Chinese Journal of Integrative Medicine
Available online at link.springer.com/journal/11655
Journal homepage: www.cjim.cn/zxyjhen/zxyjhen/ch/index.aspx
E-mail: cjim_en@cjim.cn

Herbal and Botanical Review

Therapeutic Application, Phytoactives and Pharmacology of *Tinospora cordifolia*: An Evocative Review

Rabiya Ahsan[1], Anuradha Mishra[2], Badruddeen Badar[1], Mohammad Owais[1], and Vijayshwari Mishra[3]

ABSTRACT ***Tinospora cordifolia*** **(Guduchi or Gurjo), a herbaceous vine or climbing deciduous shrub, is consider as an important medicine in the Ayurvedic system of medication, which is available in India, China, Myanmar, Bangladesh and Srilanka.** ***Menispermaceae*** **is the family of this compound.** ***T. cordifolia*** **have a variety of properties to treat various ailments such as fevers, jaundice, diabetes, dysentery, urinary infections, and skin diseases. This compound has been subjected to many chemicals, pharmacological, pre-clinical, or clinical investigations and some new therapeutic potential effects have been indicated. This review aims to summarize the critical information concerning in areas of chemical constituents, chemical structure, and pharmacokinetic activities such as anti-diabetic, anticancer, immune-modulatory, antivirus (especially** ***in silico*** **study about COVID-19), antioxidant, antimicrobial, hepatoprotective and its effect on cardiovascular and neurological disorders as well as rheumatoid arthritis. This traditional herb needs more experimental study on the clinical, pre-clinical study, and clinical efficacy of these compounds for the prevention and treatment of COVID-19 and needs large-scale clinical studies to prove the clinical efficacy of this compound, especially in stress-related diseases and other neuronal disorders.**

KEYWORDS ***Tinospora cordifolia*****, Guduchi,** ***menispermaceae*****, pharmacology**

Tinospora cordifolia (Guduchi) is an important medicine in the Ayurvedic system of medication and is found in numerous classical texts for the treatment of various disorders such as jaundice, fever, skin diseases and diabetes.[1] *T. cordifolia* is a large, green glabrous, deciduous herbaceous plant. It belongs to the *Menispermaceae* family.[2] *T. cordifolia* is spread throughout India and China. Guduchi is the Hindi name of *T. cordifolia*, and it is a Hindu mythological term that refers to the heavenly elixir which is maintained the body in old age and helps to make it young. *T. cordifolia* is commonly known as Amrita, Guduchi Madhuparni, Amritavalli, Chinnobhava, Guduchika, Vatsadani, Kundalini, Chakralakshanika, Gurcha, Giloe, Tantrika, Gulancha, Thippateega, Amrutavalli, Garo, Galac, Amrita, Gilo, Gulvel, Guluchi, Chittamrutu, Gilo, Seendal Siddhilata, Amarlata, Heartleaf moonseed, Seendil kodi, and Tinospora.[3] *T. cordifolia* is a common climbing shrub found in the tropical deciduous forest of south Indian peninsular plains. The plant has been reported to contain tinosporin, columbin, tinosporin acid, and berberine. It is well-reputed in the traditional system of medicine to treat various ailments.[4] *T. cordifolia* is a deciduous herbaceous vine shrub with greenish-yellow typical flowers. This type of plant is found at higher altitudes. Male or female flowers are formed on separate branches. Female flower are solitary while male flowers are clustered. Cultivation of *T. cordifolia* flowers expands over summers and winters, mostly in the tropical parts of plants climbing to an altitude of 300 m in India and China. Various active constituents are derived from the *T. cordifolia* plant like diterpenoid lactones, alkaloids, glycosides, steroids, and aliphatics. These constituents are found in different parts of *T. cordifolia* plant, including whole plant, root, and stem (Table 1). Recently, this plant was reported on various activities like anti-periodic, immunomodulatory, anti-diabetic, anti-leprotic, anti-inflammatory, anti-spasmodic, antioxidant, anti-arthritic, anti-allergic, anti-malarial, anti-stress, anti-neoplastic activities and have

1. Research Scholar, Faculty of Pharmacy, Integral University, Lucknow, UP, 226022, India; 2. Department of Pharmacology, Amity Institute of Pharmacy, Lucknow, Amity University Uttar Pradesh, Sector 125,Noida, 201313, India; 3. Research Scholar, Rameshwaram Institute of Technology, Lucknow, India
Correspondence to: Dr. Anuradha Mishra, E-mail: misra.anuradha@gmail.com
DOI: https://doi.org/10.1007/s11655-023-3733-2

Chin J Integr Med 2023 Jun;29(6):549-555

Table 1. *T. cordifolia* Chemical Constituents

Plant common name & biological source	Parts	Chemicals constituents
Gurjo Heart-leaved moonseed Guduchi Giloy *T. cordifolia*	Root	**Alkaloids:** tembetarine, magnoflorine, choline, tinosporin, isocolumbin, palmatine, tetrahydropalmatine
	Stem	**Alkaloids:** berberine, palmatine **Glycosides:** cordifoliside A, B, C, D, E, tinocordiside, furanoid diterpene glucoside, 18-norclerodane glucoside, tinocordifolioside, cordioside, palmatosides F, syringin, palmatosides C **Steroids:** hydroxy ecdysone, ecdysterone, makisterone A, giloinsterol **Sesquiterpenoid:** tinocordifolin
	Aerial part	**Steroids:** β -sitosterol, δ -sitosterol
	Whole plant	**Diterpenoid lactones:** furanolactone, clerodane derivatives, tinosporon, tinosporides, jateorine, columbin **Aliphatic compound:** heptacosanol and octacosanol **Miscellaneous:** nonacosan-15-one, jatrorrhizine, tetrahydrofuran, cordifelone, tinosporidine, cordifol, N-trans-feruloyl tyramine as tinosporic acid, diacetate, giloinin, and giloin

protective properties against neurological disorders and hepatoprotective activities (Figure 1).[5]

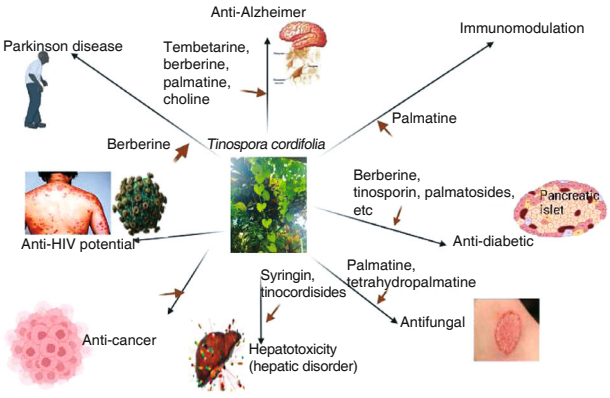

Figure 1. Schematics Representation of Active Constituents of *T. cordifolia* with Their Medicinal Value

Active Constituents of *T. cordifolia*

A variety of active constituents were isolated from *T. cordifolia* plant (Figure 2). All components belong to different drug categories such as glycosides, alkaloids, aliphatic compounds, steroids, sesquiterpenoid, polysaccharides, diterpenoid lactones, and phenolics. *T. cordifolia* plants leaves are fully rich with protein, and good for phosphorus and calcium. Different constituents reported include glycoside, alkaloids, bitter principles, crystalline components, etc. The bitter principles have been identified as columbin, chasmanthin, and palmarin. The alkaloid tinosporin, borapetoside F, borapetoside B, syringin, polypodine B 20,22-acetonide, angelicoidenol2-O- β -D-apiofuranosyl-(1→6)- β -D-glucopyranoside, secoisolariciresinol-9'-O- β -D-glucopyranoside, and pinoresinol-di-O-glycoside also have been isolated from *T.* cordifolia. The active constituents are diterpene compounds including tinosporone, tinosporic acid, cordifolisides A to E, the yellow alkaloid, berberine, giloin, crude giloininand, a glucosidal bitter principle as well as polysaccharides, including arabinogalactan polysaccharide. Picrotene and bergenin were also found in the plant.[6,7]

Extraction of *T. cordifolia* different parts has been carried out for extraction of lorophylls, carotenoids, phenols flavonoids and aminoacids. [8-10] Identified phytoconstituents are cordifolioside A, cordifolioside B, berberin and palmatine. These are the main phytoconstituents of *T. cordifolia*.[11,12]

Pharmacological Activity of *T. cordifolia*

Immunomodulators

Dhama K, et al[13] investigated about immunomodulatory activity of *T. cordifolia*, as it has been used as an adjuvant in the treatment of tumours as immunotherapy. Palmatine is an active constituent of *T. cordifolia*, and it can reduce B-cell lymphoma-2 expression and stimulate characteristic apoptotic features related to constitutive expression of caspase-activated deoxyribonucleic acid in the nucleus and cytoplasm. Palmatine has a pharmacophore group of octacosanol (aliphatic alcohol) which exhibited angio-inhibitory and antimetastatic effects.[13] *T. cordifolia* downregulated vascular endothelial growth factor gene expression by inhibiting nuclear factor-kB (NF- κ B) then suppressed sprouting of new blood vessels and protected against neuroblastoma. Stem aqueous ethanolic extract (AEC) of *T. cordifolia* has the potential to restrain neuroblastoma cell proliferation via modulating expression of proliferating cell nuclear antigen and cyclin D1. *T. cordifolia* stimulated expression of mortalin and RelA subunit of NF- κ B with

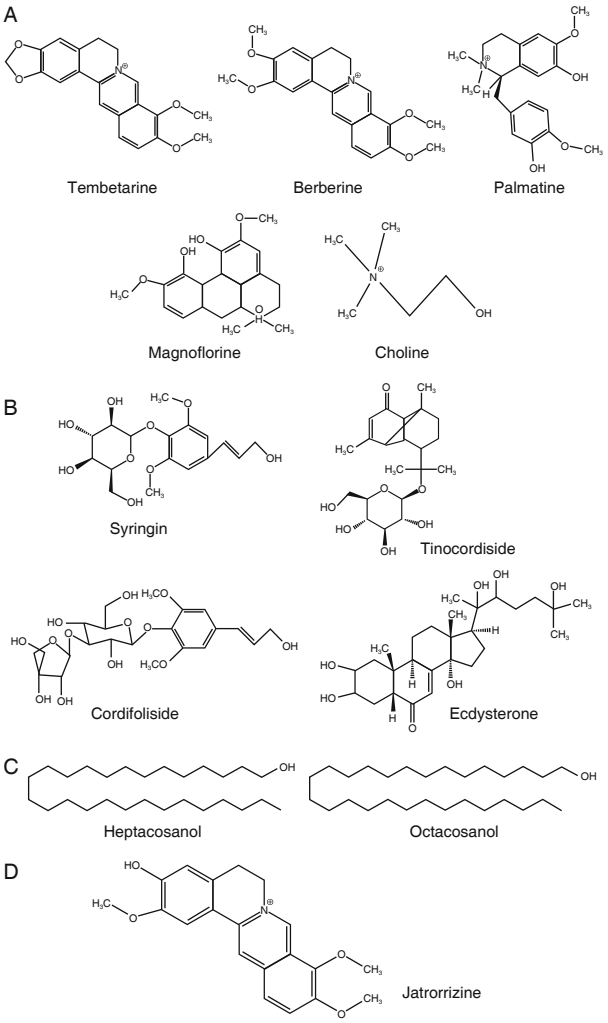

Figure 2. *T. cordifolia* Active Constituents

Notes: A: alkaloids, uses: anti-Alzheimer, anticancer, anti-cholesterol and diabetes; B: glycosides, uses: antineoplastic, antioxidant, hepatoprotective & hypolipidemic, C: liphatic compounds, uses: food-flavoring and inhibiting tremor in essential tremor; D: miscellaneous, uses: promoting blood flow, mitotic activity, antimicrobial and antifungal activity

downregulation of B-cell lymphoma-extra large (Bcl-xl).[14]

Hepatoprotective Activity

T. cordifolia water extract (TCE) intervention effectively reversed the excretion of vitamins, altered the excretion of metabolic intermediates of vitamins, and restored normal vitamin metabolism. TCE intervention normalized vitamin metabolism by reducing oxidative stress through antioxidant compounds present in it. Additionally, magnoflorine and columbin triggered liver regeneration through dopamine receptors and PPAR α activation.[15] Furthermore, TCE enhanced glutathione synthesis and lipoamide levels, which decrease inflammation and were used fully in liver regeneration that retained vitamins. TCE also enhanced the uptake of biotin and calcium. TCE ameliorated the effect of alcohol on vitamin metabolism in an alcoholic person due to its capability to fight oxidative stress, regenerate liver, expand intestinal absorption, and modulate lipid metabolism.[16]

Antioxidant Activity

Water extract of *T. cordifolia* leaf and stem exhibited good antioxidant property. 2,2-diphenyl-1-picrylhydrazyl (DPPH) is a stable free radical.[17] The *in vitro* study carried out on this radical was based on the measurement of scavenging ability of antioxidants towards stable radical DPPH. This radical reacts with suitable reducing agents, the electrons become paired off and the solution loses color stoichiometrically depending on the number of electrons taken up. *T. cordifolia* reduced the radical to the corresponding hydrazine when they react with hydrogen donors in antioxidant principles.[18] *T. cordifolia* inhibited or scavenged 2,2-azino-bis (3-etilbenzotiazolin)-6-sulfonic acid radical and also reduced nitric oxide. *T. cordifolia* increased superoxide dismutase, reduced glutathione, glutathione-S-transferase, glutathione peroxidase and glutathione reductase.[19] *T. cordifolia* extract has phenolic compound that exert pro-oxidant effects by interacting with iron. O-phenanthroline quantitatively forms complexes with ferric ions which help to disrupt the presence of chelating agents. *T. cordifolia* extracts interfered with the formation of ferrous-O-phenanthroline complex, which shown that *T. cordifolia* extract has metal chelating activity. *T. cordifolia* extract has phenolics, flavonoids, and tannins constituents, which are responsible for antioxidant activity.[20]

Anti-rheumatoid Arthritis Activity

Rheumatoid arthritis (RA) is a chronic inflammatory disease leading to joint destruction mediated by migration of $CD4^+$ T cells and macrophages infiltrating synovial tissue. TCE reduced spleen adherent cells, e.g., interleukin (IL)-1 β, IL-6, IL-23, and tumor necrosis factor (TNF) α and reduced draining lymph node cells (e.g., IL-17).[21] Study on stem extract of *T. cordifolia* showed that the pro-inflammatory cytokines were also reduced in synovial-infiltrating cells culture supernatants (e.g., IL-1 β, IL-17, IL-6, and TNF α) and sera (e.g., IL-1 β and IL-17) but not much change in levels of anti-inflammatory IL-10 and other cytokines. Thus, TCE altered the balance of pro- *versus* anti-inflammatory cytokines primarily by downregulating pro-inflammatory cytokines, particularly IL-17 and IL-1 β. TCE-induced

Chin J Integr Med 2023 Jun;29(6):549-555

suppression of arthritis might be mediated in part by altering the chemotactic cellular migration of immune cells into the joints. TCE inhibits pro-inflammatory cytokines and chemokines along with the mediators of bone remodeling.[22] A statistically significant decrease in IL-17-producing T cells was observed, but that difference was primarily in IL-17^{+}IFN-γ^{+} (double producer) cells of the spleen but not in IL-17^{+} (single producer) cells in periphery (spleen) or target organ (joints). Nevertheless, the reduced frequency of IL-17^{+}IFN-γ^{+} (double producer) cells correlates with reduced production of IL-17. TCE reduced the expression of receptor activator of nuclear factor-κB ligand (RANKL). TCE treatment reduced the osteoclastic mediators such as macrophage colony-stimulating factor and osteopontin.[23] TCE enhanced the mineralization of bone matrix on human osteoblast cells and proliferation of osteoblast cells. TCE might inhibit MMP-9 either by a direct effect on enzyme or by an indirect effect via inhibiting the key inducers of MMP-9. TCE reduced 3 of positive inducers of MMP-9, such as IL-6, IL-17, and RANKL.[24]

Antidiabetic Activity

T. cordifolia is well explored in most available diabetes models in animals which were also substantiated in clinical subjects.[3] *T. cordifolia* constituents (berberine, palmatosides and palmetine) have highly anti-diabetic activity. *T. cordifolia* suppressed the glucose consumption efficiency which concludes the anti-diabetic activity is mediated through an insulin-dependent pathway through the activation of insulin reuptake tyrosine kinase and phosphatidyl inositol-OH-kinase. However, these inhibitors did not completely arrest the glucose consumption efficiency. *T. cordifolia* mediated its action majorly through insulin pathway and to some extent by other pathways like activated protein kinase, Ras-Raf-MEK-ERK, c-Jun N-terminal kinase, or peroxisome proliferator-activated receptors (Figure 3).[25] *T. cordifolia* constituents (alkaloids) are considered to share similar activity in mediating anti-diabetic properties. Palmatine and *T. cordifolia* improved Glut-4 expression, suppressed PPARγ (lipogenic gene) and simultaneously up-regulated PPARα expression. The expression of PPARα is downregulated by *T. cordifolin* treatment (Figure 3).[26]

Anti-microbial Activity

T. cordifolia is effective at a lower concentration and higher volume with a maximum antibacterial activity (40 μL at 2% concentration). The aqueous extracts

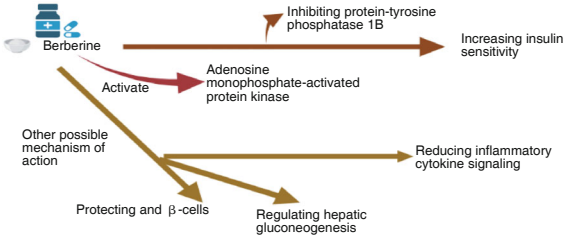

Figure 3. Mechanism of Berberine as Hypoglycemic Agent

of *T. cordifolia* exhibit effective antimicrobial activity against microorganisms.[27] Stem extract of *T. cordifolia* has secondary metabolites and the phytochemicals present in it such as quinones, polyphenols, alkaloids (berberine, palmatine), flavonoids, tannins, coumarins, terpenoids, lectins, and polypeptides.[28] *T. cordifolia* constituents such as quinones and flavonoids bind to adhesins form complexes with cell wall, terpenoids, polyphenols, and tannins cause membrane disruption and forme metal ion complexes, thus inactivating the bacterial enzymes.[29]

Anti-viral Activity

Berberine is the main constituent of *T. cordifolia*, and it was used as a natural dye. This constituent is helpful for staining heparin in mast cells. Berberine is relatively toxic parenterally but used orally for the treatment of numerous parasitic and fungal infections. Berberine, β-sitosterol, tetrahydropalmatine, octacosanol and coline have anti-viral property against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[30.31] Berberine reduced the cholesterol levels and β-sitosterol can be used in the inflammation. Octacosanol belongs alcohol category of "straight-chain aliphatic 28-carbon primary fatty alcohol" which is used in the health industry for nutritional supplements. Choline supports numerous vital bodily functions, including cellular growth and metabolism. A molecular docking study has proven that *T. cordifolia* (giloy) is an inhibitor for SARS CoV-2.[32] Berberine, β-sitosterol, octacosanol, tetrahydropalmatine, and choline are selected for 3CLpro targets Ⅰ and Ⅱ of main protease enzymes. The main chemical constituents of *T. cordifolia* (e.g. berberine and β-sitosterol) can be used as an anti-viral drug against SARS-CoV-2, and act like a good inhibitor towards SARS CoV-2 protein as compared to other inhibitors. The stem extract of *T. cordifolia* constituents are good inhibitors in regulating 3CL protease activity and provide good effects in controlling against virus replication and multiplication.[33]

Antiarrhythmic Activity

Tembetarine and berberine are important constituents of *T. cordifolia*. These constituents are known as adaptogens, as they enhanced the resistance of body to physio-chemical, and biological stress and build energy. Arrhythmias produced by $CaCl_2$ is severe and recalcitrant to manipulation, and high doses of antiarrhythmic agents have to be given to produce a significant effect.[34] Calcium concentration instigates a hyperpolarization of resting potential in cells of sinoatrial node and reduces the excitability of Purkinje cells due to a less negative value of the threshold potential.[35] *T. cordifolia* extract increased the effect as reflected by a progressive decrease in plasma calcium and sodium levels, and improved potassium levels at higher doses.[36] *T. cordifolia* normalized the arrhythmogenic calcium overload, reduced calcium-induced sodium levels, and enhanced anti-arrhythmic potassium levels.[37] The stem extract of *T. cordifolia* showed potent antiarrhythmic activity by normalization in PQRST waves as indicated by percentage of protection.[38]

Neuroprotective Activity

Kosaraju, et al[39] investigated the neuroprotective activity of *T. cordifolia* ethanolic extract (TCEE) on 6-hydroxy dopamine-induced Parkinsonism.[39] The increased levels of dopamine by the treatment of TCEE are due to the reduced metabolism of dopamine or enhanced biosynthesis of dopamine by dopaminergic neurons of substantia nigra.[40] The increased dopamine levels by TCEE is furthered supported by anti-stress and anti-depression activity of *T. cordifolia* root extract in which dopamine levels were normalized after treatment. TCEE prevents dopaminergic neurodegeneration by decreasing iron-induced damage. Reduction in glutathione might impair H_2O_2 clearance and improve OH radical's formation and produce oxidative stress. TCEE possess significant neuroprotection in 6-hydroxydopamine-induced Parkinson's disease by protecting dopaminergic neurons and reducing the iron accumulation.[41]

Conclusion

This review discusses the pharmacokinetic properties, chemical constituent, and pharmacological and therapeutic effects of *T. cordifolia* as a promising herbal drug because of its safety and effectiveness. *T. cordifolia* is an important medicinal plant having various traditional importance as it is used in the indigenous system of medicines like Ayurveda, Sidha, and Unani. Traditional practices have been proven by various experimental and research studies. This review illustrates the plant with tremendous potential in both healthcare and trade. Considerable work has been done to explore the pharmacological activity and medicinal uses of the plant. The plant has a various number of therapeutic applications *viz*. cardio-protective, diuretic, antidepressant, antiepileptic, neurodegenerative, antibacterial, antioxidant, antitussive, anti-HIV, immunostimulant, hepatoprotective, and anti-ulcerative. The major research studies were reported using extracts of the plant; still, the active principle process involved in these activities needs to be explored.

The safety profile analysis showed that *T. cordifolia* is a safe dose to use during pregnancy with caution. Thus, the above findings indicate that the traditional use of *T. cordifolia* has a logical and scientific basis in studies. *In silico* molecular docking approach provides insight into the screened molecules that might prove to be an effective inhibitor for SARS-CoV-2. Large-scale clinical studies are required to check the preclinical and clinical efficacy of these compounds for the prevention and treatment of SARS-CoV-2 and also need to prove the clinical efficacy of these agents, especially in stress-related diseases and other neurological diseases.

Conflict of Interest

The authors declare no potential conflicts of interest concerning the review, authorship, and/or publication of this article.

Author Contributions

Ahsan R and Mishra A conceived and Badar B modified this manuscript, Ahsan R, Owais M and Mishra V have collected the literature. Ahsan R wrote the manuscript. Reviewers helped to revise the manuscript. All authors read and approved the manuscript.

Acknowledgment

Author is thankful to Integral University Lucknow for providing manuscript number IU/R&D/2022-MCN0001444.

REFERENCES

1. Sinha K, Mishra NP, Singh J, Khanuja SP. *Tinospora cordifolia* (Guduchi), a reservoir plant for therapeutic applications: a review. Ind J Tradit Knowl 2004;3:257-270.
2. Bharathi C, Reddy AH, Nageswari G, Lakshmi BS, Soumya M, Vanisri DS, Venkatappa B. A review on medicinal properties

of *Tinospora cordifolia*. Int J Res Rev 2018;7:585-598.
3. Upadhyay A, Kumar K, Kumar A, Mishra H. *Tinospora cordifolia* (Willd.) Hook. f. and Thoms (Guduchi)—validation of the Ayurvedic pharmacology through experimental and clinical studies. Int J Ayu Res 2010;1:112.
4. Jeyachandran R, Xavier TF, Anand SP. Antibacterial activity of stem extracts of *Tinospora cordifolia* (Willd) Hook. f & Thomson. Ancient Sci Life 2003;23:40.
5. Saha S, Ghosh S. *Tinospora cordifolia*: one plant, many roles. Ancient Sci Life 2012;4:151.
6. Gupta S, Singh, Ashwlayan VD. Pharmacological activity of *Tiospora cordifolia*. Pharmacologyonlin 2011;644-652.
7. Sharma P, Dwivedee BP, Bisht D, Dash AK, Kumar D. The chemical constituents and diverse pharmacological importance of *Tinospora cordifolia*. Heliyon 2019;5:e02437.
8. Bharathi C, Reddy AH, Nageswari G, Sri Laxmi B, Soumya M, Vanisri DS, et al. A review on medicinal properties of *Tinospora cordifolia*. Int J Sci Res Rev 2018;7:585-598.
9. Pathan A, Kamble A, Chowdhury S, Laware S. Sequential extraction, and quantification of *Tinospora cordifolia* leaf pigments and metabolites. Int J Curr Microbiol Appl Sci 2015;4:638-644.
10. Reddi KK, Tetali SD. Dry leaf extracts of *Tinospora cordifolia* (Willd.) Miers attenuate oxidative stress and inflammatory condition in human monocytic (THP-1) cells. Phytomedicine 2019;61:152831.
11. Sardhara RA, Gopal S. Qualitative phytochemical screening of different solvent extracts of *Tinospora cordifolia* stem and lantana camara flower. Int Res J Pharm Appl Sci 2013;3:210-213.
12. Kumar V, Singh S, Singh A, Dixit AK, Srivastava B, Sidhu GK, et al. Phytochemical, antioxidant, antimicrobial, and protein binding qualities of hydro-ethanolic extract of *Tinospora cordifolia*. J Biolog Active Prod Nature 2018;8:192-200.
13. Dhama K, Sachan S, Khandia R, Munjal A, MN Iqbal HK, Latheef S, et al. Medicinal and beneficial health applications of *Tinospora cordifolia* (Guduchi): a miraculous herb countering various diseases/disorders and its immunomodulatory effects. Rec Patents Endocr Metab Immune Drug Discov 2016;10:96-111.
14. Pandey VK, Amin PJ, Shankar BS. G1-4A, a polysaccharide from *Tinospora cordifolia* induces peroxynitrite dependent killer dendritic cell (KDC) activity against tumor cells. Int Immunopharm 2014;23:480-488.
15. Bishayi B, Roychowdhury S, Ghosh S, Sengupta M. Hepatoprotective and immunomodulatory properties of *Tinospora cordifolia* in CCl_4 intoxicated mature *albino* rats. J Toxicolog Sci 2002;27:139-146.
16. Sharma B, Dabur R. Protective effects of *Tinospora cordifolia* on hepatic and gastrointestinal toxicity induced by chronic and moderate alcoholism. Alcohol Alcoholism 2016;51:1-10.
17. Sarala M, Velu V, Anandharamakrishnan C, Singh RP. Spray drying of *Tinospora cordifolia* leaf and stem extract and evaluation of antioxidant activity. J Food Sci Technol 2012;49:119-122.
18. Upadhyay N, Ganie SA, Agnihotri RK, Sharma R. Free radical scavenging activity of *Tinospora cordifolia* (Willd.) Miers. J Pharm Phytochem 2014;3:63-69.
19. Gupta R, Sharma V. Ameliorative effects of *Tinospora cordifolia* root extract on histopathological and biochemical changes induced by aflatoxin-B1 in mice kidney. Toxicol Int 2011;18:94.
20. Jain S, Sherlekar B, Barik R. Evaluation of antioxidant potential of *Tinospora cordifolia* and *T. sinensis*. Int J Pharm Sci Res 2010;1:122.
21. Paval J, Kaitheri SK, Govindan S, Mohammed CA, Kumar RS, Narayanan SN, et al. Anti-arthritic activity of the plant *Tinospora cordifolia* Willd. J Herb Med Toxicol 2011;5:11-16.
22. Bharathi C, Reddy AH, Nageswari G, Sri Laxmi B, Soumya M, Vanisri DS, et al. A review on medicinal properties of *Tinospora cordifolia*. Int J Sci Res Rev 2018;7:585-598.
23. Sannegowda KM, Venkatesha SH, Moudgil KD. *Tinospora cordifolia* inhibits autoimmune arthritis by regulating key immune mediators of inflammation and bone damage. Int J Immunopathol Pharmacol 2015;28:521-531.
24. Abiramasundari G, Sumalatha KR, Sreepriya M. Effects of *Tinospora cordifolia* (Menispermaceae) on the proliferation, osteogenic differentiation and mineralization of osteoblast model systems *in vitro*. J Ethnopharmacol 2012;141:474-480.
25. Rajalakshmi M, Eliza J, Priya CE, Nirmala A, Daisy P. Anti-diabetic properties of *Tinospora cordifolia* stem extracts on streptozotocin-induced diabetic rats. Afr J Pharm Pharmacol 2009;3:171-180.
26. Sangeetha MK, Priya CM, Vasanthi HR. Anti-diabetic property of *Tinospora cordifolia* and its active compound is mediated through the expression of Glut-4 in L6 myotubes. Phytomedicine 2013;20:246-248.
27. Nethravathi PC, Kumar MP, Suresh D, Lingaraju K, Rajanaika H, Nagabhushana H, et al. *Tinospora cordifolia* mediated facile green synthesis of cupric oxide nanoparticles and their photocatalytic, antioxidant and antibacterial properties. Mater Sci Semiconduct Proc 2015;33:81-88.
28. Mishra A, Kumar S, Pandey AK. Scientific validation of the medicinal efficacy of *Tinospora cordifolia*. Sci World J 2013;2013.
29. Agarwal S, Ramamurthy PH, Fernandes B, Rath A, Sidhu P. Assessment of antimicrobial activity of different concentrations of *Tinospora cordifolia* against *Streptococcus* mutans: an *in vitro* study. Dental Res J 2019;16:24.
30. Thakkar SS, Shelat F, Thakor P. Magical bullets from an indigenous Indian medicinal plant *Tinospora cordifolia*: an

in-silico approach for the antidote of SARS-CoV-2. Egyp J Petroleum 2021;30:53-66.
31. Sapra L, Bhardwaj A, Azam Z, Madhry D, Verma B, Rathore S, Srivastava RK. Phytotherapy for treatment of cytokine storm in COVID-19. Frontiers Biosci 2021;26:51-75.
32. Shree P, Mishra P, Selvaraj C, Singh SK, Chaube R, Garg N, et al. Targeting COVID-19 (SARS-CoV-2) main protease through active phytochemicals of ayurvedic medicinal plants—*Withania somnifera* (Ashwagandha), *Tinospora cordifolia* (Giloy) and *Ocimum sanctum* (Tulsi)—a molecular docking study. J Biomolec Struct Dynamics 2020;40:1-14.
33. Chowdhury P. *In silico* investigation of phytoconstituents from Indian medicinal herb '*Tinospora cordifolia* (giloy)' against SARS-CoV-2 (COVID-19) by molecular dynamics approach. J Biomol Struct Dynamics 2020;39:1-8.
34. Rao PR, Kumar VK, Viswanath RK, Subbaraju GV. Cardioprotective activity of alcoholic extract of *Tinospora cordifolia* in ischemia-reperfusion induced myocardial infarction in rats. Biol Pharm Bull 2005;28:2319-2322.
35. Salve BA, Tripathi RK, Petare AU, Raut AA, Rege NN. Effect of *Tinospora cordifolia* on physical and cardiovascular performance induced by physical stress in healthy human volunteers. Ayurveda 2015;36:265.
36. Spandana U, Ali SL, Nirmala T, Santhi M, Babu SS. A review on *Tinospora cordifolia*. Int J Curr Pharm Rev Res 2013;4:61-68.
37. Sharma AK, Kishore K, Sharma D, Srinivasan BP, Agarwal SS, Sharma A, et al. Cardioprotective activity of alcoholic extract of *Tinospora cordifolia* (Willd.) Miers in calcium chloride-induced cardiac arrhythmia in rats. J Biomed Res 2011;25:280-286.
38. Antul K, Amandeep P, Gurwinder S, Anuj C. Review on pharmacological profile of medicinal vine: *Tinospora cordifolia*. Curr J Appl Sci Technol 2019:1.
39. Kosaraju J, Chinni S, Roy PD, Kannan E, Antony AS, Kumar MS. Neuroprotective effect of *Tinospora cordifolia* ethanol extract on 6-hydroxydopamine induced Parkinsonism. Ind J Pharmacol 2014;46:176.
40. Jain VK, Shete A. Antipsychotic activity of aqueous ethanolic extract of *Tinospora cordifolia* in amphetamine challenged mice model. J Adv Pharm Technol Res 2010;1:30.
41. Mishra R, Manchanda S, Gupta M, Kaur T, Saini V, Sharma A, et al. *Tinospora cordifolia* ameliorates anxiety-like behavior and improves cognitive functions in acute sleep deprived rats. Sci Rep 2016;6:1-5.

(Accepted July 27, 2022; First Online April 5, 2023)
Edited by WANG Wei-xia