antioxidant in comparison of ethanolic extract [176].

7.2. Antidiabetic activity and renoprotective activity

Tinospora cordifolia were used in combination to treat diabetes and several research studies confirmed that it causes significant reduction in blood glucose level[116] and its renoprotective activity [211]. Research study confirmed that, both the aqueous and alcoholic extracts of *T. cordifolia* could ameliorate the metabolic derangements in lipid metabolism caused by STZ induced diabetes in rats. Efficacy of this activity is appreciably good when compared to standard drug insulin[250]. The ethanolic extract of *T. cordifolia* stem have inhibitory effect on CaOx crystallization thus may be beneficial in the treatment of urolithiasis [145].

7.3. Antimutagenic, anticarcinogenic, radioprotective and chemopreventive activity

Research study in experimental animals confirmed Anticarcinogenic and Antimutagenic activity of *T. cordifolia* extract [288]. Research also confirmed that the extract of it shows potent chemopreventive activity [207]. Extract of the plant also showed effective radioprotective activity [274]. Arya & Sharma reported that extract (in 50% alcohol + 50% distilled water) of *T. Cordifolia* Provides Protection against Radiation Induced Alterations in Intestinal Mucosa of *Swiss Albino* Mouse [394].

7.4. Hepatoprotective activity

There are a good number of references cited in this article which support the Hepatoprotective activity of *T. cordifolia*, vide (Table 3). It is very

interesting to note that tinosporine and tinosponone, identified in the stem and roots of *Tinospora cordifolia* are reported as hepatoprotective agents and have exhibited *in vitro* inactivating property against Hepatitis-B and E[170]. Alcoholic *T. cordifolia* root extract (TCREt) administered at a dose of 100 mg/kg body weight to diabetic rats orally for six weeks normalized the antioxidant status of liver and kidney. The effect of *T. cordifolia* root extract was found more potent than glibenclamide (600 microg/kg body weight) [292]. Here are some of the Trade names and manufacturers of multiple herbal preparations containing *T. cordifolia*, used for hepatoprotection:- LIV-52, M/S The Himalaya Drug Co., Makali, Bangalore; LIV-77, M/S Globe Pharmaceuticals, Jullandar; LIVA-16, M/S Maduna Pharmaceuticals Research, Calcutta; LIVIN, M/S Arya Audhadhi Pharm. Works, Indore; LIVODIN, M/S Madona Pharm. Res. Calcutta; LIVOMYN, M/S Charak Pharmaceuticals (India) Ltd. Samalkha; LIVOTRIT, M/S Zandu Pharmaceuticals, Bombay; LIVOZON, M/S Hind Chemicals, Kanpur [387]. In a crude multi-herb formulation (*Boerhavia diffusa*, *Tinospora cordifolia*, *Berberis aristata*, *Terminalia chebula* and *Zingiber officinale*) a maximum cure rate of 73% (dose: 800 mg/kg/day) in hepatic amoebiasis reducing the average degree of infection to 1.3 as compared to 4.2 for sham-treated controls has been reported [388]. A compound formulation having *T. cordifolia* has been observed to express hepatoprotective properties in adult goats of either sex [389]. Recent research has demonstrated that a combination of *T. cordifolia* extract and turmeric extract is effective in preventing the hepatotoxicity which is otherwise produced as a side effect of conventional pharmaceutical treatments for tuberculosis using available drugs such as isoniazid and rifampicin [330].

7.5. Cardioprotective activity

Research studies using alcoholic extract of *T. cordifolia* in ischemia-reperfusion induced myocardial infarction in rats suggests the cardioprotective activity of *T. cordifolia*[347]. The cardioprotective activity of an herbal formulation "Caps HT2" that contains methanol extract of *T. cordifolia*, having antioxidant, anticoagulant, platelet antiaggregatory, lipoprotein lipase releasing, anti-inflammatory and hypolipidaemic activity in experimental animals, the rats [385].

Table 3: Different Pharmacological activities of *T. cordifolia*

S. No	Pharmacological Activities	References cited in the article
1	Adaptogenic	4,5,220,336,
2	Antiallergic	19,141,142,165,200,206-to-208,357
3	Antiarthritic	196,197,261,
4	Antibacterial / Antimicrobial	132,136,146,148,159,234,283,311,317-to-323,
5	Anticancer	124,133,147,170,182,207,272-to-300
6	Anticarcinogenic	207,288,314,325
7	Anti-depression	377
8	Antidiabetic	22,117-to-122,141,142,165,166, 240-to-263,292
9	Antidiarrhoel	369
10	Antidote to snake-bite	139
11	Antifertility	367
12	Antifungal	132
13	Anti-HIV 1	326
14	Antiinflammatory	155,193,195-to-205,229,
15	Anti-ischemic	347
16	Antileprosy	155,208,357
17	Antimalarial	141-to-143,145,
18	Antimutagenic	288
19	Antioxidant	22,118,121,141,142,151,165,172,175,176,183,234,252,258,259,281,292,295,296,305-316,
20	Antiprotozoal	228
21	Antipyretic	65,74,77,132,198,208,267,311,380,381,
22	Antispasmodic	155,201,208,352,353,
23	Anti-stress	155,350,373-to-376
24	Antituberculosis	140,329,330,
25	Antiulcer	155,250,347,
26	Antiviral	41,70,207,326
27	Aphrodisiac	13,89,140,152,272,368,382,
28	Cardioprotective/ Cardiotonic	93,250,347,
29	Chemopreventive	207
30	Cytoprotective	275,322,358,
31	Diuretic	378,379
32	Gastrointestinal / stomach troubles	69,123,
33	Hepatoprotective	145,160,170,303,304,373,328-to-332,
34	Hypocholesterolemic	250
35	Hypoglycaemic	165,246,248,253,259
36	Hypolipidemic	116,156,226,
37	Immunostimulator / immunomodulator	134,141,142,153,158,165,171,173,200,202,282,284, 285,290,298, 300-304,315, 318, 331-346
38	Learning & memory enhance	370,371,372,

39	Radioprotective	174,272,274,294,327,
40	Renoprotective	116,211,249,292,
41	Wound healing	354,355,392,

7.6. Cytoprotective activity

Research confirmed that Carbon tetrachloride extracts are better than that of Petroleum ether and Chloroform extracts of *T. cordifolia* in respect to their antimicrobial activity and cytotoxicity and makes it a promising indigenous drug [322].

7.7. Antibacterial & Antifungal activity

Both Hot and cold methanol extracts of *T. cordifolia* stem contain significant antibacterial activity against all test bacterial strains of *Salmonella typhi, Pseudomonas aeruginosa, Staphylococcus aureus* and *Shigella dysenteriae* [317]. Research work supported the claim in the traditional medicine that the plant can be used in the treatment of various infectious diseases as fever, diarrhea, dysentery, cough etc. which are of bacterial origin and skin diseases caused by fungi[132]. It is revealed that the ethanolic extracts exhibited significant antibacterial activity against *Proteus vulgaris, Escherichia coli* and moderate activity was observed against *Enterobacter faecalis* [146].

7.8. Antiviral activity

The leaves of *T. cordifolia* extracts show anti-HIV 1 activity and this plant has great potential for developing useful drugs. Extraction of important biologically-active phytochemicals from this plant will certainly be helpful in protecting and treating various viral diseases in human beings [326].

7.9. Anti-inflammatory and anti-arthritic activities

Antiinflammatory and antiarthritic activities of *T. cordifolia* were reported by Gulati OD [197, 198] & Hazarika Ridip [97].

7.10. Anti-allergic activity

Clinical trials confirmed *T. cordifolia* significantly decreased all symptoms of allergic rhinitis [206]. Nayampalli *et al*. [19], Lagachu *et al*. [63], Chinaware [141], Desai *et al*. [142], Choudhary N *et al*. [165], Leyon [200], Nayampalli *et al*.[208], reported antiallergic activities of *T. cordifolia*.

7.11. Adaptogenic activity

Sipahimalani AT reported the adaptogenic activity of the plant drugs, *Tinospora cordifolia* and *Drypetes roxburghii* [220]. The alcoholic and aqueous extracts of *T. cordifolia* have been tested successfully for adaptogenic and immuno-modulatory activity[336].

7.12. Hypoglycemic, Hypolipidemic and hypocholesterolemic acivities

Stanely et al. reported hypoglycemic and hypolipidemic action of alcohol extract of roots of *T. cordifolia* in alloxan-induced diabetic rats[257].

7.13. Gastrointestinal motility improving and antiulcerogenic activity

Abdul Rashid reported the use of *T. cordifolia* in the Treatment of Gastrointestinal Disorders [69]. The alcoholic extract of the whole plant *T. cordifolia* possesses gastric ulcer protective principles[349]. Chandan *et al*., reported *T. cordifolia* having anti-ulcer activity in the three models tested [348]. Abdul M. Uyub *et al*, reported about the Plants screened for anti-*Helicobacter pylori* activity. *Helicobacter pylori* is the major agent in the etiology of chronic active gastritis, duodenal and gastric ulcers and has been linked to gastric carcinoma too; the selection of those Plants was based on ethnobotanical information obtained from traditional medicine practitioners in Malaysia [393].

7.14. Antispasmodic activity

Kamble et al. [352], Lather *et al*. [353], Singh *et al*.[155] and Ikram *et al*. [198] reported antispasmodic activity of the dry barks/stems of *T. cordifolia*.

7.15. Improving cognition, concentration and memory & cerebral ischemia

Central antioxidant properties are thought to be a key mechanism in improving cognition, concentration and memory, which provides potential benefits in Alzheimer's disease and attemtion-deficit-hyperactivity disorder. *T. cordifolia* has also been shown to be beneficial in improving cerebral ischemia by possible mechanisms of preventing oxidative stress injury and cytokine regulation [390. Studies have shown that herbal formulations having the properties that can improve memory and function as a brain tonic, one such synergistic formulation is comprised of alcoholic extracts/juice of stems of *Tinospora cordifolia*, leaves of *Centella asiatica*, roots of *Withania somnifera*, seeds of *Mucuna pruriens* plus the rhizomes of *Curcuma longa*, mixed in the ratio ranging from 1:0.5:1:1:2 and 1:1:1:1:2 by weight balance. These substances were found to produce enhancement in the catalase, superoxide dismutase and glutathione peroxidase in frontal cortex as well as striatum of rats [391].

7.16. Immunomodulatory activity

Research work of Upadhyaya R. *et al*. confirmed the multifaceted immunomodulatory potential of

the aqueous extract of *T. cordifolia*[158]. Sipahimalani AT reported the adaptogenic activity of the plant drugs, *Tinospora cordifolia* and *Drypetes roxburghii* [220]. The alcoholic and aqueous extracts of *T. cordifolia* have been tested successfully for adaptogenic and immuno-modulatory activity [336].

7.17. Wound healing activity

T. cordifolia is used in numerous Ayurvedic preparations such as GUDUCHYADI CHURNA, GUDUCHI TAILA, DASHMOOLARISHTA, SANJIVANI VATI, KANTA-KARI AVLEHA, CHYAVANPRASHA, GUDUCHI SAATVA, BRIHAT GUDUCHI TAILA, STANYASHODHANA KASHAYA CHURANA, PUNEHNIMBA CHURNA, GUDUCHI GHRITA, AMRITA GUGGULU, AMRITASHTAKA CHURANA, etc., Khan [20] and Nema *et al.* [392] reported that it has a potent wound healing activity [20]. Girish M, Kamdod M A. Effect of topical *Tinospora cordifolia* on excisional wound in albino rats [354]. Meravanige [356, 395] reported that *T. cordifolia* significantly ($P<0.05$) promoted the healing process in the wound models studied. Mohammed Rahmatullah et al. reported the significant improvement for wound healing in foot ulcers of diabetic patients using this plant as an adjuvant therapy [116].

8. CLINICAL STUDIES

Clinical trials confirmed *T. cordifolia* significantly decreased all symptoms of allergic rhinitis [206]. Clinical study clearly indicated that *T. cordifolia* is safe at dose of 500mg per day for a period 21 days in healthy volunteers for the parameters studied and the safety assessment was done with the help of haematological and biochemical investigations [386]. *T. cordifolia* showed healing potential on excisional wound with the tested formulation and this property could possibly be used clinically in the healing of open wounds [354]. Clinical studies established the anticancer property of *T. cordifolia*[279]. Research work of Upadhyaya R. et al. confirmed the multifaceted immunomodulatory potential of the aqueous extract of *T. cordifolia* [158]. Clinical studies have confirmed the hepatoprotective action of *T. cordifolia*; the experimental animals, goats, showed significant improvement in CCl_4 induced hepatopathy.

9. SAFETY EVALUATION

T. cordifolia is marketed globally in various kinds of dosage such as powders, tablets & capsules either as a single herb or in poly-herbal formulations. The estimation of protoberberine alkaloids can be used for routine quality control of crude drugs and polyherbal formulations having *T. cordifolia* because it is essential to detect counterfeits and ensure quality, safety and efficacy of herbal materials and formulations [346]. Acute toxicity studies revealed the non-toxic nature of methanol extract of *T. cordifolia*. Experiment was carried out on normal healthy male rats and no mortality was observed in the extract-treated rats, behavior of the treated rats also appeared normal. There was no toxic reaction found at any dose selected until the end of the study [255]. From the literature it has been noted that *T. cordifolia* exhibited various pharmacological effects, vide (Table 3). These above findings indicated that it is a safe substance to be used as medicine.

10. CONCLUSIONS AND RECOMMENDATIONS

T. cordifolia is one of the well-adapted ethnomedicinal plants having a wide spectrum of pharmacological and medicinal activities. This versatile medicinal plant is the unique source of various types of Phytoconstituents having diverse chemical nature and thus, it has a number of pharmacological properties, still more research work has to be carried out for better medicinal applications of this wonder-plant against various diseases. Currently the worldwide scenario is changing towards the use of nontoxic plant products having traditional medicinal uses. Today's drug development programme should be undertaken to make more advanced safe & effective modern drugs with compounds isolated from the medicinal plants like *T. cordifolia*.

CONFLICT OF INTEREST STATEMENT

We declare that we have no conflict of interest.

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