ISSN:1624-1940
http://magellanes.com/

Phytochemistry and pharmacological importance of *Tinospora cordifolia*

Faiza Irshad[1], Aroosa Ahmed[1], Shafia Arshad[1], Saif Ahmed[3], Zahida Yaseen[2], Muhammad Zakaria[3]

[1]University College of Conventional Medicine, Faculty of Medicine and Allied Health Sciences, The Islamia University of Bahawalpur, 63100, Pakistan

[2]Center for Research and Development (CRD), Minhaj University, Lahore. Pakistan

[3]Department of Eastern Medicine, University of Balochistan, Quetta. Pakistan

***Corresponding Author**

Shafia Arshad, University College of Conventional Medicine, Faculty of Medicine and Allied Health Sciences, The Islamia University of Bahawalpur, 63100, Pakistan
shafia.arshad@iub.edu.pk

Abstract

Introduction: This review paper highlights the significance of *Tinospora cordifolia* (*T. cordifolia*) in the therapeutics, chemical constituents, and pharmacological activities. *Tinospora cordifolia* is an evergreen shrub belonging to the family of Menispermaceae and is broadly used in traditional medicine systems. This woody climbing shrub is generally recognized as “Guduchi” and “Amrita” and is disseminated in China, India, Srilanka and Myanmar. **Method:** The review data of *T. cordifolia* was collected from various scientific online search engines in particular PubMed, Science central, Web of Science, Science Direct, Scilit as well as Google Scholar. Various in vitro, in vivo, and clinical studies were added in this review by using different keywords like *Tinospora cordifolia*, Guduchi and Amrita. **Results:** The extract of numerous components of this plant such as stems, leaves, bark, and

roots show potent antioxidant properties. In addition, Tinospora is reputed to possess antiallergic, antispasmodic, antiperiodic, anti-inflammatory, antipyretic, immunomodulatory and antitumor activities. *T. cordifolia* possesses a diverse range of active biological compounds from different phytochemical classes inclusive of alkaloids, sitosterols flavonoids, phenolic acids and terpenoids. **Conclusion:** T. cordifolia can be used as an effective therapeutic agent for the treatment of illnesses. Therapeutic properties of this plant led to the development of remedial products to cure a broad spectrum of illnesses.

Keywords

Medicinal Plant; *Tinospora cordifolia*; Antioxidant; Pharmacological actions; Chemical constituents; Menispermeaceae

1-Introduction

According to the WHO reports, a substantial majority of the global population, approximately 80 percent, rely on traditional remedies, encompassing the utilization of plant extracts and active components.(Arunachalam et al., 2022) Herbal preparations are medicinal formulations made from one or more herbs in a specific ratio to offer benefits for diagnosis and treatment of illnesses in humans and animals and aesthetic purposes (Bijauliya et al., 2017). It is also often denoted to as herbal medicine, botanic medicine or phytomedicine. Natural medicine was the only medicine available in the early 20th century because of the lack of analgesic and antibiotics at that time. By the time allopathic medicine system surged in popularity owing to its quick therapeutic actions and phytomedicine steadily lost favor among individuals (Taylor, 2022). Owing to improved harmony coupled with the body and less adverse effects, 70-80% population is still using natural medicine for basic health (Wagenlehner et al., 2018). Herbal remedies have captured interest and is believed to be superior in effectiveness compared to chemically synthesized medications.

Both in industrialized as well as emerging nations, there is a rising need for therapeutic plants due to abundance of natural compounds present in them, effective part of alternative medicine and economic importance (Jamshidi-Kia et al., 2017). Medicinal plants are the most important and trending topic of research worldwide. Development of various medications and chemotherapeutic drugs and the extraction of medicinal plants and traditionally used plants led to the increased consumption of these plants in industrialized countries. Among the wide variety of medicinal plants, *Tinospora cordifolia* belonging to Family Menispermaceae is a highly valuable plant with chemical constituents and pharmacology(Rushikesh et al., 2023). It has longstanding history in traditional medicine systems to relieve a broad spectrum of health conditions like diabetes, jaundice, anemia, inflammation, rheumatic disorders, allergic reactions, skin issues, gout, and urinary diseases (Meena et al., 2010; Preeti, 2011; Sonkamble & Kamble, 2015). *T. cordifolia* roots are utilized to treat intestinal obstruction and are known to have potent emetic properties. The starch obtained from this plant is used as useful remedy for burning sensation, relieves chronic fever, boosts energy and stimulates appetite (Ahsan et al., 2023; Sinha et al., 2004). Tinospora also serves as beneficial remedy to cure cardiovascular diseases, rheumatoid arthritis, helminthiasis, leprosy, increase body's resistance to various infections, boost immune health and maintain normal levels of white blood cells (Sharma et al., 2019a). Additionally, it aids in the treatment of liver diseases like hepatitis as well as digestive problems like hyperacidity, lack of appetite, colitis, worm infestations, abdominal pain, excessive thirst, and vomiting(Salkar et al., 2017; Upreti & Chauhan, 2018).

According to this viewpoint, Tinospora is regarded as a nectar plant and in Sanskrit it is named amrita due to its purifying, reviving and immune-boosting activities(Kumar et al., 2023) (B. Kumar et al., 2020). The potential application of the well-known medicinal herb *T. cordifolia* in contemporary medicine has been highlighted by recent scientific studies. This review directs attention to the chemical constituents, phytochemical studies, as well as

pharmacological aspects of *T. cordifolia* and its potential for scientific exploration to flourish in the field of natural medicine.

2-Methodology

For this report, scientific literature regarding current advancements in scholarly studies on *T. cordifolia*, inclusive of original articles as well as publications in Google Scholar, Pubmed, Web of Science, Harvard Library, Pubmed, Science Central, Mendeley, Pubmed Central databases, WorldCat, Crossref, Scilit, as well as Cite Factor were collected. Information was extracted from 317 published papers comprising of research, reviews and clinical trials from the last few decades using the keywords *Tinospora cordifolia*, guduchi, amrita, chemical constituents, pharmacological properties, traditional medicine, medicinal plants, and Menispermeaceae. Research articles from the last 13 years are included, the rest of the articles were omitted and this review is written by considering the latest research in this field.

All of the reports of investigations using various animal and human model systems (in vitro, ex vivo, as well as in vivo) were put into the use. For the purpose of this study, reported data was examined and depicted using figures and tables. The chemical structures were drawn using ChemDraw Ultra12.0 Software by Cambridge Soft Life Science Enterprise Solutions and their systemic name, molecular formulas and molecular weight were taken from Pubchem.

3-Plant Description

3.1-Tinospora genus

Tinospora, among the largest genera in the Menispermaceae, with about 15 species. Important classes of medicinal plants include *Tinospora cordifolia*, *Tinopspora malabarica*, *Tinospora tomentosa*, *Tinospora crispa* and *Tinospora uliginosa* (Modi et al., 2020).

3.2-Species

Tinospora cordifolia (wild) is a deciduous rising shrub originating all over India, Sri Lanka, China and Bangladesh(Sajith & Farhan, 2022). The common names in different languages are known as (Saha & Ghosh, 2012)

- Latin: *Tinospora cordifolia*
- English: Gulancha/ Indian tinospora
- Hindi: Giloya, Guduchi
- Bengali: Gulancha
- Tamil: Shindilakodi, seendal
- Telugu: Tippatiga
- Marathi: Dhindilakodi
- Gujrathi: Galo
- Kannada: Amrita balli
- Punjab: Gilo
- Assamese: Amarlata
- Sanskrit: Guduchi, Madhuparni, Vastadaani, Amrita, Tantrika, Chinnaruha, Kundalini & Chakralakshanika

With juicy stems and peppery bark, the enormous, widely-spreading, glabrous, perennial deciduous vine known as tinospora is common in Sri Lanka, India, and Myanmar. *T.cordifolia* is indigenous to India's tropical areas, rising to a height of 500 meters at temperatures between 25^{o} C and 450^{o} C (Singh et al., 2020). It possesses dark green, heart-shaped, and simple leaves. It is also alternating, estipulate, and entire with a broadly elliptical lamina with a length of 10 -12 cm and width of 8-15 cm and has multicoated reticular venation (Doley, 2020). The epidermis is characterized by longitudinal fissure, spanning 3-5

cm in length and 3-8 mm in width, and stem surface looks to be heavily covered with unsmooth tubercle. Large rosette-like lenticels and deep clefts are seen in succulent bark. The bark bears either a grey or creamy white color. The branches sprout long aerial roots that resemble thread. The branches are long and bear either pale greyish brown or filthy white color(Bharathi et al., 2018).

On auxiliary and terminal pyramids, the unisexual, tiny, and greenish-yellow flowers are borne. Female flowers often appear in a solitary inflorescence, while male flowers are grouped. A flower features membranous and oval 6 petals that are separate from each other and of lesser size than the sepals, as well as six sepals that are free and arranged in two series of three each(Gupta, 2019). Fruits mature over the winter (November) while flowers blossoms during the summer (March to June). Fruits have an orange-red color, are juicy, and are grouped into one to three smooth, ovoid droplets on a robust stalk with subterminal scars (Singh et al., 2020). There are curved seeds and embryos seen in tinospora (Modi et al., 2020). Figure 1 shows the different sections of *T. cordifolia's* plant.

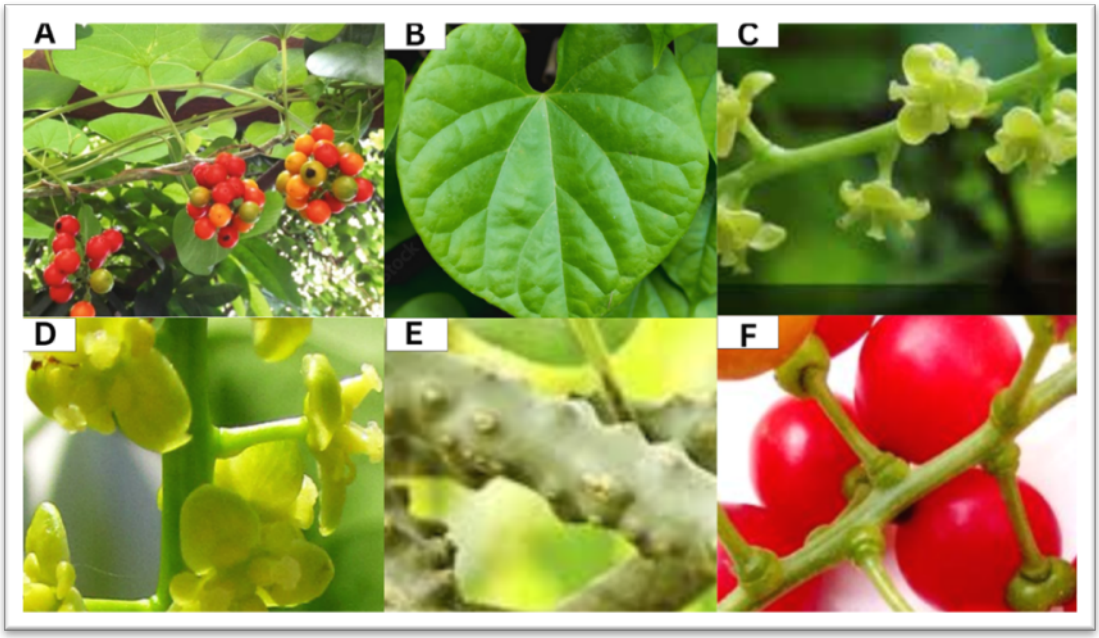


Fig 3.1- Different plant sections of *T. cordifolia's* morphology include **(A)** The entire plant, **(B)** The leaf, **(C)** Inflorescence, **(D)** The Flower, **(E)** The Stem, **(F)** and The Fruit

3.3-Chemical Constituents

The Chemical compounds in *T. cordifolia* are of several types including alkaloids, phenolics, steroids, glycosides, polysaccharides, and aliphatic compounds. Tinospora leaves provide high quantities of minerals (phosphorus as well as calcium) and protein.(Choudhary et al., 2014; Singh & Chaudhuri, 2017) Tinospora stem possesses substances including clerodane furono diterpene glucoside (comprising of amritoside A, B, C, as well as D), also spectroscopic analysis was used to establish the structure of the stem. (Islam et al., 2023; Sharma et al., 2019b).The essential component and active compounds with biological activities and chemical constituents with their chemical structures are depicted in the table 1 and 2.

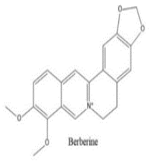
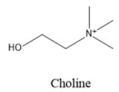
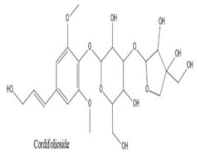
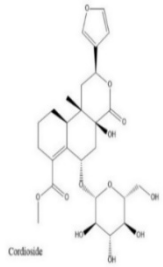
Table 1- Bioactive substances found in various *T. cordifolia* components and their biological effects.

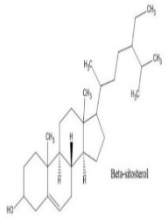
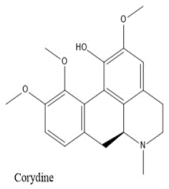
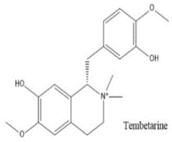
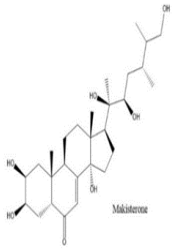
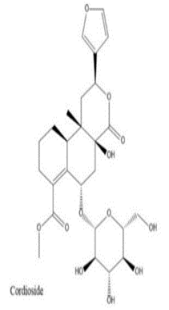
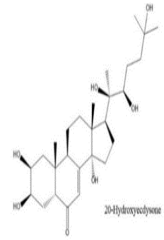
Active compounds	Active constituents	Plant part	Biological actions	References
Alkaloids	Magnoflorine, choline, berberine, palmatine, pyrrolidine, tinosporine, jatrorrhizine, tembeterine, corydine. Tetrahydropalmatine, tinosporine, isocolumbin, aporphine alkaloids, (tinoscorside A, 1 and tinoscorside B 2).	Stem, root	Respiratory tract infections, skin diseases, hypoglycemic activity, anticancer, antiviral, anti-inflammatory, psychiatric conditions, immunomodulatory effect.	[21-22], (Shamsuzzaman & Hasan, 2019; Upadhyay et al., 2010)

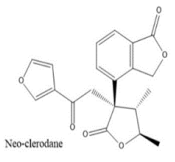
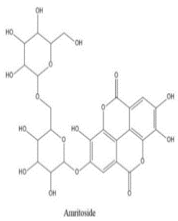
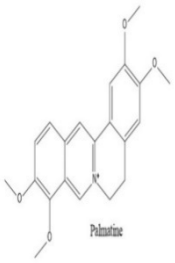
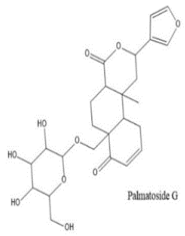
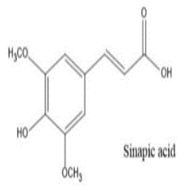
Terpenoids	Tinocodioside, sesquiterpene tinocordifolin, Cordifolioside (A, B, C, D as well as E), poly acetate, coprdioside, tinocordifolin, furanolactone, ecdysterone, furanoid diterpene, Tinosporide, palmatosides C and F, clerodane derivatives {[(5R,10R)-4R-8R-dihydroxy-2S-3R:15,16-diepoxy-cleroda-13(16), 14-dieno-17. 12S: 18,1S-dilactone]}.	Entire plant	Anticancer, Antioxidant properties. anti-inflammatory, and antihypertensive properties, Anti-microbial, vasodilatory effect	(Choudhary et al., 2013; Sinha et al., 2017; Tiwari et al., 2018) (Islam et al., 2023; Sharma et al., 2019b)
Steroids	Giloinsterol, ß-sitosterol, δ-sitosterol, Ecdysterone, hydroxy ecdysone.	Stem, arial parts	Relaxing properties, Antiosteoporotic activity	(Lee et al., 2012; McKeown et al., 2012; Modi et al., 2020; Sharma et al., 2019b)
Polysaccharides	Xylose, Galactose, Glucose, Arabinose, Mannose.	Stem	Analgesic neuroprotective, Antihyperglycemic, Antihyperuricemic, Hypocholesterolemic, Antipyretic, Anticancer, antileprotic	(Gupta et al., 2017; Singh & Chaudhuri, 2017; Upadhyay et al., 2010)
Glycoside	Furanoid diterpene glycoside, Palmatosides, pregnane glycoside, cordioside, cordiofolioside syringin, 18-norclerodane glucoside.	Stem	Neuroprotective activities, Immunomodulatory activities.	(P. Kumar et al., 2020; Pan et al., 2012; M. Pandey et al., 2012; H. Sharma et al., 2021; Singh & Saxena, 2017)

Aliphatic Compounds and Others	Octacosanol, Giloinin, tinosporic acid, jatrorrhizine, nonacason-15-one dichloromethane, N-transferuloyltyramine, cordifol, Giloin, tinosporidine, Heptacosanol, tinosporion acetate, arabinogalactan, Sinapic acid, {[3, (a-4-dihydoxy-3-methoxy-benzyl)-tetrahydrofuran]}.	Entire plant	Anti-inflammatory, Antinociceptive, Antiviral activities	(Choudhary et al., 2013; Naik et al., 2014; Sharma et al., 2019b; Singh & Chaudhuri, 2017; Spandana et al., 2013)

Table 2- Structures of some major chemical constituents of *Tinospora cordifolia***.**

Compound name	IUPAC name	Molecular formula	Molecular weight	Structural formula
Berberine Pubchem ID (2353)	{16,17-(dimethoxy-5,7-dioxa-13-azoniapentacyclo) [11.8.0.02,10.04,8.015,20] henicosa-1(13),2,4(8),9,14,16,18,20-octaene}	C20H18NO4	336.4	
Choline Pubchem ID (305)	2-hydroxyethyl(trimethyl)azanium	C5H14NO	104.17	
Cordifolioside Pubchem ID (75111036)	{4-[3,4-dihydroxy-4-(hydroxymethyl) oxolan-2-yl]} oxy-2-(hydroxymethyl)-6-{[4-(3-hydroxyprop-1-enyl)-2,6-dimethoxyphenoxy] oxane-3,5-diol	C22H32O13	504.5	
Cordioside Pubchem ID (101915817)	(methyl (2S,4aS,6S,10aR,10bS)-2-(furan-3-yl)-4a-hydroxy-10b-methyl-4-oxo-6-[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxy-1,2,5,6,8,9,10,10a-octahydrobenzo[f]isochromene-7-carboxylate)	C26H34O12	538.5	

Beta-Sitosterol Pubchem ID (222284)	[(3S,8S,9S,10R,13R,14S,17R)-17-[(2R,5R)-5-ethyl-6-methylheptan-2-yl]-10,13-dimethyl-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol]	C29H50O	415	
Corydine Pubchem ID (10153)	{(6aS)-2,10,11-trimethoxy-6-methyl-5,6,6a,7-tetrahydro-4H-dibenzo [de, g] quinolin-1-ol}	C20H23NO4	341.4	
Tembetarine Pubchem ID (167718	[(1S)-1-[(3-hydroxy-4-methoxyphenyl) methyl]-6-methoxy-2,2-dimethyl-3,4-dihydro-1H-isoquinolin-2-ium-7-ol]	C20H26NO4	344.4	
Makisterone Pubchem ID (441830)	[(2S,3R,5R,9R,10R,13R,14S,17S)-2,3,14-trihydroxy-10,13-dimethyl-17-[(2R,3R,5R)-2,3,7-trihydroxy-5,6-dimethylheptan-2-yl]-2,3,4,5,9,11,12,15,16,17-decahydro-1H-cyclopenta[a]phenanthren-6-one]	C28H46O7	494.7	
Cordioside Pubchem ID (101915817)	[methyl (2S,4aS,6S,10aR,10bS)-2-(furan-3-yl)-4a-hydroxy-10b-methyl-4-oxo-6-[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxy-1,2,5,6,8,9,10,10a-octahydrobenzo[f]isochromene-7-carboxylate]	C26H34O12	538.5	
20-Hydroxyecdysone Pubchem ID (5459840)	[(2S,3R,5R,9R,10R,13R,14S,17S)-2,3,14-trihydroxy-10,13-dimethyl-17-[(2R,3R)-2,3,6-trihydroxy-6-methylheptan-2-yl]-2,3,4,5,9,11,12,15,16,17-decahydro-1H-cyclopenta[a]phenanthren-6-one]	C27H44O7	481	

Neo-clerodane Pubchem ID (139057371)	{4-[(3R,4S,5R)-3-[2-(furan-3-yl)-2-oxoethyl]-4,5-dimethyl-2-oxooxolan-3-yl]-3H-2-benzofuran-1-one}	C20H18O6	354.4	 Neo-clerodane
Amritoside A Pubchem ID (73981613)	[6,7,14-trihydroxy-13-[3,4,5-trihydroxy-6-[[3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxymethyl] oxan-2-yl] oxy-2,9-dioxatetracyclo [6.6.2.04,16.011,15]hexadeca-1(15),4,6,8(16),11,13-hexaene-3,10-dione]	C26H26O18	626.5	 Amritoside
Palmatine Pubchem ID (19009)	(2,3,9,10-tetramethoxy-5,6-dihydroisoquinolino[2,1-b] isoquinolin-7-ium)	C21H22NO4	352.4	 Palmatine
Palmatoside G Pubchem ID (184515)	[(2S,4aR,6aR,10aS,10bS)-2-(furan-3-yl)-10b-methyl-6a-[[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxymethyl]-2,4a,5,6,10,10a-(hexahydro)-1H-benzo[f]isochromene-4,7-dione]	C25H32O10	492.5	 Palmatoside G
Sinapic acid Pubchem ID (637775)	[(E)-3-(4-hydroxy-3,5-dimethoxyphenyl) prop-2-enoic acid]	C11H12O5	224.21	 Sinapic acid

4-Pharmacological Aspects

T. cordifolia's spasmolytic, allergen-free, and antidiabetic properties have earned its recognition as a most widely used plant in traditional medicine. The herb greatly boost

immunity and possesses a perk of beneficial qualities. The stem of this plant possesses diuretic properties and used as a bitter stomachic, while roots are well recognized for its ability to reduce stress and antimalarial effects. It improves blood quality, promotes biliary secretion, and treats jaundice. The following are some of *T. cordifolia's* main biological functions. The bioactive compounds of *T. cordifolia* with their medicinal effects are mentioned in fig 2.

4.1-Antioxidant Potential

Several extracts as well as formulations of Tinospora demonstrate potent antioxidant potential by neutralizing the harmful effects of free radicals (Alam & Sharma, 2020). (5R, 10R)-4R, 8R-dihydroxy-2S, 3R: 15, 16-diepoxycleroda-13 (16), 17, 12S: 18,1S-dilactone (ECD), a terpene isolated from Tinospora declared to have antioxidant and chemoprotective activity in rats (Dhanasekaran et al., 2009). Various solvents were used for extraction of tinospora and studies were conducted by using Tinospora extract methanol, water and ethanol (Murshid et al., 2022) (Sharma et al., 2019b). Anti-lipid peroxidation potential, Superoxide radical inhibition effects, DPPH antioxidant effect, as well as antioxidant experiments were carried out using several laboratory studies(Preety et al., 2022; Sharma et al., 2019b). The radical quenching potential of the stem extracts from Tinospora, in ethanolic, aqueous, as well as methanolic forms, exhibited effects on lipid peroxidation of erythrocyte membranes, leading to elevated catalase activity. However, methanolic extract of *T. cordifolia* in human showed highest antioxidant activity than other solvents with DPPH at IC50 of 14.18ug/ml (Manne et al., 2021).

Moreover, tinospora extract boosted the activity of an antioxidant enzyme and decreased the number of unstable molecules in diabetic rats (Kannadhasan & Venkataraman, 2013; Upadhyay et al., 2014) . *T. cordifolia* was reported to have effects in growth performance, immunomodulatory response, antioxidant potential and Nile tilapia’s resistance against hypoxia stress.

4.2-Antimicrobial Activity

Tinospora's antimicrobial properties with various solvents were used on different micro-organisms and showed good anti-bacterial, antiviral and antifungal activities (Duraipandiyan et al., 2012). Bioactive compounds such as palmatine and jatrorrhizine extracted from *T. cordifolia* noted to hold antimicrobial properties(Chi et al., 2016).

Anti-bacterial activities: The stem of *T. cordifolia* is renowned to possess high curative efficiency to combat infections resulting from both gram-negative as well as gram-positive bacteria likewise is effective against various bacteria like *Proteus vulgaris*, *Salmonella typhi Serratia marcesenses*, *Staphylococcus aureus Salmonella paratyphi*, *Shigella flexneri*, *Escherichia coli*, *Enterobacter aerogene*, *Klebsiella pneumoniae*, *Salmonella typhimurium* as well as *Pseudomonas aeruginosa* at dose of 500mg/ml in in-vitro study(Paray et al., 2018; Pratihast et al., 2019). The ethanol, acetone and hydrous extract of *T.cordifolia* restrained the actions of urinary pathogens including *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* (Shanthi & Nelson, 2013).

Antifungal activities*: T. cordifolia* extract was reported to possess antifungal activities through agar well plate diffusion technique. The water extract of Tinospora exhibited potential activity against several fungal species such as *Aspergillus fumigatus*, *Aspergillus nigar* and *Aspergillus flavus* (Alrumaihi et al., 2019). Tinospora ethanolic extract at different concentrations showed antifungal activities against *Streptococcus mutans* in agar media for a general-purpose medium, the brain-heart infusion in animal studies. The ethanolic extract of this plant showed area of inhibition 0.2% chlorhexidine as positive and a negative control with dimethylformamide (Agarwal et al., 2019).

Antiviral effect: *T. cordifolia* possesses bioactive compound known as tinosporin possesses viricidal action due to its immunoregulatory potential and differential suppression of the virion to attack helper T lymphocytes, which makes it effective HTLV, HIV, and various other viral infections (Ansary et al., 2020). Tinospora's bioactive compounds namely

tinocordiside, berberine, magnoflorine as well as isocolumbin exhibited IC50 value of <1uM against SARS-COV-2 virus evaluated by computational method.(Sagar & Kumar, 2020)

Antiparasitic Activity: *T. cordifolia* is effective against parasitic infections. *T. cordifolia* alcoholic extract was reported to show highest mortality of 100% with concentration of 100mg/ml against *Gastrothylax crumenifer*(Jogpal et al., 2021). In a single blinded, randomized control clinical study comprising of 66 scabies infected individuals, consumption of *T. cordifolia* lotion for three repeated days over the period of 14 days resulted in a substantial improvement in symptoms of scabies in these individuals. Efficacy of lotion prepared from *T. cordifolia* is as effective as permethrin lotion in reducing the symptoms of scabies(Castillo et al., 2013).

4.3-Hypoglycemic activity

The bioactive compounds that have been identified from tinospora, include flavonoids, steroids, alkaloids, saponins, cardiac glycoside, and tannins, have hypoglycemic properties. As a conclusion, it allows wide applicability in experimental as well as clinical research. Bioactive compounds like alkaloids including palmatine, jatrorrhizine, and magnoflorine from *T. cordifolia* have been claimed to have activities like those of insulin and to be insulin-mediated (R. Sharma et al., 2021). Increased levels of GSH and other reactive species, which increased the risk for baby as well as the mother, can occur as a result of gestational diabetes. *T. cordifolia* has a defensive ability by lowering the oxidative stress, subsequently reducing the risk of illnesses and any kind of birth defect when fed daily to a diabetic rat. Tinospora root extracts decrease blood sugar and urine glucose levels in diabetic rat models while attenuating brain-mediated cholesterol levels, underscoring the plant's anti-diabetic and lipid-lowering action (Dwivedi & Daspaul, 2013; Rani et al., 2023). However, the clinical trials are recommended to evaluate *T. cordifolia* effects on gestational diabetes in humans. *T.*

cordifolia powder is reported to lower blood glucose levels, beta lipoproteins, triglycerides, and total cholesterol at a particular dose of 50mg/kg b.w for 2 weeks(Kumar et al., 2016).

4.4-Antihypertriglyceridemic Activity

Compounds extracted from Tinospora namely tinosporin, tinosporaside as well as polysaccharides have ability to reduce triglyceride (TG) levels. *T. cordifolia* aqueous extract reported to reduce TG levels in twenty individuals with high TG levels more than 499 mg/dl as well as 130-230 mg/dl. Basal parameters remained checked prior and after intervention of TC. Omics analysis revealed that *T. cordifolia* regulate the TG levels by modulating the signaling pathways associated with TG(Shirolkar et al., 2022).

4.5-Anxiolytic Activity

The capability of *T. cordifolia* extract in ethanolic form to alleviate anxiety was investigated. (Gururaja & Joshi, 2022). Isoquinolin alkaloids such as palmatine and berberine work by inhibiting AChE which help reduce stress and anxiety(Arunachalam et al., 2022). *T. cordifolia* ethanolic extract at the concentration of 100mg/kg reported to show remarkable reduction in all stress symptoms comparted to conventional medication diazepam (2.5mg/kg) (Sharma et al., 2019b). The plant extract results in mild behavioral problems and mental deficits. Various clinical studies showed that it also increased I.Q. levels. Due to its abilities to enhance memory and recall, tinospora serves as brain tonic (Baghel, 2017).

4.6-Antihyperlipidemic Activity

T. cordifolia also regulate lipid profile levels. Diterpenoids and diterpene glycoside such as such as tinosporin and tinosporaside are shown to have hypolipidemic effects(Ahsan et al., 2023). Hyperlipidaemic rats treated with *T.cordifolia* extract exhibited a remarkable decrease

in LDL (bad cholesterol), VLDL, and triglycerides in their lipid profile however it showed an improvement in HDL levels (Rathi & Balasubramanian, 2018).

4.7-Antiosteoporotic activity

Indian ethnomedicine holds great history for Tinospora consumption in the management of gout and bone discontinuity. The steroid such as 20-hydroxy- β ecdysone exhibited antiosteoporotic effects and used for treatment of osteoarthritis and osteoporosis(Sharma et al., 2019a).

The impact of *T. cordifolia* extract on osteoblastic bone cells was assessed with cytopathological analysis by haematoxylin/eosin staining, Sirius red staining, osteocalcin quantification, and semiquantitative PCR (RT-PCR). The bone was analysed histopathologically (Hematoxylin/Eosin staining), biochemically (markers of bone production and resorption), radiologically (DEXA analysis), and histomorphometrically.
extract improved. The collagen synthesis, osteogenic gene expression and osteocalcin levels—all of which are favourable signs of osteoblastogenesis were increased by administering *T. cordifolia* extract. Treatment with *T. cordifolia* extract did not impact the proliferation of osteoclast(Abiramasundari et al., 2017).

4.8-Anti-HIV Activity

T. cordifolia has long been investigated for its potential to treat HIV affected individuals by enhancing the patient's responsiveness to medications related top retrovirus. *T. cordifolia's* anti-HIV actions are due to alkaloids and terpenoids which manage the illness by raising CD4 T-cell counts and lowering eosinophil counts in HIV-positive individuals. Significantly increased intracellular and phagocytic bactericidal activity was demonstrated by *T. cordifolia* extract. *T. cordifolia* similarly stimulated peritoneal macrophage. Significant amounts of

macrophages, polymorph nuclear leucocytes, and B lymphocytes are stimulated by *T. cordifolia* (Gupta et al., 2010; Patel et al., 2013; Sajith & Farhan, 2022). The toxicity study of crude extract of *T. cordifolia* with different solvents on peripheral mononuclear blood cells (PBMCs) were evaluated. The values of n-hexane and n-butanol extract of *T. cordifolia* range from 5.7 to 12.0 g/ml against PBMCs and moderate cytotoxic effects were observed. (Tiwari et al., 2018)

4.9-Anticancer Activity

The anti-cancer properties of the herb tinospora have been demonstrated using a variety of experimental animal models (Selvam et al.). A rise in the level of glutathione (GSH) along with other metabolising enzymes was observed in liver and extra hepatic organs of mice subjected to the hydroalcoholic root extract of Tinospora at 50 as well as 100 mg/kg b.w. Malonaldehyde (MLD) synthesis has also significantly decreased, indicating a decrease in the synthesis of unstable molecules and keep cell in an antioxidative state (Tiwari et al., 2018). Aqueous (TCA) fraction, ethanol extract (TCE), n-Butanol (TCB), dichloromethane (TCD) as well as petroleum ether (TCP) extract of Tinospora were reported to possess radical scavenging and antiproliferative potential. The total flavonoids, phenolic compound and antioxidant content was assessed using a variety of methods. To assess the anti-proliferative potential on cervical carcinoma (HeLa) cell lines, MTT and SRB tests were performed showing that *T. cordifolia* have anti proliferative effects (Polu et al., 2017). Berberine from *T. cordifolia*, inhibits the proliferation, differentiation, signaling pathways, and epithelial-mesenchymal transition of tumor cells. The 33 genes involved in human adenocarcinoma cells of the colon were found to be downregulated by berberine in *T.cordifolia*, according to the findings(Palmieri et al., 2019). Ethanolic or aqueous extract of *T.cordifolia* also showed anticancer effects on human neuroblastoma cells(Mishra & Kaur, 2015).

4.10-Hepatoprotective Activity

Ayurvedic medicine has traditionally employed *T. cordifolia* to treat a variety of illnesses. In an investigation, rats treated with thioacetamide (TAA) and cultured rat hepatocytes were used as test subjects for radical scavenging and liver protective properties of ethanolic extract of leaves of *T. cordifolia*. The TC extract revealed no obvious cytotoxic effect on cultured hepatocytes at IC_{50}≤500 µg/mL (subsequent to 48 hours) according to the MTT (cell viability assay) assay. The animal studies showed that the Tinospora extract considerably (P value 0.05) controlled the rise in liver enzyme namely aminotransferase as well as TAA-treated rats (at dosages 100 mg/kg body weight)(Hussien et al., 2023). Epoxy clerodane diterpene and compounds with antioxidant properties such as triterpenes, phenolics, lipids, glycosides, and organic acids flavonoids, and alkaloids, show hepatoprotective activities (Parthasarathy & Evan Prince, 2021).According to another research performed to evaluate the hepatoprotective effects of *T. cordifolia*, administration of TCME orally showed the restoration of biochemical and histological alteration to normal levels. Rats exposed to Cd also showed greater levels of protein carbonyl content and lipid peroxidation (LPO) in their liver tissues, as well as higher levels of the blood indicators AST and ALT indicating liver damage. TCME co-treatment nearly reinstated the biological and histological variations brought on by Cd intoxication (Baskaran et al., 2018).

4.11-Antithrombotic Activity

Diterpenoid lactones such as Tinosporide, tinosporaside and cordifolide are shown to have anti thrombotic activities which work by interfering with arachidonic acid pathway and inhibiting thrombus formation and platelet aggregation(Ahsan et al., 2023). In a research, platelet binding on a collagen-coated surface, thrombin inhibition test, thrombin generation assay, as well flow cytometry detection of platelet PAC1-FITC binding were all performed

and used to measure antithrombotic activity. SXME considerably reduced thrombin activity at doses of 5–20 mg/ml, but TCME dramatically reduced thrombin activity at values of 500ug/ml–5 mg/ml. Additionally, thrombin production was suppressed by SXME at doses between 2 and 20 mg/ml whereas it was significantly inhibited by TCME at 200 g/ml, indicating that TCME is more effective than SXME. Additionally, SXME did not prevent platelet adherence to a collagen-coated surface, but TCME did so at a concentration of 5 mg/ml. At 300 uM, indomethacin significantly inhibited platelet adhesion. SXME substantially reduced thrombin-induced activation of platelets (PAC1-FITC binding) nearly 80% with a dosage of 1 mg/ml, but TCME significantly suppresses platelet activation in response to thrombin (PAC1-FITC binding) by around forty percent. These findings made it clear that SXME and TCME had antithrombotic properties. To determine the chemical that is active and responsible for the antithrombotic action, more study is required (Lugun et al., 2018).

4.12-Neuroprotective Effect

Alzheimer's disease as well as Parkinson's disease are neuronal degenerative disorders impacting central nervous system that are triggered by oxidative stress and neuroinflammation. Diterpenoids, flavonoids, polysaccharides and other compound with antioxidant properties are proven to mitigate the risk of neurodegenerative disorders (Bhalodi & Kothari, 2023). *T.cordifolia* aqueous extract (200mg/kg b.w for 2 weeks) is known to have potential to reduce neural inflammation in (MPTP) tempted parkinsonism affected mouse(Birla et al., 2019). A biochemical compound isolated from the endophytic fungus of this medicinal plant known as G15 exhibited highest ACHE inhibition activity which help reduce the symptoms of Alzheimer's disease(Vig et al., 2022).

4.13-Antiallergic Activity

Bioactive compounds such as alkaloids and diterpenoids isolated from *T. cordifolia* exhibit beneficial effects against allergic reactions. Clinical studies revealed that *T. cordifolia* extract (300mg/kg for 8 weeks) significantly calmed sneezing in eighty three percent of individuals, pruritic nose in 71%, rhinorrhoea in 69% as well as obstructed nasal passage in 61% individual. While in case of placebo group, there is no remarkable improvement in symptoms of allergic rhinitis(Badar et al., 2005).

4.14-Immunomodulatory Activity

The Indian ayurvedic and traditional medicine systems widely used the *T. cordifolia* plant for its therapeutic properties. However, further experimental data will be helpful to demonstrate its efficacy for clinical use. Numerous pharmacological investigations have shown that *T. cordifolia* modifies important signalling pathways involved in immune regulation, inflammation, and cell proliferation(Yates et al., 2022). The immunoregulatory potential of alcohol-based extract derived from Tinospora stem were assessed in a study employing diverse experimental models, comprising neutrophil adhesion test, the phagocytic index by carbon clearance test, the titre of hemagglutinating antibodies (HA), and delayed type hypersensitivity (DTH) responses. Alcoholic stem extract of *T. cordifolia* was consumed at dosages of 50, 100, 200, and 300mg/kg, and this had a notable impact on the percentage of neutrophils adhering to nylon fibres, antibody titre values, and hypersensitivity responses. This may be because of a particular plant extract having a lot of active phytochemicals. As a conclusion, it was shown that the plant extracts improved both humoral and cell-mediated immunity (Yates et al., 2022). Bioactive compounds like alkaloids, phenyl propanoides like cordifolioside A and B, N-methyl-2-pyrrolidone, magnoflorine, 11,hydroxymuskatone, Nformylannonain, cordioside, synirgin, and caordia, and arabinogalactan and enzyme thiol amylase are considered responsible for immunoregulatory potential of *T.cordifolia* (Ansary et

al., 2020). It is reported that sesquiterpenoid glycoside, also known as tinocordiside, possesses immunity enhancing activities (Yates et al., 2022). *T. cordifolia* polysaccharide component significantly decreased the ability of B16F-10 melanocytes to spread because of its radical quenching activity against superoxide radicals and DPPH. G1-4A, an arabinogalactan-based polysaccharide derived from Tinospora stimulated immature bone marrow as well as spleen derived dendritic cells to mature via modifying cytokines, costimulatory molecules, and other molecules. As a result, clonal expression along with antigen-specific-directed T cell development enabled adaptive immunity. Galactose (32%), galacturonic acid (35%) and arabinoside (31%) are all present in G1-4A(V. K. Pandey et al., 2012). Encompassing concentrations between 0-1000 ug/mL, an alternate polysaccharide (1-4)-D-glucan extracted from *T. cordifolia* known as RR1, displayed exceptional immune modulating capabilities for being not proliferating and not cytotoxic to normal in addition to tumour cultured cells (Aranha et al., 2012). *T. cordifolia* shown immunity-boosting properties in a clinical experiment that was open-labelled, randomised, and placebo-controlled. *T. cordifolia* (100 mg/kg body weight) and placebo were administered to 400 kids between the ages of 1 and 15 in various groups. The TLC, lymphocyte count, and absolute lymphocyte count (ALC) all showed substantial improvements, and infections were also significantly reduced (Sharma & Sharma, 2015). Bioactive compounds of tinospora cordifolia with their medicinal effects are depicted in fig 2.

ISSN:1624-1940
http://magellanes.com/

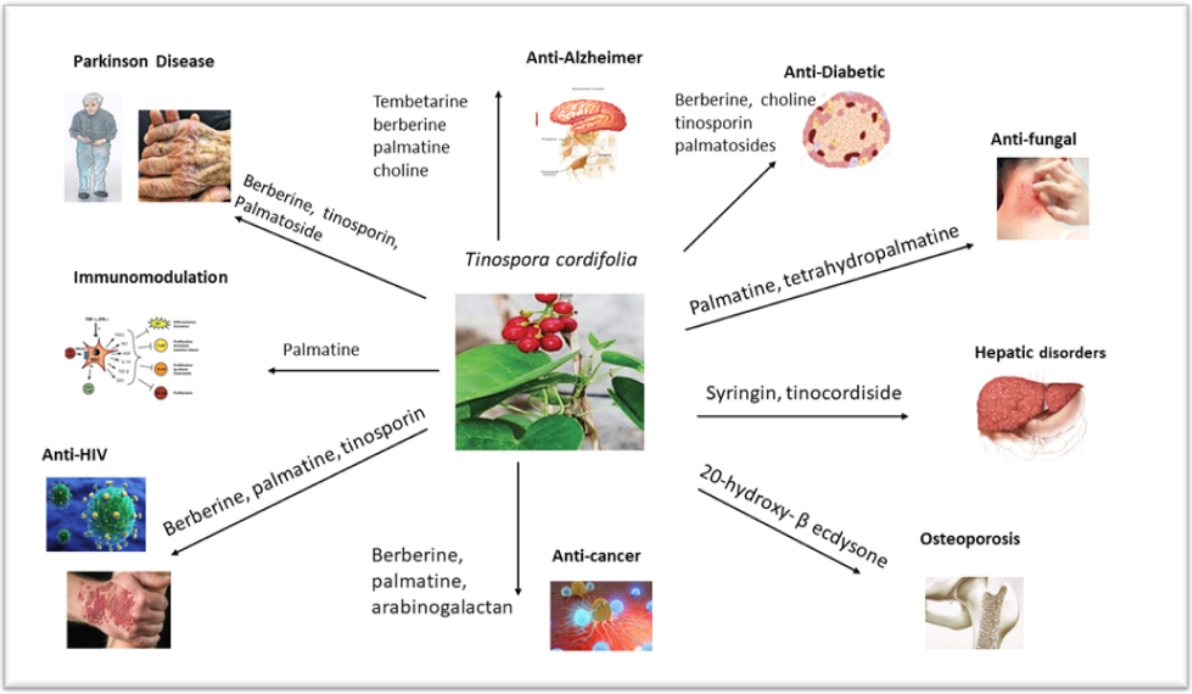


Fig 3- Schematic representation of bioactive compounds of *T. cordifolia* with their medicinal effects.

Table 3: In-vitro pharmacological aspects, in-vivo studies and clinical trials are given in table.

Pharmacological Aspects	Part Used	Key Findings	Evidence
Antioxidant activity	*T. cordifolia* extract	Strong antioxidant potential and inhibition concentration IC50 of 50g/ml	In-Vitro
	Diet incorporating *T. cordifolia*	Increased antioxidant enzyme and decrease the no. of unstable molecule.	In-vivo/ albino rats
	T. cordifolia extract	Improved antioxidative response, growth performance in Nile tilapia.	In-vivo/ fish
Antibacterial activity	Ethanol, acetone, and aqueous extract	T. cordifolia exhibited efficacy in combating various gram negative and positive bacteria.	In-Vitro
	Silver nanoparticles	Exhibited activity against urinary pathogens	In-Vitro
	Aq. Silver nano particles	The zone of inhibition falls between 10 ± 0.58 to 21 ± 0.25mm was observed with silver nano particle (6.25-200	clinical trial

		ug/ml) in combating *Pseudomonas aeruginosa* strains	
Antifungal activity	Ethanolic and hydrous extract	Exhibited antifungal potential in combating *Aspergillus fumigatus*, *Aspergillus nigar* as well as *Aspergillus flavus.* (Agar well plate diffusion technique)	in-vitro
	Whole plant extract	Oral administration of different dosages of TCAE (10, 25 and 50mg/kg) showed antifungal activity against Aspergillus fumigatus	in-vivo /mice
Antiviral activity	Whole plant extract	A diterpenoid present in *T. cordifolia,* Tinosporin showed antiviral action due to its immunoregulatory potential and specific suppression of the virion to attack helper T lymphocytes, which makes it effective against HTLV, HIV, and various other viral infections	in-vitro
Antiparasitic activity	Tinospora infused lotion	Application of Tinospora-infused lotion for 3 consecutive days over a course of two weeks resulted in significant improvement in scabies symptoms	clinical trial
Antihyperglycemic activity	*T. cordifolia* extract	The TCLF-1 and TCLF-2 ethyl acetate and n-butanol fractions of *T. cordifolia* showed significant antioxidant and anti-diabetic efficacy	in-vitro
	Root extract of plant	Decrease blood sugar and urine glucose levels in diabetic rat models, reduced risk of birth defects in diabetic rat was also observed	In-vivo/rats
	Tinospora powder	Applying Tinospora powder at dose of 50mg/kg for 15 days showed a remarkable decrease in FBG levels, beta lipoproteins, TG as well as TC levels	clinical trial
	Aqu. Ext of stem	A substantial reduction in SGPT, γ GT, SGOT, and MCV ($p< 0.01$) was observed by administration of 0.5g/kg b.w of TCAE for 2 weeks. TC, TGL were reduced and HDL level raised	clinical trial
Anxiolytic activity	Alcoholic extract	reduced stress symptoms and improved brain health	In-vivo/rats
Antihyperlipidemic activity	whole plant extract	remarkable decrease in LDL, TG, total cholesterol, and increase HDL	In-vivo/rats
Antihypertriglyceridemic activity	Aqueous extract	decreased TG and LDL levels through modulation of signaling pathways.	clinical trial
	Aqueous extract	Increased GSH and decrease in MDA along with uric acid level, decreased SLP, AST/ALT, TG and LDL level	clinical trial
Antiosteoporotic activity	whole plant extract	Improved collagen synthesis, osteogenic gene expression and regulate osteocalcin levels	In-vivo/rats

	Tinospora powder	Bone pain, stability and movement was improved with *T. cordifolia* capsule for 70 days	clinical trial
Anti-HIV activity	Whole plant extract	Lowered patient's resistance by raising CD4-T cells and decreasing eosinophil count	clinical trial
	Tinospora powder	improved clinical and biochemical responses to ART as well as recurrent HIV virus resistance to ART	clinical trial
Anticancer activity	whole plant extract	*T. cordifolia* root extract showed antitumor potential	In-vivo/rats
	Whole plant extract	Exhibited antiproliferation potential in combating IMR-32 human neuroblastic tumor cells	clinical trial
	Aqueous extract	inhibits the spread, divergence, signaling pathways, and epithelial-mesenchymal transition of adenocarcinoma cells of colon	clinical trial
Hepatoprotective activity	Ethanolic extract	Controlled the rise in plasma aminotransferases in TAA-treated rats	In-vivo/rats
Neuroprotective activity	Aqueous extract	Reduced inflammation in parkinsonian mice. Fungal isolate (G15) from T. cordifolia exhibited highest ACHE inhibition activity and reduce the symptoms of AD	in-vivo/mice
Immunomodulatory activity	Stemic extract	improved humoral and cell-mediated immunity	in-vivo/rats
	Tinospora powder	Administration of *T. cordifolia* powder in 400 kids at the dose of 100mg/kg increased TLC, ALC and LC levels.	clinical trial
	Whole plant extract	Hb percentage was significantly reduced and reduction was also observed in neutrophil as well as eosinophil levels post 6 months consumption	clinical trial
Antiallergic activity	Whole plant extract	TCAE at 300mg/kg for 8 weeks significantly alleviated sneezing in 83 percent individuals, pruritic nose in 71%, runny nose in 69% and obstruction of nose in 61% individuals.	clinical trial

T. cordifolia products available in market

There is a variety of products available in the market that contain T. cordifolia which play an important role in promoting overall health and combating illness. Giloy can be found in several forms including powder, syrup, tablets, juices and more. These products assist in strengthening the immune system and curing a variety of diseases. Dabur, Patanjali,

Baidyanath, and Himalaya are some of the renowned companies that provide giloy products used to relieve the symptoms of asthma, bronchitis, diarrhea, viral fever and common cold.

Table 4: T. cordifolia containing products in Market

Products name	**Brand name**	**Benefits**
Giloy Ghanvati tablets	Patanjali	Strengthen heart, support immunity, regulate blood sugar and relieve stress and anxiety
Brave-Heart Capsules	Brave-heart	Improve cardiac function, regulate blood pressure, lower cholesterol
Giloy Capsules	Zandu	Support liver health, improve digestive health and normalize blood sugar levels
Cirrholiv-ds Syrup	Paul medicos	Promote liver health and boost immunity
Giloy Ghan-vati	Dabur	Help in digestion and support immune health
Guduchi Ghrita	Guduchi	Boost skin health and treat Gout
Guduchi Churna	Baidyanath	Provide antioxidant support, treat malaria, swine flu and dengue, treat diabetes and improve skin health
Immuniveda Chyawanprash	Saffola	Improve respiratory health, boost energy and Vigor
Guduchi sattva	DAV Pharmacy	Effective in fever, cough, diabetes, calm burning sensation, improve liver health
Giloy juice	Kapiva	Treat fever, jaundice, gout, detoxify toxins, improve skin health
Madhu mehari	Baidyanath	Help reduce fatigue, regulate blood and urine sugar levels

5-Toxicity of *T. cordifolia*

According to Ayurvedic system, *T. cordifolia* can be used as being secure remedy, however chronic consumption of elevated doses has been associated with constipation. On its toxicity, there is no information. (Chopra et al., 2012). Swiss albino mice were used in a study to assess *T. cordifolia* for toxicity. The high dosage levels for decoction used were 9 mL/kg and for the entire plant powder was 8 g/kg. The findings revealed no demise, in addition an LD50 level was shown to surpass 1g/kg when administered orally in healthy animals devoid of impairing gastrointestinal movement.(Gautam et al., 2020). Another research by Agarwal et al. found that consumption of 3g/kg dosage of *T. cordifolia* exhibited no negative effects in animals. (Alrumaihi et al., 2019). *T. cordifolia* was administered to healthy volunteers in the early stage I experiment, and it validated its safety. As far as the toxicity studies on several animal experimental models as well as frequent utilization by professional are concerned, *T.cordifolia* is honoured as being risk free herbal treatment (Shaikh et al., 2020).

6-Discussion

T. cordifolia is a medical plant that has been well discovered in the field of biological effects of various extracts, fractions, and constituents through the measurement of biological components from many fields of study. In toxicological research, the bioactive compounds were studied in both laboratory and animal models to evaluate the biological effects of crude extract and different formulations. Moreover, bioactive compounds present in *T. cordifolia* also showed therapeutic effects against parasitic infections, hyperglycaemia, hypertriglyceridemia, cancer, HIV, and allergies. Its pharmacological effects are caused by a diversity of biological substances, comprising of glycosides, sesquiterpenoids, steroids, and alkaloids making it a crucial component of natural medicines and preparations. These

bioactive compounds extracted from *T. cordifolia* possess antidiabetic, antioxidant, immunomodulatory, antitumor, and antimicrobial activities and can be utilized to relieve a wide range of diseases either alone or with standardized form. The pharmacological studies and clinical research of Tinospora plant revealed its remarkable therapeutic potential and safety as a dietetic supplement. Furthermore, bioactive chemicals including steroids, sesquiterpenoids, glycosides and alkaloids present in *T. cordifolia* make it an essential component of natural medicine. These bioactive compounds obtained from *T. cordifolia* possess hypoglycemic, radical scavenging, immunoregulatory and antineoplastic properties and can be used for treating a variety of diseases. This review study applied to both clinical and future research projects for the development of new formulation and medicines. Further research is needed to better understand its pharmacological properties and to develop effective and safe formulations for various conditions. Additionally, studies should be conducted to further explore the efficacy of *T. cordifolia* for the management of various diseases. Future developments will need for detailed study of plant cultured tissue utilizing cutting-edge biotechnological tools like genomes as well as proteomics, empowering for efficient disease cantered approach.

7-Conclusion

T. cordifolia is a therapeutic plant comprised of a wide range of biological compounds. Steroids, alkaloids, sesquiterpenoids, glycosides, and other bioactive substances have all been explored. This anti-HIV potential, review highlights the antimicrobial, antifungal, hypolipidemic, antioxidant, antibacterial, hepatic disorder, wound-healing, anticancer, immunomodulating, antiosteoporotic, systemic infections, antitoxic, and Parkinson's disease properties of *T. cordifolia*. Since the beginning of Ayurvedic medicine, it has been effectively utilized, and its products have been employed for better financial and therapeutic usage. In this context, further research should be conducted to examine *T. cordifolia's* potential for prevention and treatment of illnesses.

Declaration of interest

We declare that there is no conflict found in this study.

Funding

No funding was received for this study.

Data availability

No additional data available for this paper.

Acknowledgement

Authors are very grateful to the University College of Conventional Medicine, The Islamia University of Bahawalpur for moral support for the completion of this study.

References

Abiramasundari, G., Gowda, C. M., Pampapathi, G., Praveen, S., Shivamurugan, S., Vijaykumar, M., Devi, A., & Sreepriya, M. (2017). Ethnomedicine based evaluation of osteoprotective properties of Tinospora cordifolia on in vitro and in vivo model systems. *Biomedicine & Pharmacotherapy*, *87*, 342-354.

Agarwal, S., Ramamurthy, P. H., Fernandes, B., Rath, A., & Sidhu, P. (2019). Assessment of antimicrobial activity of different concentrations of Tinospora cordifolia against Streptococcus mutans: An in vitro study. *Dental research journal*, *16*(1), 24.

Ahsan, R., Mishra, A., Badar, B., Owais, M., & Mishra, V. (2023). Therapeutic Application, Phytoactives and Pharmacology of Tinospora cordifolia: An Evocative Review. *Chinese Journal of Integrative Medicine*, *29*(6), 549-555.

Alam, N., & Sharma, K. (2020). Estimation of phenolic content, flavonoid content, antioxidant, and alpha-amylase inhibitory activity of some selected plants from Siraha district Nepal. *Asian J Pharm Clin Res*, *13*(4), 18-23.

Alrumaihi, F., Allemailem, K. S., Almatroudi, A., Alsahli, M. A., Khan, A., & Khan, M. A. (2019). Tinospora cordifolia aqueous extract alleviates cyclophosphamide-induced immune suppression, toxicity and systemic candidiasis in immunosuppressed mice: in vivo study in comparison to antifungal drug fluconazole. *Current Pharmaceutical Biotechnology*, *20*(12), 1055-1063.

Ansary, P., Sasidharan, A. K., & Sethu, R. (2020). A CRITICAL REVIEW ON THE ANTIVIRAL AND IMMUNOMODULATORY ACTIVITIES OF IMPORTANT AYURVEDIC DRUGS. *Kerala Journal of Ayurveda*, *5*(1), 9-17.

Aranha, I., Clement, F., & Venkatesh, Y. P. (2012). Immunostimulatory properties of the major protein from the stem of the Ayurvedic medicinal herb, guduchi (Tinospora cordifolia). *Journal of ethnopharmacology*, *139*(2), 366-372.

Arunachalam, K., Yang, X., & San, T. T. (2022). Tinospora cordifolia (Willd.) Miers: Protection mechanisms and strategies against oxidative stress-related diseases. *Journal of ethnopharmacology*, *283*, 114540.

Badar, V., Thawani, V., Wakode, P., Shrivastava, M., Gharpure, K., Hingorani, L., & Khiyani, R. (2005). Efficacy of Tinospora cordifolia in allergic rhinitis. *Journal of ethnopharmacology*, *96*(3), 445-449.

Baghel, P. (2017). Plant of versatile properties: A review of Tinospora Cordifolia (Guduchi). *International Journal of Agriculture Innovations and Research*, *5*(5), 2319-1473.

Bajaj, P., & Kaur, G. (2022). Acute Sleep Deprivation-Induced Anxiety and Disruption of Hypothalamic Cell Survival and Plasticity: A Mechanistic Study of Protection by Butanol Extract of Tinospora cordifolia. *Neurochemical Research*, *47*(6), 1692-1706.

Baskaran, R., Priya, L. B., Kumar, V. S., & Padma, V. V. (2018). Tinospora cordifolia extract prevents cadmium-induced oxidative stress and hepatotoxicity in experimental rats. *Journal of Ayurveda and integrative medicine*, *9*(4), 252-257.

Bhalodi, K., & Kothari, C. S. (2023). Tinospora cordifolia: A New Perspective on Alzheimer's Disease and Green Nanotechnology. *The Natural Products Journal*, *13*(2), 26-39.

Bharathi, C., Reddy, A. H., Nageswari, G., Lakshmi, B. S., Soumya, M., Vanisri, D., & Venkatappa, B. (2018). A review on medicinal properties of Tinospora cordifolia. *International Journal of Scientific Research and Review*, *7*(12), 585-598.

Bijauliya, R. K., Alok, S., Kumar, M., Chanchal, D. K., & Yadav, S. (2017). A comprehensive review on herbal cosmetics. *International Journal of Pharmaceutical Sciences and Research*, *8*(12), 4930-4949.

Birla, H., Rai, S. N., Singh, S. S., Zahra, W., Rawat, A., Tiwari, N., Singh, R. K., Pathak, A., & Singh, S. P. (2019). Tinospora cordifolia Suppresses Neuroinflammation in Parkinsonian Mouse Model. *NeuroMolecular Medicine*, *21*(1), 42-53. https://doi.org/10.1007/s12017-018-08521-7

Castillo, A. L., Osi, M. O., Ramos, J. D. A., De Francia, J. L., Dujunco, M. U., & Quilala, P. F. (2013). Efficacy and safety of Tinospora cordifolia lotion in Sarcoptes scabiei var hominis-infected pediatric patients: A single blind, randomized controlled trial. *Journal of pharmacology and pharmacotherapeutics*, *4*(1), 39-46.

Chi, S., She, G., Han, D., Wang, W., Liu, Z., & Liu, B. (2016). Genus Tinospora: ethnopharmacology, phytochemistry, and pharmacology. *Evidence-Based Complementary and Alternative Medicine*, *2016*.

Chopra, A., Saluja, M., Tillu, G., Venugopalan, A., Narsimulu, G., Sarmukaddam, S., & Patwardhan, B. (2012). Evaluating higher doses of Shunthi-Guduchi formulations for safety in treatment of osteoarthritis knees: A Government of India NMITLI arthritis project. *Journal of Ayurveda and integrative medicine*, *3*(1), 38.

Choudhary, N., Siddiqui, M., Azmat, S., & Khatoon, S. (2013). Tinospora cordifolia: ethnobotany, phytopharmacology and phytochemistry aspects. *International Journal of Pharmaceutical Sciences and Research*, *4*(3), 891.

Choudhary, N., Siddiqui, M., & Khatoon, S. (2014). Pharmacognostic evaluation of Tinospora cordifolia (Willd.) Miers and identification of biomarkers.

Dhanasekaran, M., Baskar, A.-A., Ignacimuthu, S., Agastian, P., & Duraipandiyan, V. (2009). Chemopreventive potential of Epoxy clerodane diterpene from Tinospora cordifolia against diethylnitrosamine-induced hepatocellular carcinoma. *Investigational new drugs*, *27*, 347-355.

Doley, P. (2020). Chapter-7 Giloy: The Green Genie. *Chief Editor*, 107.

Duraipandiyan, V., Ignacimuthu, S., Balakrishna, K., & AL-Harbi, N. A. (2012). Antimicrobial activity of Tinospora cordifolia: an ethnomedicinal plant. *□洲□□医□*, *7*(2), 59-65.

Dwivedi, C., & Daspaul, S. (2013). Antidiabetic herbal drugs and polyherbal formulation used for diabetes: A review. *J Phytopharmacol*, *2*(3), 44-51.

El Basuini, M. F., Teiba, I. I., Shahin, S. A., Mourad, M. M., Zaki, M. A., Labib, E. M., Azra, M. N., Sewilam, H., El-Dakroury, M., & Dawood, M. A. (2022). Dietary Guduchi (Tinospora cordifolia) enhanced the growth performance, antioxidative capacity, immune response and ameliorated stress-related markers induced by hypoxia stress in Nile tilapia (Oreochromis niloticus). *Fish & shellfish immunology*, *120*, 337-344.

Gautam, A., Kaur, H., Kaur, A., Prashar, P. K., Sood, A., Singh, S. K., Gulati, M., Pandey, N. K., & Kumar, B. (2020). Tinospora cordifolia: A Successful Story from Botanical background to Pharmaceutical Product. *Research Journal of Pharmacy and Technology*, *13*(11), 5620-5630.

George, M., Josepha, L., & Mathew, M. (2016). A research on screening of learning and memory enhancing the activity of whole plant extract of Tinospora cordifolia (Willd). *Pharma Innovation*, *5*, 104-107.

Gupta, G., Sujatha, N., Dhanik, A., & Rai, N. (2010). Clinical evaluation of Shilajatu Rasayana in patients with HIV infection. *Ayu*, *31*(1), 28.

Gupta, P. (2019). A review on therapeutic multipurpose medicinal use of Tinospora cordifolia. *IJTSRD*.

Gupta, P. K., Rajan, M., & Kulkarni, S. (2017). Activation of murine macrophages by G1-4A, a polysaccharide from Tinospora cordifolia, in TLR4/MyD88 dependent manner. *International immunopharmacology*, *50*, 168-177.

Gururaja, M., & Joshi, H. (2022). Evaluation of Anti-anxiety Potential of Tinospora cordifolia (Willd.) Leaf Extract in Mice Using Experimental Models. *Journal of Young Pharmacists*, *14*(1), 46.

Habbu, P. V., Madagundi, S. D., & Kulkarni, V. H. (2021). Antioxidant and Antidiabetic Potential of Endophytic Fungal Fractions Recovered from Tinospora Cordifolia (Willd.) Leaves. *RGUHS Journal of Pharmaceutical Sciences*, *11*(2).

Hussien, H. T., Tag, H. M., Ahmed, E., Nabil, Z. I., & El-Naggar, M. S. (2022). THE ANTIOXIDANT AND HEPATOPROTECTIVE ACTIVITIES OF THE ETHANOLIC EXTRACT OF TINOSPORA CORDIFOLIA LEAVES: IN VITRO AND IN VIVO STUDIES. *Egyptian Journal of Zoology*(Articles in Press).

Hussien, H. T., Tag, H. M., Ahmed, E., Nabil, Z. I., & El-Naggar, M. S. (2023). THE ANTIOXIDANT AND HEPATOPROTECTIVE ACTIVITIES OF THE ETHANOLIC EXTRACT OF TINOSPORA CORDIFOLIA LEAVES: IN VITRO AND IN VIVO STUDIES. *Egyptian Journal of Zoology*, *79*(79), 48-65.

Islam, A., Singh, H., & Sharma, A. (2023). Impact of Regional Quality Assessment of Tinospora cordifolia: A Scientific Perspective for Exploration of Harvest Strategy as a Quality Marker. *Agricultural Research*, 1-8.

Jamshidi-Kia, F., Lorigooini, Z., & Amini-Khoei, H. (2017). Medicinal plants: Past history and future perspective. *Journal of herbmed pharmacology*, *7*(1), 1-7.

Jogpal, B., Swarnakar, G., Chouhan, H. S., & Roat, K. (2021). In vitro anthelmintic activity of medicinal plant Tinospora cordifolia extract on amphistome Gastrothylax crumenifer. *Ecology. Environment and Conservation*, *27*, 231-234.

Kalikar, M., Thawani, V., Varadpande, U., Sontakke, S., Singh, R., & Khiyani, R. (2008). Immunomodulatory effect of Tinospora cordifolia extract in human immuno-deficiency virus positive patients. *Indian Journal of Pharmacology*, *40*(3), 107.

Kannadhasan, R., & Venkataraman, S. (2013). In vitro capacity and in vivo antioxidant potency of sedimental extract of Tinospora cordifolia in streptozotocin induced type 2 diabetes. *Avicenna Journal of Phytomedicine*, *3*(1), 7.

Khan, M. A. (2019). Tinospora cordifolia aqueous extract ameliorates the systemic infection of aspergillus fumigatus in balb/c mice. *Asian J Pharm Clin Res*, *12*(3), 525-528.

Kumar, B., Bajpai, V., & Kumar, N. (2020). *Phytochemistry of Tinospora cordifolia*. CRC Press.

Kumar, N., Kumar, G., Prabhakar, P. K., Sahu, J. K., & Naik, S. (2023). Ultrasound-assisted extraction of bioactive compounds from giloy (Tinospora cordifolia) stem: Quantitative process optimization and bioactives analysis. *Journal of Food Process Engineering*, e14259.

Kumar, P., Kamle, M., Mahato, D. K., Bora, H., Sharma, B., Rasane, P., & Bajpai, V. K. (2020). Tinospora cordifolia (Giloy): phytochemistry, ethnopharmacology, clinical application and conservation strategies. *Current Pharmaceutical Biotechnology*, *21*(12), 1165-1175.

Kumar, V., Mahdi, F., Singh, R., Mahdi, A. A., & Singh, R. K. (2016). A clinical trial to assess the antidiabetic, antidyslipidemic and antioxidant activities of Tinospora cordifolia in management of type-2 diabetes mellitus. *International Journal of Pharmaceutical Sciences and Research*, *7*(2), 757.

Kurian, G. A., Manjusha, V., Nair, S. S., Varghese, T., & Padikkala, J. (2014). Short-term effect of G-400, polyherbal formulation in the management of hyperglycemia and hyperlipidemia conditions in patients with type 2 diabetes mellitus. *Nutrition*, *30*(10), 1158-1164.

Lee, I.-A., Kim, E.-J., & Kim, D.-H. (2012). Inhibitory effect of β-sitosterol on TNBS-induced colitis in mice. *Planta medica*, *78*(09), 896-898.

Lugun, O., Bhoi, S., Kujur, P., Kumar, D. V., & Surin, W. R. (2018). Evaluation of Antithrombotic Activities of Solanum xanthocarpum and Tinospora cordifolia. *Pharmacognosy Research*, *10*(1), 98.

Manne, M., Goudar, G., Varikasuvu, S. R., Khetagoudar, M. C., Kanipakam, H., Natarajan, P., Ummiti, M. D., Yenagi, V. A., Chinthakindi, S., & Dharani, P. (2021). Cordifolioside: potent inhibitor against M pro of SARS-CoV-2 and immunomodulatory through human TGF-β and TNF-α. *3 Biotech*, *11*, 1-25.

McKeown, E., Bykerk, V. P., De Leon, F., Bonner, A., Thorne, C., Hitchon, C. A., Boire, G., Haraoui, B., Ferland, D. S., & Keystone, E. C. (2012). Quality assurance study of the use of preventative therapies in glucocorticoid-induced osteoporosis in early inflammatory arthritis: results from the CATCH cohort. *Rheumatology*, *51*(9), 1662-1669.

Meena, A., Singh, A., Panda, P., Mishra, S., & Rao, M. (2010). Tinospora cordifolia: its bioactivities & evaluation of physicochemical properties. *IJPPR*, *2*, 50-55.

Mishra, R., & Kaur, G. (2015). Tinospora cordifolia Induces Differentiation and Senescence Pathways in Neuroblastoma Cells. *Molecular Neurobiology*, *52*(1), 719-733. https://doi.org/10.1007/s12035-014-8892-5

Modi, B., Kumari Shah, K., Shrestha, J., Shrestha, P., Basnet, A., Tiwari, I., & Prasad Aryal, S. (2020). Morphology, Biological Activity, Chemical Composition, and Medicinal Value of Tinospora Cordifolia (willd.) Miers. *Advanced Journal of Chemistry-Section B*, *2020*, 36-54.

Murshid, G. M., Kundu, S. K., Sohrab, M. H., & Mazid, M. A. (2022). Pharmacological Overview of Tinospora cordifolia, an Ethnologically Important Plant of Bangladesh. *Pharmacology & Pharmacy*, *13*(3), 93-106.

Naik, D., Dandge, C., & Rupanar, S. (2014). Determination of chemical composition and evaluation of antioxidant activity of essential oil from Tinospora cordifolia (Willd.) Leaf. *Journal of Essential Oil Bearing Plants*, *17*(2), 228-236.

Palmieri, A., Scapoli, L., Iapichino, A., Mercolini, L., Mandrone, M., Poli, F., Giannì, A. B., Baserga, C., & Martinelli, M. (2019). Berberine and Tinospora cordifolia exert a potential anticancer effect on colon cancer cells by acting on specific pathways. *International journal of immunopathology and pharmacology*, *33*, 2058738419855567.

Pan, L., Terrazas, C., Lezama-Davila, C. M., Rege, N., Gallucci, J. C., Satoskar, A. R., & Kinghorn, A. D. (2012). Cordifolide A, a sulfur-containing clerodane diterpene glycoside from Tinospora cordifolia. *Organic letters*, *14*(8), 2118-2121.

Pandey, M., Chikara, S. K., Vyas, M. K., Sharma, R., Thakur, G. S., & Bisen, P. (2012). Tinospora cordifolia: A climbing shrub in health care management. *Int J Pharm Bio Sci*, *3*(4), 612-628.

Pandey, V. K., Shankar, B. S., & Sainis, K. B. (2012). G1-4 A, an arabinogalactan polysaccharide from Tinospora cordifolia increases dendritic cell immunogenicity in a murine lymphoma model. *International immunopharmacology*, *14*(4), 641-649.

Paray, A. R., Bhakat, M., Mohanty, T. K., Parry, U. R., & Lone, S. A. (2018). Antimicrobial activity of Indian medicinal plants, Azadirachta indica, Carica papaya, Curcuma longa, Moringa oleifera and Tinospora cordifolia: A review. *The Pharma Innovation Journal*, *7*(10), 523-531.

Parthasarathy, M., & Evan Prince, S. (2021). The potential effect of phytochemicals and herbal plant remedies for treating drug-induced hepatotoxicity: a review. *Molecular Biology Reports*, *48*, 4767-4788.

Patel, A., Bigoniya, P., Singh, C. S., & Patel, N. S. (2013). Radioprotective and cytoprotective activity of Tinospora cordifolia stem enriched extract containing cordifolioside-A. *Indian Journal of Pharmacology*, *45*(3), 237.

Perera, P. K., Perera, M., & Kumarasinghe, N. (2014). Effect of Sri Lankan traditional medicine and Ayurveda on Sandhigata Vata (osteoarthritis of knee joint). *Ayu*, *35*(4), 411.

Polu, P. R., Nayanbhirama, U., Khan, S., & Maheswari, R. (2017). Assessment of free radical scavenging and anti-proliferative activities of Tinospora cordifolia Miers (Willd). *BMC complementary and alternative medicine*, *17*(1), 1-12.

Pratihast, K., Kumar, R., & Bharti, S. K. (2019). Comparative antimicrobial activity of ethanolic and aqueous extract of Tinospora cordifolia. *Pharma Innov J*, *8*(3), 129-136.

Preeti, S. (2011). Tinospora cordifolia (Amrita)-a miracle herb and lifeline to many diseases. *International Journal of Medicinal and Aromatic Plants*, *1*(2), 57-61.

Preety, D., Deepak, S., Mradu, B., & Nalini, S. (2022). Evaluation of in vitro cytoprotective and antioxidant effects of Tinospora cordifolia in cultured HepG2 cells. *Journal of Herbal Medicine*, *31*, 100529.

Raina Mehra, T. N., Arora, M., & Madan, S. (2013). Standardization and Evaluation of Formulation Parameters of Tinospora Cordifolia Tablet. *Journal of Advanced Pharmacy Education & Research Oct-Dec*, *3*(4).

Rani, R., Chitme, H., & Sharma, A. K. (2023). Effect of Tinospora cordifolia on gestational diabetes mellitus and its complications. *Women & Health*, 1-11.

Rathi, D., & Balasubramanian, P. (2018). EVALUATION OF HYPOLIPIDEMIC ACTION ON TINOSPORA CORDIFOLIA.

Rushikesh, S., Jadhav, S., & Kamble, S. (2023). Tinospora cordifolia a Medicinal plant with many roles: A Review. *Research Journal of Pharmacognosy and Phytochemistry*, *15*(1), 87-90.

Sagar, V., & Kumar, A. H. (2020). Efficacy of natural compounds from Tinospora cordifolia against SARS-CoV-2 protease, surface glycoprotein and RNA polymerase. *Biology, Engineering, Medicine and Science Reports*, *6*(1), 06-08.

Saha, S., & Ghosh, S. (2012). Tinospora cordifolia: One plant, many roles. *Ancient science of life*, *31*(4), 151.

Sajith, K., & Farhan, H. (2022). Pharmacological effects of Tinospora cordifolia:(Giloy) in human body. *The Pharma Innovation Journal*, *11*(7), 07-10.

Salkar, K., Chotalia, C., & Salvi, R. (2017). Tinospora cordifolia: an antimicrobial and immunity enhancer plant. *Int. J. Sci. Res*, *6*, 1603-1607.

Selvam, P., Illanjiam, S., Ramesh, T., Aravindh, R., & Vasanthraj, R. Investigation of anticancer and antimicrobial activities of Kabasura Kudineer: A polyherbal formulation. *EVIDENCE BASED HERBAL MEDICINE–PART-V*.

Shaikh, A. S., Thomas, A. B., & Chitlange, S. S. (2020). Herb–drug interaction studies of herbs used in treatment of cardiovascular disorders—A narrative review of preclinical and clinical studies. *Phytotherapy research*, *34*(5), 1008-1026.

Shamsuzzaman, M., & Hasan, M. R. (2019). A review of anticancer potential medicinal plants. *J. sci. Facts*, *5*, 1-4.

Shanthi, V., & Nelson, R. (2013). Anitbacterial activity of Tinospora cordifolia (Willd) Hook. F. Thoms on urinary tract pathogens. *Int J Curr Microbiol App Sci*, *2*(6), 190-194.

Sharma, D. N., & Sharma, A. (2015). Tinospora cordifolia Enhances Vyadhikshamatwa (immunity) in children. *The Journal of Phytopharmacology*, *4*(4), 227-230.

Sharma, H., Rao, P. S., & Singh, A. K. (2021). Fifty years of research on Tinospora cordifolia: From botanical plant to functional ingredient in foods. *Trends in Food Science & Technology*, *118*, 189-206.

Sharma, P., Dwivedee, B. P., Bisht, D., Dash, A. K., & Kumar, D. (2019a). The chemical constituents and diverse pharmacological importance of Tinospora cordifolia. *Heliyon*, *5*(9).

Sharma, P., Dwivedee, B. P., Bisht, D., Dash, A. K., & Kumar, D. (2019b). The chemical constituents and diverse pharmacological importance of Tinospora cordifolia. *Heliyon*, *5*(9), e02437.

Sharma, R., Bolleddu, R., Maji, J. K., Ruknuddin, G., & Prajapati, P. K. (2021). In-Vitro α-amylase, α-glucosidase inhibitory activities and in-vivo anti-hyperglycemic potential of different dosage forms of guduchi (tinospora cordifolia [willd.] miers) prepared with ayurvedic bhavana process. *Frontiers in Pharmacology*, 903.

Shirolkar, A., Sharma, B., Lata, S., & Dabur, R. (2016). Guduchi Sawras (Tinospora cordifolia): An Ayurvedic drug treatment modulates the impaired lipid metabolism in alcoholics through dopaminergic neurotransmission and anti-oxidant defense system. *Biomedicine & Pharmacotherapy*, *83*, 1265-1277.

Shirolkar, A., Yadav, A., Nale, A., Phogat, J., & Dabur, R. (2022). Integrated omics analysis revealed the Tinospora cordifolia intervention modulated multiple signaling pathways in hypertriglyceridemia patients-a pilot clinical trial. *Journal of Diabetes & Metabolic Disorders*, *21*(1), 379-397.

Singh, A., Saxena, S., & Babu, A. (2020). A pharmacological and chemical constituents review on Tinospora cordifolia-a medicinal herb. *World Journal of Pharmaceutical Research*, *9*(14), 472-491.

Singh, D., & Chaudhuri, P. K. (2017). Chemistry and pharmacology of Tinospora cordifolia. *Natural product communications*, *12*(2), 1934578X1701200240.

Singh, G., & Saxena, R. (2017). Medicinal properties of Tinospora cordifolia (Guduchi). *Inter J Adv Res, Ideas and Innovations in Technology*, *3*, 227-231.

Singh, K., Panghal, M., Kadyan, S., Chaudhary, U., & Yadav, J. P. (2014). Antibacterial activity of synthesized silver nanoparticles from Tinospora cordifolia against multi drug resistant strains of Pseudomonas aeruginosa isolated from burn patients. *Journal of Nanomedicine & Nanotechnology*, *5*(2), 1.

Sinha, A., Sharma, H., Singh, B., & Patnaik, A. (2017). Phyto-chemical studies of methanol extracts of tinospora cordifolia stem by GC-MS. *World Journal of Pharmaceutical Research*, *6*(4), 1319-1326.

Sinha, K., Mishra, N., Singh, J., & Khanuja, S. (2004). Tinospora cordifolia (Guduchi), a reservoir plant for therapeutic applications: A Review.

Sonkamble, V. V., & Kamble, L. H. (2015). Antidiabetic potential and identification of phytochemicals from Tinospora cordifolia. *American Journal of Phytomedicine and Clinical Therapeutics*, *3*(1), 097-110.

Spandana, U., Ali, S. L., Nirmala, T., Santhi, M., & Babu, S. (2013). A review on Tinospora cordifolia. *International Journal of Current Pharmaceutical Review and Research*, *4*(2), 61-68.

Taylor, R. C. (2022). Alternative medicine and the medical encounter in Britain and the United States. In *Alternative Medicines* (pp. 191-228). Routledge.

Tiwari, P., Nayak, P., Prusty, S. K., & Sahu, P. K. (2018). Phytochemistry and pharmacology of Tinospora cordifolia: A review. *Systematic Reviews in Pharmacy*, *9*(1), 70-78.

Upadhyay, A. K., Kumar, K., Kumar, A., & Mishra, H. S. (2010). Tinospora cordifolia (Willd.) Hook. f. and Thoms.(Guduchi)–validation of the Ayurvedic pharmacology through experimental and clinical studies. *International journal of Ayurveda research*, *1*(2), 112.

Upadhyay, N., Ganie, S. A., Agnihotri, R. K., & Sharma, R. (2014). Free radical scavenging activity of Tinospora cordifolia (Willd.) Miers. *Journal of Pharmacognosy and Phytochemistry*, *3*(2), 63-69.

Upreti, P., & Chauhan, R. (2018). Effect of leaf powder of giloy (Tinospora cordifolia) in fish feed on survival and growth of post larvae of Catla catla. *Journal of Applied and Natural Science*, *10*(1), 144-148.

Vig, R., Bhadra, F., Gupta, S. K., Sairam, K., & Vasundhara, M. (2022). Neuroprotective effects of quercetin produced by an endophytic fungus Nigrospora oryzae isolated from Tinospora cordifolia. *Journal of Applied Microbiology*, *132*(1), 365-380.

Wagenlehner, F., Wullt, B., Ballarini, S., Zingg, D., & Naber, K. G. (2018). Social and economic burden of recurrent urinary tract infections and quality of life: a patient web-based study (GESPRIT). *Expert review of pharmacoeconomics & outcomes research*, *18*(1), 107-117.

Yates, C. R., Bruno, E. J., & Yates, M. E. (2022). Tinospora Cordifolia: A review of its immunomodulatory properties. *Journal of Dietary Supplements*, *19*(2), 271-285.