REVIEW ARTICLE

Giloy (Amrita) *Tinospora cordifolia:* Its phytochemical, therapeutic, and disease prevention potential

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Abstract

Present review article describes phytochemicals, disease prevention, and biological effects of *Tinospora cordifolia* commonly known as Giloy or Giloe" or "Guduchi." This plant is indigenous to tropical regions of the Indian subcontinent and widely used in Ayurvedic medicines since time immemorial. This article emphasized important biological activities such as anti-toxic, antipyretic, anti-inflammatory, antidiabetic, antioxidant, Antimicrobial, anti-stress, hypolipidaemic, hepatic disorder, anti-cancer, anti-HIV, anti-complementary, antitoxic effects, wound healing, anti-complementary, and immune stimulatory and immunomodulating activities. Plant is widely used by local people for treatment of fever, cough, cold, allergic rhinitis, and diabetes. Regular used of Giloy leaf juice cut down sugar, it induces generation of insulin that regulates blood sugar levels. Giloy juice is highly beneficial in liver disease, urinary tract infections, ulcer, kidney problems, and heart-related issues. Giloy juice acts as an appetizer, digestive, and help to remove cough and as immunity booster. It is also used to detoxify skin, improves digestion, and reduces digestion-related problems like diarrhea, colitis, vomiting, and hyperacidity. Giloy is unique plant and depository of hundreds of diverse bioactive constituents. These are used to prepare diverse rasayana' for therapeutic purposes mainly for saving the life of people. Due to life saving natural attributes, this plant is known as Amrita "that provides immortality" to people and immunity booster. Giloy plant hot concoction and extracts were proved boon for people as it has saved millions of lives during corona virus epidemics. Plant is used for the various human diseases and ailments related to liver, gastric, respiratory, urinary tract infections, ulcer, kidney and heart and skin.

Key words: Giloy, Guduchi, phytochemicals, therapeutic and nutritional uses, *Tinospora cordifolia*, traditional medicines

INTRODUCTION

Giloy or Giloe or "Guduchi" plant (*Tinospora cordifolia* [Tc]) is a herbaceous dioecious creeper found climbing on large trees.[1] Plant belongs to family Menispermaceae indigenous to tropical regions of the Indian subcontinent. Tc (Thunb.) Miers, (Guduchi) is a large, glabrous, perennial, deciduous, and climbing shrub of weak and fleshy stem having green-yellow heart-shaped leaves. It is a climbing shrub with green-yellow heart-shaped leaves. It is a widely used plant in folk and Ayurvedic systems of medicine. Plant grows at high altitude and bears flowers that are greenish to yellow, found at higher altitude.[2-4] Tc (Willd.) Miers; known as guduchi in Sanskrit and amrutha balli in Kannada. This is an herbaceous vine belongs to family Menispermaceae and well known as "rasayana" plant [Figure 1].

Giloy is mentioned in shloka of Charak Samhita, where its name is characterized by having heart-shaped leaves with reddish fruit. Giloy or Amrita is a very popular medicinal plant and is used in several traditional medicines to cure various diseases. Plant is known by so many local and regional names. In Northern India plant is known as Amrita and Guduchi while in other parts of India, it is known as Madhuparni, Amruta, Amritavallari, Chhinnaruha, Chakralakshanika, Somvalli, Rasayani, Devnirmita, Gulvel, Vatsadani, Jwarari, Bahuchinna, and Amrita. The genus Tinospora includes 34 species, in which several herbs were used as traditional medicines by indigenous groups throughout the tropical and

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Figure 1: (a-f)Floral and vegetative parts of *Tinospora crdifolia* (Amrita or Guduchi) a climbing shrub

subtropical parts of Asia, Africa, and Australia Giloy plant is indigenous to tropical regions of the Indian subcontinent. Giloy species are particular to India and some parts of China and grow in the tropical and subtropical regions.[5]

Giloy is an important vital depository of natural medicines having many diverse therapeutic compounds. This is widely used in preparation of thousands of Ayurvedic medicines in India since a very long past. Giloy is used for medicinal purposes by local people and possesses immense potentially beneficial properties.[6,7] In Ayurveda, it is a well practiced medicine that is used for treatment of fever, would heal, allergy, and body pain. Giloy is one of the main herbs with a bitter taste. It is used in various disorders and also helps alleviate Vata and Kapha dosha. It's hot kadha is used to relieve in cold and fever.[6,7] Giloy and Tulsi leaf hot extract proves highly beneficial in dengue fever. It assists in increasing platelet count in dengue fever and reduces the chances of complications. It reduces the symptoms such as runny nose, sneezing, nasal obstruction, watering of eyes. Giloy leaves and stem extract act as anti-toxic, antipyretic (that reduces fever), anti-inflammatory, and antioxidant. Giloy is very useful in hay fever also known as allergic rhinitis.

Giloy is used in preparation of many medicinal formulations for the treatment of several diseases, that is, pyrexia, dyspepsia, syphilis, gonorrhea, diseases of the urinary tract, gout, viral hepatitis, anemia, general weakness, urinary tract infections, dermatological diseases, loss of appetite, asthma.[8-11] Giloy-based Ayurvedic preparations are highly useful to cure diabetes. Giloy leaf extract is used to cut down sugar; it is a well known Madhunashini. It starts generation of insulin which regulates blood sugar levels. Giloy is also used for liver diseases, urinary tract infections, ulcer, kidney problems, and heart-related issues. Giloy juice acts as an appetizer, digestive, and help to remove cough. Fresh Giloy juice prepared by blending leaves and stems work as immunity booster. It is also used to detoxify skin, improves digestion, and reduces digestion-related problems such as diarrhea, colitis, vomiting, and hyperacidity. Giloy contains anti-inflammatory and anti-arthritic properties which help to reduce arthritis and gout. Giloy is also used to treat Hay fever and provide relief in nasal discharge, sneezing, nasal itching, and nasal obstruction. It also increases the count of the leukocytes (white blood cells) to fight against infection.[12]

Giloy contains natural products such as alkaloids, glycosides, steroids, and other compounds, these were found highly effective against various disorders, such as diabetes, cancer, neurological problems, and fever. Giloy does lowering of total cholesterol level in the liver. It also improves the level of antioxidant enzymes (reduces damage by free radicals) and oxidative-stress markers thereby enhancing overall liver function.[13] Giloy is an excellent remedy to reduce mental stress and anxiety. This is also used to enhance memory and cognitive functions. Giloy leaf paste on the skin to fasten the wound healing process as it helps increases collagen production and skin regeneration.[14] Giloy is very effective to improve eye-sight when applying topically.

Giloy contains rutin and quercetin present in inhibit cell proliferation and growth of breast cancer cells due to its anti-cancer property [Figure 2]. It also shows anti-proliferative activities It also changes the expression of apoptotic genes and induces apoptosis (cell death) in breast cancer cells.[15] Giloy obstructs growth and spread of cancer cells. Giloy helps to control high cholesterol level in the body by improving the metabolism and eliminating toxins from the body which are responsible for high cholesterol. Giloy leaves are blood purifier, and relive pain and inflammation in arthritis. Giloy suppresses arthritic inflammation by inhibiting the production of pro-inflammatory cytokines (molecules that promote inflammation). Plant contains highly active chemical constituents such as diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds, essential oils, a mixture of fatty acids, and polysaccharides different parts including root, stem, and whole part[16] [Figure 2]**.** Tc has immense application in the treatment of various diseases in the traditional ayurvedic literature.[17]

SOURCE OF INFORMATION

For writing this comprehensive research review on Amrita or Guduchi "Tc," various databases were searched. For collection of relevant information, specific terms such as medical subject headings and key text words, such as Guduchi "Tc" and its therapeutic uses published till 2023 were used in MEDLINE. Tc is one such plant and has shown to exhibit anti-carcinogenic properties. Most specially for retrieving all articles pertaining to the traditional uses of Tc for therapeutics, electronic bibliographic databases were searched and abstracts of published studies with relevant information on the Tc were collected. Furthermore, additional references were included through searching the references cited by the studies done on the present topic. Relevant terms were used individually and in combination to ensure an extensive literature search. For updating the

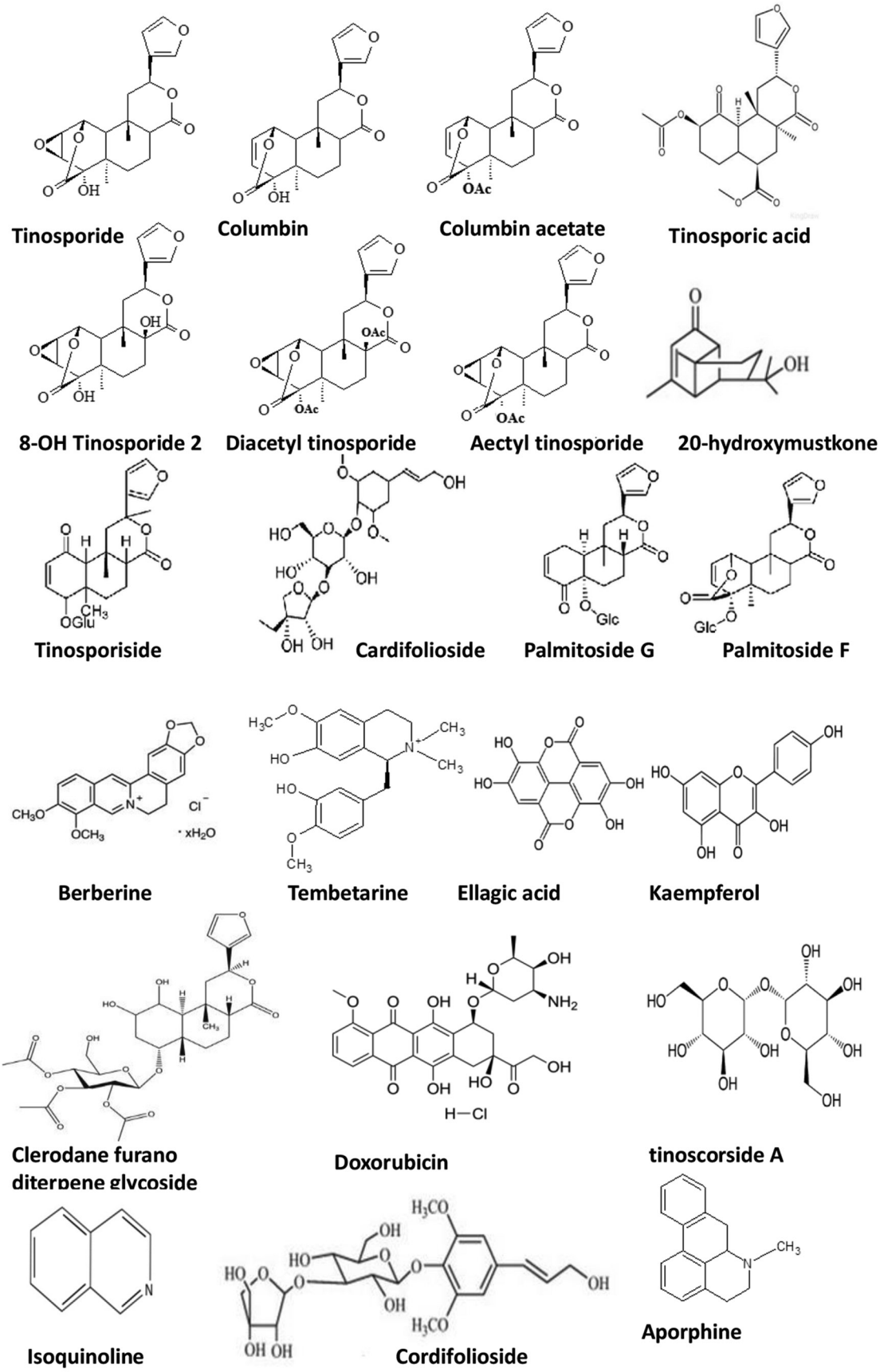

Figure 2: *(Continued)*

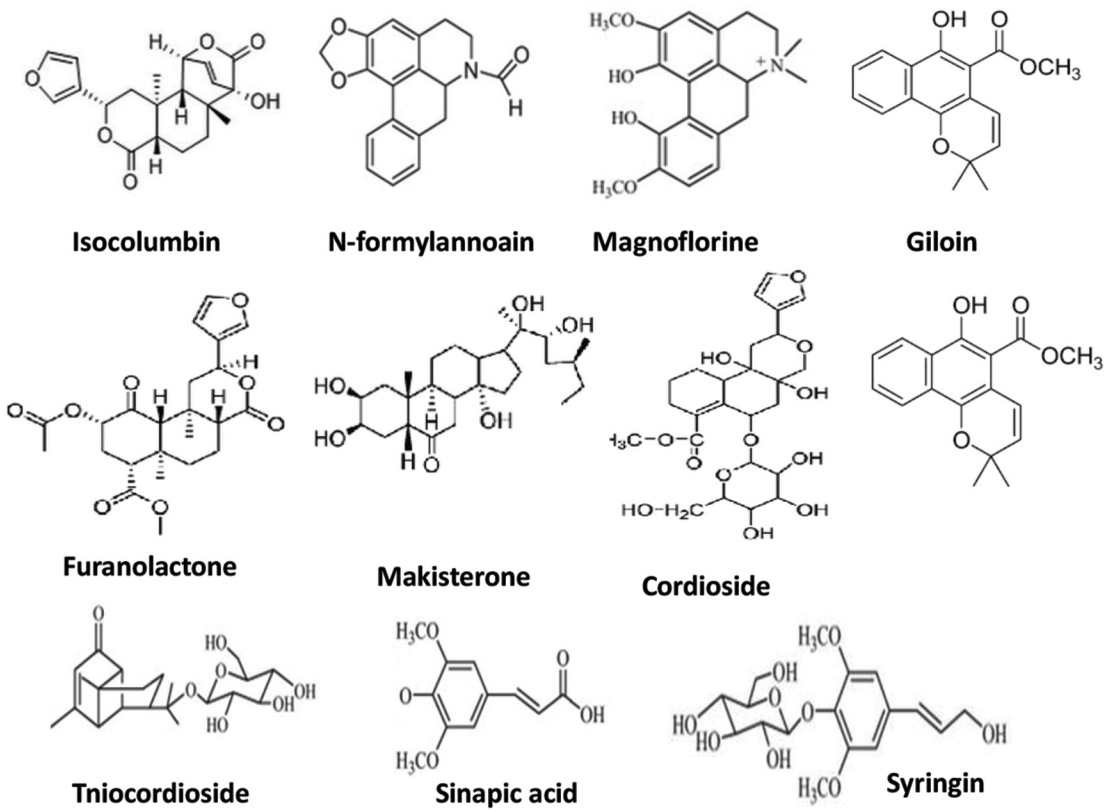

Figure 2: Important biologically active compounds isolated from *Tinospora cordifolia* which are responsible for the diverse medicinal and therapeutic activities

information about a subject and incorporation of recent knowledge, relevant research articles, books, conferences proceedings, and public health organization survey reports were selected and collated based on the broader objective of the review. The present review aimed to systematically analyze published data on the effect of Tc -derived phytocomponents on cancer. This was achieved by searching databases, including SCOPUS, Web of Science, and EMBASE, PubMed, Swissprot, Google searches and Cochrane library were searched. From this common methodology, discoveries and findings were identified and summarized in this final review.

PHYTOCHEMISTRY

Giloy is a rich source of protein and micronutrients, such as iron, zinc, copper, calcium, phosphorus, and manganese. It also contains many secondary plant metabolites, such as terpenes, alkaloids, flavonoids, steroids, and glycosides [Figure 2].[18] Tc contains chemical compounds alkaloids, terpenoids, lignans, and steroids and is a source of many enzymes such as hydrolysates (trypsin, papain, pepsin, α-chymotrypsin.[19] *Tinospora crispa* contains alkaloids, flavonoids, and flavone glycosides, triterpenes, diterpenes and diterpene glycosides, cis clerodane-type furanoditerpenoids, lactones, sterols, lignans, and nucleosides.[20] Tc also contains berberine (BBR).[21] It also contains cordifolide A and is a sulfur-containing clerodane diterpene glycoside.[22] This is a potent inhibitor against Mpro of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and immunomodulatory through human TGF-β and tumor necrosis factor-alpha (TNF-α).[23] Pepsin-pancreatin stem proteins are also isolated from Tc [Figure 2].[24]

This papain hydrolysates shows free radical scavenging capacity and possess low molecular weight hydrophobic peptides.[24] Phytochemical analyses of *T. crispa* revealed the presence of alkaloids, flavonoids, and flavone glycosides, triterpenes, diterpenes and diterpene glycosides, cis clerodane-type furanoditerpenoids, lactones, sterols, lignans, and nucleosides.[20] Active cordioside, quercetin, eicosenoic acid (paullinic acid), and boldine are also isolated from *T. crispa* [Figure 2].[25] *T. crispa* contains more unique bioactive agents, that is, clerodane furanodiptherineglycosidae, elligic acid, kaempferol, N-formylannonain, magnoflorine, jatrorrhizine palmatine, 11-hydroxymustakone, cordifolioside A, tinocordiside, yangambin, anthraquinones, terpenoids, saponins and phenol, pyrrole-based small molecules, quercetin and rutin, arabinogalectian, palmatine, and clerodane-derived diterpenoids.[26] Most of the chemical constituents reported from this shrub belong to different classes, such as alkaloids, diterpenoid lactones, glycosides,

steroids, sesquiterpenoid, phenolics, aliphatic compounds, and polysaccharides [Figure 2].[11]

NUTRITIONAL VALUE

Local people use Guduchi (Tc) as fodder for cattle. Guduchi is a rich source of protein and micronutrients, such as iron, zinc, copper, calcium, phosphorus, and manganese. It also contains many secondary plant metabolites, such as terpenes, alkaloids, flavonoids, steroids, and glycosides. Guduchi is used in poultry, as supplementation material from 1 to 5 g/kg of diet (different sources, such as powder, extracts, roots, and leaves, have been used). It is also suggested for birds. In general, dietary supplementation of poultry broilers with Tc yielded positive impacts on growth performance, body gains (increased by 4.8%), dressing percentage (increased by 7.1%), meat quality traits, and the shelf life of the meat.[18] Guduchi (Tc) as an eco-friendly feed supplement in human and poultry nutrition.[18] Guduchi is a rich source of protein and micronutrients, such as iron, zinc, copper, calcium, phosphorus, and manganese. It also contains many secondary plant metabolites, such as terpenes, alkaloids, flavonoids, steroids, and glycosides.

The stem of Giloy is considered highly effective because of its high nutritional content and the alkaloids found in it but the root and leaves also can be used. Tc exerted a palliative effect on the general health status of the birds through reducing live enzymes and plasma uric acids and enhancing the immune response, as indicated by the leukocyte count, hemagglutinin titer, interleukin (IL) activity, and mortality levels.[18] In general, dietary supplementation of poultry broilers with Tc yielded positive impacts on growth performance, body gains (increased by 4.8%), dressing percentage (increased by 7.1%), meat quality traits, and the shelf life of the meat. In addition, Tc exerted a palliative effect on the genera.[18] Its hot leaf decoction showed potential antiviral property and boost up immunity against COVID-19. This plant was enormously used for preparation homemade kada. Most people (86.1%) think that there is no side effect of kadha while 13.9% think vice versa for curing coronavirus and improvement and boosting the immunity. Most people are using tulsi drops, Vitamin C, and chyawanprash for boosting their immunity. Therefore, we conclude from the survey and available literature that spices and herbs play a significant role against viral infections.[27]

THERAPEUTIC USES

Guduchi is a multipurpose plant that possesses wider therapeutic properties such as antioxidant activity, antimicrobial activity, antibacterial activity, antifungal activity, anti-diabetic activity, antistress activity, hypolipidaemic effect, and hepatic disorder, anticancer anti HIV potential, antiosteoporotic effects, antitoxic effects, wound healing, anti-complementary activity, and immunomodulating activity, systemic infection, and Parkinson's disease (PD).[19] Tc shows multiple biological activities, that is, antioxidative, antimicrobial, antihyperglycemic, anti-inflammatory, osteoprotective, hepatoprotective, antidiarrheal, and antistress effects.[18] Plant also shows antimicrobial effects against *Escherichia coli* and *Salmonella enteritidis*. This plant acts as an immunity booster and improves humoral and cell-mediated immunity against Newcastle disease, infectious anemia, gout, and Aflatoxicosis.[18] Tc exerted a palliative effect on the general health status of the birds through reducing live enzymes and plasma uric acids and enhancing the immune response, as indicated by the leukocyte count, hemagglutinin titer, IL activity, and mortality levels. Plant possesses anti-diabetic, antipyretic, antispasmodic, anti-inflammatory, anti-arthritic, antioxidant, anti-allergic, anti-stress, anti-leprotic, antimalarial, hepato-protective, immuno-modulatory, and anti-neoplastic activities.[11] This is also in ethnomedical treatment of colds, headaches, pharyngitis, fever, diarrhea, oral ulcer, diabetes, digestive disorder, and rheumatoid arthritis [Table 1].[5]

Biological Activity

Tc contains diverse groups of chemical compounds including alkaloids, terpenoids, lignans, steroids, and enzymes. Due to presence of active constituents, Giloy is widely used in Indian system of medicine for the treatment of fever, urinary problem, dysentery, skin diseases leprosy, diabetes, and many more diseases. Tc has shown many promising biological activities, such as antioxidative, antimicrobial, antihyperglycemic, anti-inflammatory, osteoprotective, hepatoprotective, antidiarrheal, and antistress effects.[18] Giloya is useful in the treatment of helminthiasis, heart diseases, leprosy, and rheumatoid arthritis, support the immune system, the body's resistance to infections, supports standard white blood cell structure, function, and levels.[28] It also helps in digestive ailments such as hyperacidity, colitis, worm infestations, loss of appetite, abdominal pain, excessive thirst, and vomiting, and even liver disorders like hepatitis.[29,30] *Tinospora* species exhibit antidiabetic, antioxidation, antitumor, anti-inflammation, antimicrobial, antiosteoporosis, and immunostimulation activities. The present review explained antioxidant activity, antimicrobial activity, antibacterial activity, antifungal activity, anti-diabetic activity, antistress activity, hypolipidaemic effect, anticancer anti-HIV potential, antiosteoporotic effects, antitoxic effects, wound healing, anticomplementary activity, and immunomodulating activity [Table 1].[19]

Antioxidant Activity

Tc stem contains anti-oxidant properties. Its daily oral administration of 500 mg/kg of body weight for 40 days in alloxan-induced diabetic rats increase the erythrocytes membrane lipid peroxide and catalase (CAT) activity

Table 1: The different active constituents isolated from Giloy (*Tinospora cordifolia*) plant

Chemical nature	Plant part	Active ingredient	Biological activity	References
Alkaloids	Whole plant	Berberine, tinosporin, palmitine, jatrorrhizine, tembeterine, magnoflorine, isocolmbin	Anti-diabetic, Antioxidant activity	[9,13,21]
Alkaloid, diterpinoids, lactone,	Leaves and stem	Epicatechin, tinosporin, tinosporide, jeteorine,	Anti-inflammatory, antioxidant	[18,21]
Glycosides	Fruits and leaves	Cordifolioside A, Tinocordiside, Syrgin,	Immunomodulatory activity, anticancer	[19]
Alkaloids	Whole plant	jatrorrhizine, tembeterine, magnoflorine	Anti-oxidant, anti- diabetic	[31-33]
Alkaloids, terpenoids	Whole plant Leaves and stem	Berberine tetrahydroplamitine, isocolumbin, palmetine, temebetarine, Magnoflorine, tinosporin, palmetine, aporphine, jatrorrhizine,	Inducer and sensitizers of insulin production in pancreatic cells, antidyslipidemic activity	[36,37,38,43]
Diterpinoid lactones:	Whole plant	Furanolactone, tinosporin, jateorine, columbin	Antimicrobial activity	[40-45]
Alkaloids	Whole plant Leaves and stem	Magnoflorine, tinsporin, isocolumbin, palmetine, tetrahydroplamitine	Antimalarial. Antiviral, antibacterial, Anthelminthic, Anti-filarial activity, Anticoccidial	[40,47,51,53-57,60,61,64,70]
Clerodane derivative	Leaves and stem	Furnolactone, Tinosporin, isocolumbin, palmitine, jateorine, columbin,	Cardioprotective, immunomodulatory, analgesic	[75-77]
Terpinoid	Leaves	Cordifoliosid eA	Immunestimulatory, radioprotective activity	[78,82]
Steroids	Whole plant	beta sitosterol, makisterone A. Giloinsterol, Hydroxy ecdysone. Ecdysterone	Antiarthitic activity	[87]
Diterpene	Leaves and stem	Epoxyclerodane, Tinocardin, Tinosporide, Columbin, 8 hydroxy columbin	Gastroprotective activity	[90]
Alkaloids, terpinoids	Leaves and stem	Tinosporin, isocolumbin, palmitine, magnoflorin, tetrahydroplamitine	Ameliorative activity	[92,93]
Alkaloids	Whole plant	Magnoflorine, tinsporin,	hepatoprotective agents analgesic	[83,89]
Alkaloids, terpenoids	Whole plant, Leaves and stem	Magnoflorine, palmetine, tinocordiside, Cordifolioside A	Anticancer	[96-98]
Alkaloids	Whole plant	Berberine, choline, tembeterine, tinosporin, palmitine, jatrorrhizine	Neuroprotective, antidepressant	[99,100,102]
Polysaccharide	Stem and root	Arabinogalactan	Immuno-protector	[79]
Aliphatic compounds	Stem and root	Ootaoosanol Heptacosanol Nonacosan-15-one	Radio-sensitizing activity, anti-tumor, anti-nociceptive and anti inflammatory	[104]
Amine	Whole plant	N-trans-feruloyl tyramine, giloin, tinosporic acid	Protease inhibitors, neuro-modulator. Insulin mimicking and insulin releasing effect	[105]

while superoxide dismutase (SOD), glutathione (GSH) peroxidase were found to be decreased significantly ($P < 0.01$).[31] Its leaf extract powder showed strong antioxidant activity.[32] Plant also possesses phenolic compounds in stem extract (−) epicatechin has been reported for the first time in Tc stem extract.[33] *Tinospora sinensis* (Lour.) contains BBR that possesses diverse biological activities [Table 1].[21]

Antidiabetic Activity

Tc (Thunb.) Miers possesses phytoconstituents tinosporaside and BBR which show very strong antidiabetic activity.[1,34] Plant extract or Satva restore and work in both conditions hypoglycemic and hyperglycemic state.[35] Guduchi Churna (GC) and extracted juice, decoction, and GC prepared from its leaves is used to treat diabetes. Tc consumption ameliorates changes in kidney chondroitin sulfate/dermatan sulfate in diabetic rats.[36] Plant possesses nutraceuticals most of them are antidiabetic.[37] Tc stem bio-organic compounds act as inducer and sensitizers of insulin production in pancreatic cells [Table 1].[38]

Antimicrobial Activity

Tinospora cardifolia (Giloy) extracts were found active against *Streptococcus mutans, Enterococcus faecalis* and *staphylococcus aureus* at 2% of concentration with a zone of inhibition of 19 mm.[39] Tinospora exhibited antimicrobial activity against *S. mutans*.[40] Tc acetone and ethyl acetate extracts were found active against *Klebsiella pneumoniae* and Pseudomonas spp. These have shown a minimum bactericidal concentration values between 1.29 and 22.73 mg/mL.[41] Tc shade dried and powdered leaves showed anti-microbial property against E. coli.[42]

Tinospora sagittata (Oliv.) Gagnep. var. craveniana (S.Y.Hu) Lo (TSG) is a traditional Chinese herb. This is used for the treatment of upper respiratory tract infection and has anti-bacterial and anti-ulcer activity. It shows bactericidal effects due to presence of major component, palmatine, against *Helicobacter pylori* SS1 *in vitro* and *in vivo*.[43] PMT derivatives showed antibacterial activities against six metronidazole resistant *H. pylori* strains. It also exhibited a good safety profile with a half-lethal dose (LD_{50}) of over 1000 mg/kg.[44] Tc extracts were found active against *Mycobacterium tuberculosis.* These showed dose-dependent inhibitory activity with maximum effect of 18–32% [Table 1].[45]

Antiprotozoan Activity

Tc leaf extract showed good anti-plasmodial activity.[46] *T. crispa*, found in Indonesia is used for the traditional treatment of malaria and Leishmaniasis by local people. It was found highly active against *Plasmodium falciparum* and also against *Babesia divergens* and *Leishmania infantum.* It shows cytotoxicity to sporozoites activity (IC_{50} values <3 µg/mL).[20] *T. crispa* possessed a broad antimalarial activity[20] while Tc shows anti-trypansomiasis, anti-leishmaniasis, and anti-malaria activity.[47] Both plant derivatives including the crude extracts, and bioorganic compounds are used in preparation of anti-leishmanial medicines.[48] Its natural compounds inhibit the cell cycle arrest have proven effective for killing cancer cells *in vitro*.[49] It inhibits the activities of cyclins and cyclin-dependent kinases, as well as other proteins and enzymes involved in proper regulation of cell cycle leading to controlled cell proliferation.[50] Plant possesses novel antimalarial compounds that could serve as a leads for the development of new and effective antiplasmodial drugs [Table 1].[51]

Antiviral activity

Hot extract of Tc shows potential antiviral preventive and immunity booster activity against COVID-19. Giloy Ghanvati shows strong therapeutic potential against viral diseases.[52] Tc, BBR can regulate 3CLpro protein's function due to its easy inhibition and thus can control viral replication. These are proved potential drug candidates for COVID-19.[53] More specifically, secondary metabolites were found highly active against SARS-CoV-2. Chemicals in Tc may activate Nrf2, which leads to the overexpression of antioxidant enzymes such as CAT, GSH peroxidase (GPx), GSH-S-transferase (GST), and GSH reductase (GR), and thereby induces the adaptive response to oxidative stress. Tc is also able to reduce NF-κB signaling by inhibiting PI3K/Akt, activating AMPK and sirtuins, and downregulating PI3K/Akt. It can be used for treatment of astrointestinal diseases, inflammatory processes, and microbial infections, as immunostimulants, and in chemotherapy [Table 1].[54]

Diterpenoids found in spices and herbs play a significant role against viral infections.[27] These are potent compounds found in natural medicines.[55] Tc also contains various classes of alkaloids, lignans, steroids, and terpenoids. Diterpenoids are considered the major active compounds in *T. sinensis* with unique structures and activities.

Antibacterial Activity

Tc shows antibacterial activity against *S. mutans*.[40] Its stem extract was found active against drug resistant *S. auerus*.[56] Its subminimum inhibitory concentrations (MICs) of AuNPs (50, 100, and 150 µg/mL) greatly affected the biofilm-forming ability of *Pseudomonas aeruginosa*.[57] Ethanolic extract of Tc showed growth inhibitory potential *Salmonella* Typhi (Gram-negative), *S. aureus,* and *Serratia marcesenses* (Gram-positive).[58] Tc, and studied the action of AuNPs against *P. aeruginosa* PAO1 biofilm. Solvent extracts of Tc, showed antibacterial potential against *E. coli, S. aureus, K. pneumoniae, Proteus vulgaris, S.* Typhi*, Shigella flexneri, Salmonella* Paratyphi*, Salmonella* Typhimurium*, P. aeruginosa, and Enterobacter aerogenes* by disc diffusion method [Table 1].[59]

Anti-parasitic Activity

Amphistome *Gastrothylax crumenifer* parasites with the treatment of medicinal plants Tc.[60] *In vitro* anthelmintic

activity of plants have been studied on trematode parasites liver fluke Fasciola gigantica[61,62] tegument of *G. crumenifer* and on amphistome *Orthocoelium scoliocoelium, F. gigantica. G. crumenifer*[63-67] and intestinal helminthes [Table 1].[68]

ANTICOCCIDOSIS

Tinospora rumphii stem extract possess potential to cutdown the Eimeria species oocysts per gram counts of naturally infected goats [Table 1].[69]

Antifilarial Activity

Similarly, dried stems (ST) of *T. crispa* and four other plants slowed anti-filarial activity, these have cut down relative movability of adult worms of subperiodic *Brugia malayi* [Table 1].[70]

Immunomodulatory and Immune Stimulatory Activity

Aaqueous and methanolic extracts of Tc (AETC and METC) were found active against *Salmonella typhimurium*. Tc stem parts contain major bioactive compounds, and activate the peritoneal macrophages and boost the non-specific host defenses).[71] These extracts showed immune-stimulating activity and enhance the level of gamma-interferon (IFN-γ), TNF-α, and IL-1β.[72] Tc also shows immunomodulatory effects.[73] Its ethanolic extract (100 mg/Kg/p.o.) increased the level of liver mitochondrial enzymes such as GSH, CAT, and SOD but decreased the level of LPO in liver as compared to the vehicle.[74] This immune-stimuatory activity is due to presence of Cordifolioside A and syringing in Tc. Its extracts showed significant enhancement in phagocytic activity and increase in nitric oxide and reactive oxygen species generation at concentration 0.1–2.5 μg/mL.[75] Plant extracts from giloy are used for preparation of so many Ayurvedic medicinal mainly to cure infectious diseases [Table 1].[1,45]

T. crispa possesses important phytochemicals, that is, cordioside, quercetin, eicosenoic acid (paullinic acid), and boldine,[25] polysaccharides, terpenoids, flavonoids, alkaloids, glycosides, and lactones which are responsible for immunomodulation activity.[45] This activity is also reported in aqueous extracts of the stem and root of Tc.[76-78] A drug (1,4)-alpha-D-glucan (alpha-DG), from Tc, showed novel immune stimulatory effects and induced the level of pro- and anti-inflammatory cytokines (IL-1beta, IL-6, TNF-α, IFN-γ, and IL-10) in the lung and spleen of endotoxin-stimulated juvenile rats.[79] Further, a polysaccharide (G1-4A) isolated from guduchi has shown promising adjuvant activity.[80] More specifically, Neem-guduchi has more immunomodulatory potential.[81] Guduchi Ghana prepared by classically was found to possess significant immunostimulatory action on immune system [Table 1].[81]

Radioprotective and Cytoprotective Activity

Tc n-butanol fraction contains cordifolioside-A that shows radioprotective and cytoprotective potential against 4 Gy-γ radiation in mice and cyclophosphamide induced genotoxicity.[82] It protects from protect radiation-induced lethality, lipid peroxidation, and DNA damage [Table 1].[82]

Antipyretic and Hepatoprotective Activity

Guduchi Tc shows antipyretic activity.[18] Metabolism-mediated interaction potential of standardized extract of Tc causes herb-drug interactions through rat and human liver cytochrome enzymes through rat and human liver microsomes. Consumption of Tc may not cause any adverse effects when consumed along with other xenobiotics [Table 1].[83]

T. crispa possess phytoconstituents, which showed hepatoprotective effects, it significantly reduced Malondialdehyde (MDA) levels and increases SOD levels in CCl4-induced hepatotoxicity. *T. crispa* contains genkwanin and reduces pyrexia and as a source of potential hepatoprotective agents.[84] Aqueous extracts Tc significantly reduce the deleterious effects of paracetamol and exhibit significant antioxidant and hepatoprotective activities.[46] Guduchi ghrita formulations in albino rats against yeast induced pyrexia Guduchi ghrita formulations having significant anti-pyretic activity [Table 1].[85]

ANTI-GOUT PROPERTIES

Nineteen fungal endophytes were isolated from the medicinal plant Tc and evaluated for their XO inhibitory activity. Basically xanthine oxidase inhibition is required to restore hyperuricemic condition and for treatment gout [Table 1].[86]

Analgesic Activity

Tc extract acts as good analgesics, it significantly ($P < 0.05$) increased the response time and decreased the number of writhes in hot plate method and abdominal writhing.[87] Tc shows peripheral analgesic effect and marked central analgesic effect vis-à-vis standard modern antipyretics.[88,89] TSY exhibits combined analgesic, sedative, and anti-gastric cancer activities. *In vivo* experiments TSY extract exhibits good analgesic and sedative effects.[90] Polysaccharide rich extract (PRE) isolated from Tc, on the survival of intracellular MTB strains and activation of macrophages, was investigated. PRE treatment up regulated the expression of pro-inflammatory cytokines such as IL-β, TNF-α, IL-6, IL-12, and IFN-γ in RAW 264.7 cell line. This classical activation of macrophages

by PRE treatment and killing of intracellular MTB is due to NO induction [Table 1].[91]

AMELIORATIVE EFFECTS

Tc showed protection against aflatoxin-induced nephrotoxicity due to the presence of alkaloids such as a choline, tinosporin, isocolumbin, palmatine, tetrahydropalmatine, and magnoflorine.[92] Tc to scavenge free radicals generated during aflatoxicosis.[92] AFB1 exposure led to significant rise in thiobarbituric acid reactive substances and fall in SOD, CAT, reduced GSH, GST, GPx, GR, ascorbic acid, and protein content. Tc ameliorates urotoxic effect (CP induced toxicities) of cyclophosphamide by modulating GSH and cytokine levels [Table 1].[93]

Adaptogenic Activity

Guduchi ghrita' (SGG) is prepared from Tc (Willd.) Miers was found to produce significant inhibition of stress hypothermia and gastric ulceration. Guduchi ghrita also shows adaptogenic effects.[94] Adaptogens exhibit a biphasic dose-effect response; at low doses they function as mild stress-mimetics, which activate the adaptive stress-response signaling pathways to cope with severe stress.[95] These also show pleiotropic effects on the neuroendocrine-immune system [Table 1].

Anticancer Activity

Tc (Thunb.) Miers (Giloy) inhibits oral cancer cells in a dose-dependent manner by inducing apoptosis and attenuating epithelial-mesenchymal transition.[96] Methanolic extract of Tc possess cytotoxic activity against human breast cancer cell line MDA-MB-231 and normal Vero epithelial cell line.[97] BBR found in Tc extract significantly contributes to its antiproliferative activity. This compound targets multiple cell signaling pathways, including proliferation, differentiation, and epithelial–mesenchymal transition.[97] BBR is a natural active principle with potential antitumor activity. The presence of BBR in Tc extract significantly contributes to its antiproliferative activity in human colon adenocarcinoma [Table 1].[98]

NEUROPROTECTIVE EFFECT

Tc ethanol extract shows neuroprotective against 6-hydroxy dopamine (6-OHDA) lesion rat model of PD. Its ethanolic extract exhibited significant neuroprotection by increasing the dopamine levels up to 2.45 ± 0.40 ng/mg of protein and complex I activity up to 78.50 ± 0.96 nmol/min/mg of protein) at 200 and 400 mg/kg in comparison to control. It shows significant neuroprotection in 6-OHDA-induced PD by protecting dopaminergic neurons and reducing the iron accumulation.[99] Natural products or phytoconstituents, such as polyphenolic, potentially suppress neuro-degeneration and improve memory as well as cognitive functions of the brain.[100] Tc as a potential neuroregenerative candidate against glutamate induced excitotoxicity *in vitro*. T cordifolia (B-TCE) exhibited neuroprotective potential by preventing degeneration of neurons induced by glutamate.[101] Ethanol extract of *Tinospora cordifolia* (Tc)aerial parts shows neuroprotective activity against 6-hydroxy dopamine (6-OHDA) lesion rat model of Parkinson's disease.[99] Results show that TCEE possess significant neuroprotection in 6-OHDA induced PD by protecting dopaminergic neurons and reducing the iron accumulation [Table 1].

Antidepressant-like Activity

Tc (Wild.) Miers petroleum ether extract shows antidepressant-like effect, it has significantly reversed by depressant effect in pretreatment of animals with prazosin (a α1-adrenoceptor antagonist), sulpiride (a selective dopamine D2-receptor antagonist), p-CPA (a serotonin synthesis inhibitor), and baclofen (GABA-B agonist), when tested in tail suspension test. Moreover, petroleum ether extract also reduced the mouse whole brain monoamine oxidase (MAO-A and MAO-B) activities as compared to control, resulting in increase in the levels of brain monoamines. It could be used in management of depressive disorders [Table 1].[102]

ANTIPYRETIC AND HEPATOPROTECTIVE POTENTIAL

T. crispa shows antipyretic and hepatoprotective properties of both a crude organic extract and various sub-fractions. Especially methanolic extract of *T. crispa* and fractions containing genkwanin, both have reduced pyrexia and possess of potential hepatoprotective agents.[84] *T. crispa* anti-pyretic activity of Guduchi ghrita formulations in albino rats against yeast-induced pyrexia in experimental groups [Table 1].[85]

Antiscabies Activity

Tc lotion was found highly effective in scabies-infected patients. Plant possesses anti-scabies agent. Tc lotion exhibits anti-scabies activity comparable with permethrin. Its incorporation as therapeutic reagent in *Sarcoptes scabiei* infections is highly recommended [Table 1].[103]

MISCELLANEOUS

Polysaccharide G1-4A, isolated from Indian medicinal plant, Tc enhanced surface expression of CD40, CD80, CD86, MHCII by BMDC in vitro and splenic DC in vivo. It shows immunopharmcological effects against murine lymphoma.[79] Tc is used for treatment of various ailments. It shows radiosensitization and does depletion of GSH and GST,

accompanied by elevated levels of lipid peroxidation and DNA damage of tumor cells.[104] Few compounds tinosponone, xanosporic acid, cardiofolioside B, tembetarine, and BBR in Tc. are potent inhibitors of main protease of SARS-CoV-2.[105]

CONCLUSION

Amrita is a green depository of diverse groups of natural plant products which possess multiple therapeutic and medicinal potential. This plant is not only a medicinal plant but also an eco-friendly important feed supplement in human and poultry nutrition. In addition, dietary supplementation of poultry broilers with Tc yielded positive impacts on growth performance and body gains. Plant is used in India in folk and Ayurvedic systems of medicine and well known as "rasayana" plant. Giloy and Tulsi leaf hot extract proves highly beneficial in dengue fever. It assists in increasing platelet count in dengue fever and reduces the chances of complications. It reduces the symptoms like runny nose, sneezing, nasal obstruction, and watering of eyes. Giloy leaves and stem extract acts as anti-toxic, antipyretic (that reduces fever), anti-inflammatory, and antioxidant.

Giloy or Amrita is an important vital depository of natural medicines having many diverse therapeutic compounds. This is widely used in preparation of thousands of Ayurvedic medicines India since a very long past. Giloy is used for medicinal purposes by local people and possesses immense potentially beneficial properties. Giloy is used for medicinal purposes by local people and possesses immense potentially beneficial properties. Giloy leaves and stem extract possess anti-toxic, antipyretic (that reduces fever), anti-inflammatory, and agents. Giloy is very useful in hay fever also known as allergic rhinitis. Giloy contains natural products such as alkaloids, glycosides, steroids, and other compounds, these were found highly effective against various disorders, such as diabetes, cancer, neurological problems, and fever. Giloy helps to control high cholesterol level in the body by improving the metabolism and eliminating toxins from the body which are responsible for high cholesterol. This is a very popular medicinal plant and is used in several traditional medicines to cure various diseases. Tc has immense application in the treatment of various diseases in the traditional ayurvedic literature.

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