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Phyto-Therapeutic Review of *Tinospora cordifolia* Linn. in Competence to Immunomodulation and Antiviral Potential to Deal with COVID



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ABSTRACT

Covid-19 necessitates immunity-boosting remedies or herbals like the use of Tinospora cordifolia Linn. It is a deciduous climbing shrub from tropical Asia, belonging to the family Menispermaceae. Several phytochemicals like alkaloids, diterpenoid lactones, steroids, glycosides, aliphatic chemicals, polysaccharides, etc. have been isolated from all parts of the plant. It is used and recommended for centuries in Indian medicine. According to findings it has proved, that drinking fresh Giloy juice strengthens immunity by enhancing the activity of macrophages. It has shown efficacy against upper respiratory tract infections and has shown anti-diabetic, antipyretic, antispasmodic, anti-inflammatory, anti-arthritic, antioxidant, anti-allergic, anti-stress, anti-leprotic, antimalarial, hepato-protective, immuno-modulatory, and anti-neoplastic effects according to various scientific studies. Since covid-19 an immunity boosting and antiviral herbs like Giloy have been accepted by the population. Thus, the immunomodulatory and antiviral activities of Giloy are systematically reviewed in the present article.

INTRODUCTION

Herbs have played a vital role in therapeutic applications and they are studied and utilized for ages. They are called "fountain of life energy". In Vedic and Ayurvedic literature, the usage of this therapeutic herb is documented in great detail. These practices have greatly influenced human life color along with the regular hits hold life along with the scientific know–how's in the molecular level with the biochemical and phytochemical composition of the plant and the plant compounds have finished a great deal in the sympathetic of this miraculous plant. ^[1,2]

Giloy or *Tinospora cordifolia* Linn. has a significant place in these literatures. It is a perennial climbing shrub, belonging to the moonseed family, Menispermaceae; which contains 70 genera and 400 species. It is commonly called Guduchi, Amrita, Gurach, and Tinospora. The plant may be found in India's tropical areas, reaching a height of 300 meters from Kumaon through Assam and Myanmar, Bihar, Konkan, and Sri Lanka. ^[3,4]

It is widely used as a powerful tonic and its frequent use has shown considerable enhancement in the immune system which is equipped to battle a variety of common health problems like anti-diabetic, antipyretic, antispasmodic, anti-inflammatory, anti-arthritic, antioxidant, anti-allergic, anti-stress, anti-leprotic, antimalarial, hepato-protective, immuno-modulatory, and anti-neoplastic effects have been documented by various scientific studies. The active components from Giloy increase the growth of stem cells in our bodies. Its frequent ingestion raises the overall number of WBCs as well as the number of antibodies. It is one of the naturally immuno-modulator herbs and hence gained more attention since the Covid-19 pandemic situation. The immunomodulatory activity of Giloy is carried out by phytoconstituents with the ability to activate, enhance, repair immune systems and help to combat both common or chronic health issues.^[5] It also aids in the treatment of autoimmune illnesses like cancer, rheumatoid arthritis and the removal of toxins from our liver and kidneys, therefore avoiding the development of chronic liver disorders. ^[6]

Although it shows multifunctional characteristics, it's immunomodulatory and antiviral activity is most appreciated during Covid-19 and hence focused in the present study.

MATERIALS AND METHODS

Numerous authentic printed and electronic publications are taken into account for the review of *T. cordifolia* regarding Pharmacognostic characteristics, phytoconstituents, therapeutic uses, pharmacological studies, etc. Genuine materials published in PubMed, Science Direct

Google Scholar, and Research gate were referred to assemble all the latest data. The Images of various parts of Giloy were collected by self in Maharashtra, India.

Vernacular Names of Giloy: [4,7]

1. Sanskrit: Guduchi, Amrita

2. Bengali: Golancha

3. English: Tinospora

4. Gujarati: Gulvel

5. Hindi: Gulancha

6. Kannada: Amrutaballi, Madhuparni

7. Malayalam: Amrytu, Chittamrita

8. Oriya: Giochi

9. Tamil: Amudam, Chindi.

10. Telugu: Tippateege, Guricha

11. Gilo, Satgilo

Taxonomical Classification of Giloy: [4,8]

1. Kingdom: Plantae

2. Subkingdom: Tracheobionta

3. Division: Magnoliophyta

4. Class: Magnoliopsida

5. Subclass: Ranunculidae

6. Order: Ranunuculales

7. Family: Menispermaceae

8. Genus: Tinospora

9. Species: Cordifolia

MORPHOLOGY

It is a large, slender, stretching steeple shrub with long twin branches. The stems are succulent, and the branches are formed by long Filiform mushy aerial roots. The bark is wet and grey-brown. [3, 4]

The leaves are simple, heart-shaped, alternate, and explicit with long, roundish petioles, pulvinus at the base and the apex, with the basal one lengthier, partially and halfway twisted.

The name is derived from its cardiovascular leaves and shrimp berries. The lamina is widely oblong and ovate, 10-20 cm long and 8-15 cm (3-6 in) wide and 7 nerve and deep corded at the base, cone-like, pubescent above, and a white tomentose beneath with a remarkable reticulum. Flowers are tiny, greenish-yellow, unisexual, emerges on axillary and terminal races, when the plant is leafless. Male flowers are grouped, while the female flowers are generally present as single. There are six sepals in two sets of triplets. The external flowers are smaller than the insider ones. Petals are smaller, obovate, and membranous than sepals. The fruits are aggregated in one to three clusters. Fruits are ovoid, fleshy, reddish having a single seed. Fruiting is seen in September-October. On stout stalks with sub-terminal scars, scarlets, or orange colors. They avoid smooth drupelets. [4,8]



Figure No. 1.1: Fruits of Giloy

Figure No. 1.2: Giloy leaves, stems, and roots.

PART OF THE PLANT USE

Most researchers have studied almost all parts i.e., roots, stem, leaves and fruits to show therapeutic phytoconstituents from Giloy.

PHYTO-THERAPEUTICS OF GILOY

Several reports have shown the positive effects of herbal extracts as an antiviral agent used in animal feed or as prophylaxis and remedy. Besides being a cheaper and safer alternative, the use of herbs may reduce the incidence of drug resistance and may modulate the immune system in preventing viral diseases. Different phytoconstituents have been isolated from all parts of the *T. cordifolia* plant belonging to different classes of secondary metabolites such as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds, and polysaccharides. ^[9, 10]

The whole plant of *T. cordifolia* contains diterpenoid lactones like furanolactone, tinosporin, columbin, dioscorides, neosporin, jateorine; aliphatic compounds like octacosanol, octacosanol, cleodrane derivatives [11] i.e. (5R, 10R)-4R-8R-dihydroxy-cleroda-13(16), 14-die no-17, 12S:18, 1S-dilactone and miscellaneous compounds like Nonacosan-15-one 3, a 4-dihTinosporamethoxy-benzyl)-4-(4-hydroxy-3-methoxy-benzyl)-tetrahydrofuran, tinosponidine, 6-cortisol, 6-cordifelone, 6-jatrorrhizine. Aerial parts are reported to contain steroids like b-sitosterol, d-sitosterol, g-sitosterol b-hydroxyecdysone, ecdysterone, mastertone, giloinsterol. [12] The active constituents octacosanol, nanocosan-15-one dichloromethane, heptacosanol are reported with anti-nociceptive and anti-inflammatory activity. They also inhibit TNF- α from binding to the DNA and provide protection against 6-hydroxydopamine induced Parkinsonism in rats. [13] Cleodrane derivatives showed biological actions such as vasorelaxant, anti-inflammatory, anti-microbial, anti-hypertensive, and anti-viral. [11, 12]

Leaves of the plant are rich in protein (11.2%) and are fairly rich in minerals like calcium and phosphorus.

The stem of *T. cordifolia* contains alkaloids eg: berberine, palmatine D, choline D, tinospora, magnoflorine, tetrahydropalmatine, isocolumbin, glycosides eg: furanoid diterpene glycoside, tinocordiside, syringin, syringin-apiosylglycoside, tinocordifolioside, cordioside, cordifolioside A, cordifolioside B, palmatine C31, palmatine F31, cordiofoliside B2, cordifoliside D2, cordifoliside sesquiterpenoid eg: Tinocordifolin. [13, 14] The stem also accommodates sesquiterperiods and tinocordifolin which exhibits an antiseptic activity. In both acute and subacute inflammatory models, *T. cordifolia* dried stem has demonstrated a strong anti-informational impact. The *T. cordifolia* was shown to be more efficient than acetylsalicylic acid in acute inflammation. [15]

Roots contain alkaloids such as palmatine. ^[12] Ayurvedic Indian Medicine, *T. cordifolia* is frequently used to treat diabetic mellitus. A decrease in blood glucose level and brain lipid decline was testified by oral administration of the aqueous *T. cordifolia* root extract into alloxan diabetic mice. ^[16] *T. cordifolia's* aqueous extract has demonstrated possible antioxidant activity in rats with alloxan diabetes. The treatment of *T. cordifolia* root extract (2.5, 50 mg/kg body weight) for 6 weeks resulted in a substantial decrease in blood and tissue cholesterol, phospholipids, and free fatty acids in alloxan diabetic rats. ^[17]

The stem and root parts of *T. cordifolia* are reported to contain alkaloids like terbutaline, choline, magnoflorine, berberine, neosporin, isocolumbin, palmatine, jatrorrhizine, aporphine alkaloids, tetra-dropalmatine which showed anti-ulcer, ^[18] anti-diabetes, anti-viral, anti-inflammatory, anti-psychiatric, and immunomodulatory action. ^[19, 20]

The seed constituents have shown diuretic and stomachic properties. It stimulates bile production, causes constipation, relieves hunger, searing pain, diarrhea, blood enrichment, and heals jaundice. [21, 22]

Shoot chunk of *T. cordifolia* restrain Steroids (B-sitosterol, δ -sitosterol, 20 β -hydroxyecdysone, giloinsterol, makisterone A, ecdysterone). They are effective in glucocorticoid-induced osteoporosis in early inflammatory arthritis. They induce cell cycle arrest in the G2/M phase and inhibits TNF- α , IL-1 β , IL-6, and COX-2, and apoptosis through c-Myc suppression.

Some constituents of *T. cordifolia* such as Jatrorrhizine, Tinosporic acid, 3, (a 4-dihydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxy-benzyl) tetrahydrofuran, N-trans-feruloyltyramine as diacetate, gilpin. These compounds have been reported to show protection against HIV (human immunodeficiency virus). [21, 22]

The constituents like 18-norcleodrane glucoside, tinocordifolioside, cordioside, cardio inside A, B, C, D, and E, furanoid diterpene glucoside, syringin, pregnane glycoside syringing-apiosylglycoside, palmatosides showed immunomodulation in Parkinson's disease, dementia, motor, and cognitive disorder, neurological disorders like ALS. They inhibit NF-k Band to show anti-cancer properties. [13] The secondary phytoconstituents demonstrated anti-cancer, anti-diabetes, anti-viral, anti-inflammatory, antipsychiatric, and immunomodulatory effects are terbutaline, choline, magnoflorine, berberine, neosporin, isocolumbin, palmatine, jatrorrhizine, aporphine alkaloids, and tetra-hydropalmatine. [19]

The hepatoprotective capacity of *T. cordifolia* extracts is another significant feature. An experiment showed substantial improvement in CCl4-induced hepatopathy clinically and studied hemato-biochemically in goats treated with *T. cordifolia*. It also has inactivating characteristics in-vitro against hepatitis B and E surface antigens. ^[23, 24, 25]

Giloy has demonstrated anti-inflammatory properties like indomethacin or nonsteroidal drugs. It reduces histamine-induced bronchospasm in animals. 1,4-alpha-D-glucan activates macrophages, NFB translocation, and cytokine production to boost immunity. It has shown

antipyretic $^{[26]}$ and antimicrobial $^{[25]}$ properties also. The structures of Phytoconstituents from *T. cordifolia* are mentioned in the following Figure no. 2. & 3. $^{[27,28]}$

FOLK REMEDIES

Leaves: Gout, ulcers, jaundice, fever, wounds treatments and to control blood glucose level.

Stem: Water extract or mixture with honey used for the treatment of jaundice, skin diseases, fever. Stem starch i.e., Sativa can be used as tonic, antidote to snakebite and scorpion sting.

Bark: Powder along milk is given for dealing with cancer.

Fruits: Jaundice and rheumatism.

Roots: Emetic for visceral obstructions, leprosy, diarrhea, and dysentery. Powder along milk is given for dealing with cancer.



Figure: 2: Structres of Phytoconstituents of T. cordifolia

Figure No. 3: Structres of Phytoconstituents of *T. cordifolia* [27]

Table No. 1: Essential constituents of *T. cordifolia*^[27]

Active Component	Compounds		
Terpenoids [29,30] Glycosides of Cleroden & Non-cleroden skeleton	Tinosporide, Furanolactone diterpene, Furanolactone clerodane diterpene, furanoidditerpene, Tinosporaside, ecdysteronemakisterone and several glucosides isolated as poly acetate, phenylpropene disaccharides cordifolioside A, B and C, cordifoliside D and E, tinocordioside, cordioside, palmatosides C and F, sesquiterpene glucoside tinocordifolioside, sesquiterpene tinocordifolin		
Alkaloids [12, 31]	Tinosporine, (S), Magnoflorine, (S), Berberine, (S), Choline,		
Isoquinolin, Atropine skeleton	(S), Jatrorrhizine, (S), 1,2-Substituted pyrrolidine(S), Alkaloids, viz. jatrorrhizine, palmatine, beberine, tembeterine, choline.		
Lignans [32]	3 (a, 4-dihydroxy-3-methoxybenzyl)-4-(4-hydroxy-3-methoxybenzyl)		
Steroids [33]	Giloinsterol, (S), β-Sitosterol, (S), 20a- Hydroxy ecdysone, (S),		
δ- sitosterol	2,3,14,20,22,25-hexahydroxyl-5-cholest-7-en-6-one		
Phenolics [32, 34]	Phenypropanoids, Flavonoids, benzenoid		
Essential oil & aliphatic compounds [34]	Alcohol (32.1%, phenols, aldehydes, fatty acids, alkanes, esters, terpines, hydroquinone, 2-hexenal, palmitic acid, phytol, methyl-9,12-octadecadienoate, methyl 9-octadecenoate,		
Primary Metabolites [35]	Polysaccharides like: Glucose, arabinose, galactore, mannose, rhamnose, xylose Proteins Minerals: Calcium, Phosperous		
Others [29, 36]	Giloin, Tinosporan acetate, Tinosporal acetate, Tinosporidine, Heptacosanol, Octacosanol, sinapic acid, heptacosanol, octacosanol, noncosanol-15-one, cyvlohexyl-11- heneicosanoneTinosponone, two phytoecdysones, arabinogalactan, giloinsterol, giloin, giloinin, gilo-sterol, tinosporan acetate, tinosporic acid, tinosporal acetate, tinosporone, tinosporal, tinosporide, cordifolide & furanolactone diterpines		

TOXICOLOGY

It is described as a safe drug. There are no reports of any toxicity in humans. But high doses may cause constipation. [37, 38]

IMMUNOMODULATORY COMPETENCE

Numerous diseases like arthritis, ulcerative colitis, asthma, allergy, parasites, cancer, and other infectious diseases are the cause of dysfunction of the immune system. [17, 67] T. cordifolia has been reported to induce immunomodulatory properties according to multiple researchers. [39, 40, 41] Aqueous extract has shown immunomodulatory activity. [42] The phytoconstituents like 11-hydroxymustakone, N-methyl-2-pyrrolidone, N-formylannonain, cordifolioside A, magnoflorine, tinocordiside, and syringin are active chemicals have been demonstrated for immunomodulatory and cytotoxic properties. [40, 41, 43, 44] They are proved with the function of increasing macrophage phagocytic activity, producing reactive oxygen species (ROS) in human neutrophil cells and increasing nitric oxide (NO) generation via stimulating splenocytes and macrophages, which is indicative of anti-tumor actions. [45] Aqueous Tinospora extracts have also been shown to impact cytokine synthesis, mitogenicity, immune effector cell stimulation, and activation. [45] Extracts have been found in mice to cause an increase in the cytokine IL-6, resulting in rapid responses to injury, inflammation, activation of cytotoxic T cells, and B cell differentiation. [46, 47] In an experimental rat model, active chemicals in aqueous extracts such as alkaloids, di-terpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds, or polysaccharides were shown to be cytotoxicity. [46] Extracts of dry stem effects of T. cordifolia have been reported to improve immunological response in mice by promoting IL-1 production and macrophage activation. There have also been reports of T. cordifolia being used to reduce oxidative damage. [48]

Table 2: Phyto constitution of T. cordifolia mechanism of action of some important phytochemicals and their activities. [12]

Phytoconstituents of <i>T. cordifolia</i>	Activity	Mechanism of action
Quinones	Antimicrobial	Binds to adhesions, complex with the cell wall,
		inactivate enzymes
Flavonoids	Antimicrobial	Complex with the cell wall binds to adhesins,
		inhibits release of autacoids and prostaglandins.
	Antidiarrheal	Inhibits contractions caused by spasmogens,
		stimulates normalization of the deranged water
		transport across the mucosal cells, inhibits GI
		release of acetylcholine
	Antimicrobial	Binds to adhesions, enzyme inhibition, substrate
		deprivation, complex with cell wall, membrane
		disruption, metal ion complexation
	Antidiarrheal	Makes intestinal mucosa more resistant and reduces
		secretion, stimulates normalization of deranged
Polyphenols and Tannins		water transport across the mucosal cells and
		reduction of the intestinal transit, blocks the binding
		of B subunit of heat- labile enterotoxin to GM1,
		resulting in the suppression of heat-labile
		enterotoxin-induced diarrhea, astringent action
	Anthelmintic	Increases supply of digestible proteins by animals
		by forming protein complexes in the rumen,
		interferes with energy generation by uncoupling
		oxidative phosphorylation, causes a decrease in the
		G.I. metabolism
Coumarins	Antiviral	Interaction with eukaryotic DNA
Terpenoids and	Antimicrobial	Membrane disruption
essential oils	Antidiarrheal	Inhibits release of autocoids and prostaglandins
	Antimicrobial	Intercalates into cell wall and DNA of parasites
	Antidiarrheal	Inhibits release of autocoids and prostaglandins

Alkaloids	Anthelmintic	Possess anti-oxidating effects, thus reduces nitrate generation which is useful for protein synthesis, suppresses transfer of sucrose from the stomach to the small intestine, diminishing the support of glucose to the helminths, acts on CNS causing paralysis
Lectins and	Antiviral	Blocks viral fusion or adsorption, forms disulfide
Polypeptides		bridges
Glycosides	Antidiarrheal	Inhibits release of autocoids and prostaglandins
	Antidiarrheal	Inhibits histamine release in vitro
Saponins	Anticancer	Possesses membrane permeabilizing properties
	Anthelmintic	This leads to vacuolization and disintegration of
		teguments
Steroids	Antidiarrheal	Enhance intestinal absorption of Na+ and water

Tinospora cordifolia derived (1,4)-alpha-d-glucan (alpha-d-glucan) has been demonstrated to activate human lymphocytes in vitro, with downstream production of pro-and anti-inflammatory cytokines. [49, 50, 51]

There are also reports of synergistic effects on *T. cordifolia* immunomodulatory activity of substances. ^[43] Chemotherapeutic substances are currently predominantly immunosuppressive, but the majority are cytotoxic and have a spectrum of adverse effects. Thus, medicinal plants are becoming important sources of immunomodulatory drugs, as do their active components. Several researchers have found that plant components are used to improve macrophage phagocytic capacities and to promote antibody production by B cells. ^[52]

ANTIVIRAL POTENTIAL

Viral diseases are emerging these days with multiple modifications and disasters to not only the human race but to all animals as well as plants. The most common viral disease affecting humans at a large population level comprises cholera, zeka virus, shigella, chikungunya, waste niger virus, meningitis, typhoid, yellow fever, AIDS followed by flue like SARS-Covid-SARI etc.

The crude extract of dry stem of *T. cordifolia* showed antiviral activity against herpes simplex virus which was evaluated by MTT assay. [53] Acquired Immuno-deficiency syndrome, AIDS is a deadly disease produced by HIV which breaks down the host immune system and lets the person suffer opportunistic and neurological illnesses that are lifethreatening. [54] The primary problem of HIV infections is the lack of thymus-derived cells. [55] The significant impact of immune-stimulation in the *T. cordifolia* extract was shown by research performed with an HIV-positive volunteer group (TCE). There was a decrease in eosinophil count as compared to controls, indicating the immunomodulatory action of the T. cordifolia stem extract. [55] In further research, the effects of E. coli caused peritonitis are shown for the T. cordifolia extract from a mouse study. The bacterial clearance has substantially increased and the phagocytic and intracellular bacterial capacity of neutrophils, treated mouse groups, has improved in the *T. cordifolia* extract. The treatment of plants displayed some immunomodulatory effects rather than control. [56] In addition, immunomodulators Tinospora reduces the risk and enhances the effect of obstructive jaundice following surgery and should be included in preoperative treatment for jaundiced patients. To avoid sepsis and immunosuppression, the requirement for hours is immune regulation in case of surgeries. In addition, the phagocytosis and inter-cellular killing capability are increased by improving the survival rate and polymorphonuclear leucocyte function in patients with obstructive jaundiced patients with TEC regular surgery. [57,58]

The PMNs are white blood cells from the marrow of the bone that plays an important function in protecting the body against infection. PMNs are drawn to invade micro-organisms and are inducted to phagocytose by their contact with antibodies, supplements, and chemotaxis factors. [58]

GILOY AND COVID-19

COVID-19 is a highly contagious illness caused by the virus SARS-CoV-2 that became a worldwide pandemic. In absence of exact treatment or vaccination available to combat this condition in which the primary target was the body's immune system, people were searching for herbal remedies. Many different sorts of research are being performed to produce specific immunomodulators, antiviral agents and vaccines for SARS-CoV-2. In Ayurveda, the idea of epidemic condition (Janapadodhwanasa) is described and different measures, including Rasayana dravyas, are stated for prevention and treatment of such illnesses (immunomodulatory drugs). [59, 60]

T. cordifolia (Wild.) Miers is an immune-modulator medication used in Ayurveda that possesses antioxidant, immunomodulatory, anti-inflammatory, anti-allergic, antiviral and antihyperglycemic effects. Scientific study on this medication may provide a novel strategy as well as information for COVID-19 prevention, treatment, and the creation of a new therapeutic entity. The in-silico study performed using tools of network pharmacology, molecular docking including molecular dynamics has revealed that among all considered phytochemicals in *Tinospora cordifolia*, berberine can regulate 3CL^{pro} protein's function due to its easy inhibition and thus can control viral replication. [61] In a recent study, the aqueous extracts of T. cordifolia as a means of treatment to the SARS-CoV-2 spike-protein induced disease phenotype in a humanized zebrafish model comparing to the reference compound, Dexamethasone. Findings reported morphological, cytological, and behavioral changes observed with induction of SARS-CoV-2 spike-protein were rescued to near normal levels with GG treatment. [62] The five phytoconstituents of T. cordifolia, namely, berberine, bsitosterol, coline, tetrahydropalmatine and octacosanol were evaluated using the molecular dynamics approach and berberine was found to function of regulating 3CLpro proteins by inhibition and subsequently control the viral replication. [61] Tinocordiside, one of the phytochemicals of Giloy, showed inhibition of main protease of SARS-CoV-2 in a molecular docking study. [63] Berberine, isocolumbin, magnoflorine and tinocordiside compounds isolated from Giloy showed high binding efficacy against all the four key SARS-CoV-2 target surface glycoprotein (6VSB), receptor-binding domain (6M0J), RNA dependent RNA polymerase (6M71), and main protease (6Y84) involved in virus attachment and replication. [5]

Covid-19 positive patients having signs and symptoms of Covid-19 in age group >18 years <60 years were investigated to study the efficacy of the combination Giloy, Gaumutra Capsules, Asthi Churna and Kamdhenu Aasava resulted in the Management of the Pandemic-Covid-19. [64]

CONCLUSION

The global acceptance of Ayurveda largely depends on evidence-based efforts. Providing backing up of systematic reviews is one such requisite. Giloy is a celebrated herb from the science of Ayurveda. Though much deliberation has been done on its adaptogen effects. Still, it holds a lot of potential in terms of immunomodulatory activities. The free radical scavenging activity demonstrating the importance of Giloy in the medical therapeutic field.

[65, 66] Also, its anti-viral activity on viral hepatitis and HIV is promising. *T. cordifolia's* chemical components include alkaloids, glycosides, hormones, phenolic, aliphatic chemicals, polysaccharides, protein-rich leaves, calcium, and phosphorus. Chlordane furono diterpene glucoside is found in the stem (Amrithocides). It was seen that the numbers of studies for assessing action against COVID-19 were more as compared to other studies. The phytoconstituents from Giloy like berberine, β- sitosterol, octacosanol, tetrahydropalmatine, and choline with 2CL-Protargets I, II of Protease enzyme may show the potential as a drug of choice for SARS-CoV-2 or called Covid-19. This is a welcome gesture towards government efforts to bring Giloy as prophylactic treatment of COVID19. Laboratory studies show a hopeful scenario. It can be assumed that clinical studies will be carried out and published soon in this regard. Thus, the above findings clearly indicate that the use of Giloy for activities such as immunomodulatory, anti-viral and especially against COVID-19 has a logical and scientific basis.

CONFLICT OF INTEREST STATEMENT

The Authors declare no conflict of interest.

REFERENCES

- 1. Kumar DV, Geethanjali B, Avinas KO, Kumar J. *Tinospora cordifolia:* The antimicrobial property of the leaves of amruthaballi. *Bacteriol J: Mycol.* 2017.
- 2. Sastri BN. The Wealth of India. A Dictionary of Indian Show Raw materials and Industrial Products. Raw Materials. 1962; Vol. 6: L-M 483.
- 3. Sarangi MK, Soni S. A Review on Giloy: The Magic Herb. Inventi Rapid: Planta Activa. 2013.
- 4. Nadkarni KM. Indian Materia Medica. Popular Prakashan, Bombay. 1976; Vol. 1, p. 1142.
- 5. Sagar V, Kumar AH. Efficacy of natural compounds from Tinospora cordifolia against SARS-CoV-2 protease, surface glycoprotein and RNA polymerase. *Virology*. 2020; 1-10.
- 6. Krishan S. Immunomodulatory Effect of Giloy (Tinospora cordifolia). 2020.
- 7. Yadav M, Yadav P, Shameem A, Singh P, Kumar S. Department of pharmacy 222001.U.P. INDIA. 2014.
- 8. Sinha K, Mishra N, Singh K. *Tinospora cordifolia* (Guduchi). A reservoir plant for therapeutic app. locations. *Indian Journal of Traditional Knowledge*. 2004; 3 (3),257-270.
- 9. Khan MM, Dul-Haque MS, Chowdhury MS. Medicinal use of the unique plant *Tinospora cordifolia*: evidence from traditional medicine and recent research. *Asian J Med Biol Res.* 2016; 2(4), 508–512.
- 10. Bisset NG, Nwaiwu J. Quaternary alkaloids of Tinospora species. *Planta Med.* 1983;48, 275–279.
- 11. Bhatt RK, Hanuman JB, Sabata BK. A new clerodane derivative from Tinospora cordifolia's Phytochemistry. 1988; 27, 1212-1216.
- 12. Chaudhary N, Siddiqui MB, Azmat A, Khatoon S. *Tinospora cordifolia:* Ethnobotany, Pharmacology, and Phytochemistry Aspects. *Int J pharma Sci* Res. 2013; 4(3), 891-899.
- 13. Wazir V, Maurya R, Kapil RS. Cordioside, a clerodane furano diterpene glucoside from Tinospora cordifolia. Phytochemistry. 1995 Jan 1;38(2):447-9.
- 14. Maurya R, Handa SS. Tinocordifolin, a sesquiterpene from Tinospora cordifolia. Phytochemistry. 1998 Nov 5;49(5):1343-5.

- 15. Jana U, Chattopadhyay RN, Show BP. Preliminary Studies on anti-inflammatory activity of Zingiber Officinale Rosc., Vitex negundo Linn. And *Tinospora cordifolia* (Wild) Miers in albino rats. *Indian J Pharm*. 1999; 31(3), 232-233.
- 16. Dhaliwal KS. Hepatoprotective compositions *and* composition *for* treatment *of* conditions related *to* hepatitis B and E infection. 1999; US Patent 749296. 20.
- 17. Stanely M, Prince P, Menon VP, Gunasekaran G. Hypolipidaemic action of *Tinospora cordifolia* roots in alloxan diabetic rats). *J Ethnopharmacol*. 1999; 64(1), 53-57.
- 18. Sharma DN, Khosa RL, Chansauria JP, Sahai M. Antiulcer activity of *Tinospora cordifolia* Miers and *Centella Asiatica* Linn. extracts. *Phytother Res.* 1995; 9:589.
- 19. Patel MB, Mishra S. Hypoglycemic activity of alkaloidal fraction of Tinospora cordifolia. Phytomedicine. 2011 Sep 15;18(12):1045-52.
- 20. Kundnani KM, Mahajan VR, Jolly CI. A new hypoglycaemic agent from Tinospora cordifolia: Miers. Indian Drugs. 1985;23(2):119-20.
- 21. Aiyer KN, Kolammal MM. Pharmacognosy of Ayurvedic drugs. Dept. of Pharmacognosy, University of Kerala, Trivandrum. 1963;1(7):102-5.
- 22. Raghunathan K, Mitra R. Pharmacognosy of indigenous drugs: Central Council for Research in Ayurveda and Siddha. New Delhi. 1982; 1:127-39.
- 23. Maddi R, Kandula VL, Vallepu B, Navuluri H, Kolluri H, Vunnam DT. Preliminary Phytochemical Analysis and Invitro Antiviral Activity of Ethanolic extract of Whole plant of Tinospora cordifolia (Thunb.) Miers against Hepatitis-A Virus. Int. J. Sci. Res. in Biological Sciences Vol. 2018 Jun; 5:3.
- 24. Tiwari S, Talreja S. A Concept to Treatment of Hepatitis Virus by Herbal Remedies. Journal of Pharmaceutical Sciences and Research. 2020 Aug 1;12(8):1088-92.
- 25. Kattupalli SO, Vesta VA, Vangara SA, Spandana UP. The multi-activity herbaceous vine-Tinospora cordifolia. Asian Journal of Pharmaceutical and Clinical Research. 2019;12(3):23-6.
- 26. Vedavathy S, Rao KN. Antipyretic activity of six indigenous medicinal plants of Tirumala Hills, Andhra Pradesh, India. Journal of ethnopharmacology. 1991 May 1;33(1-2):193-6.
- 27. Sharma P, Dwivedee BP, Bisht D, Dash AK, Kumar D. The chemical constituents and diverse pharmacological importance of Tinospora cordifolia. Heliyon. 2019 Sep 1;5(9): e 02437.
- 28. Pradhan D, Kar DM, Ghosh G. Bioassay-guided Fractionation of Anti-microbial principle from Ethanolic Extract of Tinospora cordifolia and its Characterization. Research Journal of Pharmacy and Technology. 2020;13(3):1415-22.
- 29. Khuda MQ, Khaleque A, Basar KA, Rouf MA, Khan MA, Roy N. Studies on Tinospora cordifolia II: Isolation of tinosporine, tinosporic acid and tinosporol from the fresh creeper, Sci Res,(Dacca), III (1966) 9. *In Chem Abstr* .1966; 65, 10549a.
- 30. Gagan VD, Pradhan P, Sipahimalan AT, Banerji A. Palmatosides C, F: Diterpene furan glucosides from *Tinospora cordifolia*-Structural elucidation by 2D NMR spectroscopy. *Indian Journal of Chemistry*. 1996;35B, 630–634.
- 31. Pathak AK, Agarwal PK, Jain DC. NMR studies of 20p-hydroxyecdysone, a steroid; isolated from Tinospora cord~ roliatt. Indian journal of chemistry. 1995 Jul;34: 674-6.
- 32. Hanuman JB, Bhatt RK, Sabata BK. A diterpenoid furanolactone from Tinospora cordifolia. Phytochemistry. 1986 Jan 1;25(7):1677-80.
- 33. Kidwai AR, Salooja KC, Sharma VN, Siddiqui S. Chemical examination of Tinospora cordifolia. Journal of Science and Indian Research. 1949; 8:115-8.
- 34. Uchejeso OM, Chinaza IR, Goodluck OA, Rinpan JI. Some Igbo Indigenous Plants with Anti-COVID-19 Properties. *In Alternative Medicine*. 2020 Nov 9.
- 35. Singh S, Maan NS, Rana V, Jyotsana J, Tewatia BS, Sheoran N. Effect of dietary inclusion of Giloy (Tinospora cordifolia) stem powder on growth performance and metabolizability in broilers. Journal of Entomology and Zoology Studies. 2018;6(5):36-40.
- 36. Chintalwar G, Jain A, Sipahimalani A, Banerji A, Sumariwalla P, Ramakrishnan R, Sainis K. An immunologically active arabinogalactan from Tinospora cordifolia. Phytochemistry. 1999 Nov 1;52(6):1089-93. 37. Singh D, Chaudhuri PK. Chemistry and pharmacology of Tinospora cordifolia. Natural product communications. 2017 Feb;12(2):1934578X1701200240.

- 38. Sunanda SN, Desai NK, Ainapure SS. Antiallergic properties of Tinospora cordifolia in animal models. Indian Journal of Pharmacology. 1986 Oct 1;18(4):250.
- 39. Bishayi B, Roychowdhury S, Ghosh S, Sengupta M. Hepatoprotective and immunomodulatory properties of Tinospora cordifolia in CCl4 intoxicated mature albino rats. The Journal of toxicological sciences. 2002;27(3):139-46.
- 40. Subramanian M, Chintalwar GJ, Chattopadhyay S. Antioxidant properties of a Tinospora cordifolia polysaccharide against iron-mediated lipid damage and γ -ray induced protein damage. Redox Report. 2002 Jun 1;7(3):137-43.
- 41. Sharma U, Bala M, Kumar N, Singh B, Munshi RK, Bhalerao S. Immunomodulatory active compounds from Tinospora cordifolia. Journal of ethnopharmacology. 2012 Jun 14;141(3):918-26.
- 42. Upadhyaya R, Pandey RP, Sharma V, Verma Anita K. Assessment of the multifaceted immunomodulatory potential of the aqueous extract of Tinospora cordifolia. Research Journal of Chemical Sciences. 2011; 2231:606X.
- 43. Kapil A, Sharma S. Immunopotentiating compounds from Tinospora cordifolia. Journal of ethnopharmacology. 1997 Oct 1;58(2):89-95.
- 44. More P, Pai K. In vitro NADH-oxidase, NADPH-oxidase and myeloperoxidase activity of macrophages after Tinospora cordifolia (guduchi) treatment. Immunopharmacology and immunotoxicology. 2012 Jun 1;34(3):368-72.
- 45. Sudhakaran DS, Srirekha P, Devasree LD, Premsingh S, Michael RD. Immunostimulatory effect of Tinospora cordifolia Miers leaf extract in Oreochromis mossambicus. *Indian J Exp Biol.* 2006; 44,726–32.
- 46. Raghu R, Sharma D, Ramakrishnan R, Khanam S, Chintalwar GJ, Sainis KB. Molecular events in the activation of B cells and macrophages by a non-microbial TLR4 agonist, G1-4A from *Tinospora cordifolia*. *Immunol Lett.* 2009; 123,60–71.
- 47. Koppada R, Norozian FM, Torbati D, Kalomiris S, Ramachandran C, Totapally BR. Physiological Effects of a Novel Immune Stimulator Drug,(1, 4)-α-d-Glucan, in Rats. Basic & clinical pharmacology & toxicology. 2009 Oct;105(4):217-21.
- 48. Jahfar M. Glycosyl composition of polysaccharide from Tinospora cordifolia. Acta pharmaceutica (Zagreb, Croatia). 2003 Mar 1;53(1):65-9.
- 49. Nair PR, Melnick SJ, Ramachandran R, Escalon E, Ramachandran C. Mechanism of macrophage activation by (1, 4)- α -D-glucan isolated from Tinospora cordifolia. International Immunopharmacology. 2006 Dec 5;6(12):1815-24.
- 50. Saha S, Ghosh S. Tinospora cordifolia: One plant, many roles. Ancient science of life. 2012 Apr;31(4):151.
- 51. Upadhyay AK, Kumar K, Kumar A, Mishra HS. Tinospora cordifolia (Willd.) Hook. f. and Thoms. (Guduchi)—validation of the Ayurvedic pharmacology through experimental and clinical studies. International Journal of Ayurveda research. 2010 Apr;1(2):112.
- 52. Sundarraj S, Thangam R, Sreevani V, Kaveri K, Gunasekaran P, Achiraman S, Kannan S. γ -Sitosterol from Acacia nilotica L. induces G2/M cell cycle arrest and apoptosis through c-Myc suppression in MCF-7 and A549 cells. Journal of ethnopharmacology. 2012 Jun 14;141(3):803-9.
- 53. Pruthvish R, Gopinatha SM. Antiviral prospective of Tinospora cordifolia on HSV-1. International Journal of Current Microbiology and Applied Sciences. 2018;7(01):3617-24.
- 54. Park, K. Preventive medicine in obtestpediatrics and Geriatrics. In: *Park's textbook on preventive and social medicine*, 24th ed. Jabalpur: M/S Banarasidas Bhanot Publishers. 2017.
- 55. Kalika MV, Thawani VR, Varadpanda UK, Sontakke SD, Singh RP, Khiyani RK, Tripathi YB, Sharma M, Manickam M. A new Antioxidant from Rubia cordifolia. Indian J Biochem Biophys. *Int J Pharma*. 1997; 34,302–6.
- 56. Thatte UM, Kulkarni MR, Dahanukar SA. Immunotherapeutic modification of Escherichia Coli peritonitis and bacteremia by *Tinospora Cordifolia*. *J Postgrad Med*. 1992; 38(1),13-15.
- 57. Bapat RD, Rege NN, Koti R, Desai NK, Dahanukar SA. We Do Away with PTBD. *HPB Surg*. 1995; 9(1), 5-11.
- 58. Roth JA, Kaberle ML. Evaluation of bovine Polymorphonuclear leukocyte function. *Vet Immunol Immunopathol.* 1981; 2(2),157-174.

- 59. Gupta A, Vedula S, Srivastava R, Tamoli S, Mundhe N, Wagh DN, Batra S, Patil M, Pawar HB, Rai RK. Prospective, randomized, open-label, blinded end point, two-arm, comparative clinical study to evaluate the efficacy and safety of a Fixed Ayurvedic Regimen (FAR) as add-on to conventional treatment in the management of mild and moderate COVID-19 patients. Journal of Pharmacy And Bioallied Sciences. 2021 Apr 1;13(2):256.
- 60. Srivastava AK, Singh VK. Tinospora cordifolia (GILOY): A MAGICAL SHRUB. Asian Journal of Advances in Medical Science. 2021 Apr 20:22-30.
- 61. Chowdhury P. In silico investigation of phytoconstituents from Indian medicinal herb 'Tinospora cordifolia (giloy)'against SARS-CoV-2 (COVID-19) by molecular dynamics approach. Journal of Biomolecular Structure and Dynamics. 2020 Aug 6:1-8.
- 62. Balkrishna A, Khandrika L, Varshney A. Giloy Ghanvati (Tinospora cordifolia (Willd.) Hook. f. and Thomson) Reversed SARS-CoV-2 Viral Spike-Protein Induced Disease Phenotype in the Xenotransplant Model of Humanized Zebrafish. Frontiers in Pharmacology. 2021 Apr 19; 12:534.
- 63. Shree P, Mishra P, Selvaraj C, Singh SK, Chaube R, Garg N, Tripathi YB. 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. Journal of Biomolecular Structure and Dynamics. 2020 Aug 26:1-4.
- 64. Gaushala BG. Giloy Gomutra Capsule, Asthi churna aur Kamdhenu Asava ka vaishvik mahamari Covid-19 par logo ka anubhav aur Chikitsakiya prabhava ka Ankalan.2020.
- 65. Tiwari P, Nayak P, Prusty SK, Sahu PK. Phytochemistry and Pharmacology of *Tinospora cordifolia*: A review. *Free Radicals and Antioxidants*. 2018; 9(1),70-80.
- 66. Sharma A, Gupta A, Singh A, Batra A. *Tinospora cordifolia* (Willd.) A plant with immense economic potential. *Journal of Chemical and Pharmaceutical Research*. 2010; 2(5), 327-333.
- 67. Saha, S., & Ghosh, S. (2012). Tinospora cordifolia: One plant, many roles. *Ancient science of life*, 31(4), 151.

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