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REVIEW

Phytochemistry, Ethnobotany and Pharmacological Uses of *Tinospora cordifolia* with Special Reference to SARS-COV-2

Shahnaz Alom, Dolly Kalita, Jesminara Ahmed, Kaifur Rahman, Manyajyoti Boruah, Murchana Sarmah, Nikusmita Das and Farak Ali*

Girijananda Chowdhury Institute of Pharmaceutical Science-Tezpur, Dekargaon, Sonitpur-784501, India

*Corresponding author: E-mail: alifarak347@gmail.com

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Medicinal plants or medicinal herbs possess therapeutic properties or exert beneficial pharmacological effects on human. From time immemorial, people have been using various medicinal plants without even knowing their phytochemistry and pharmacological properties as a medicine for treating numerous ailments. As technology developed and upgraded, people used to screen out various phytoconstituents as well as evaluate their basic pharmacological properties. *Tinospora cordifolia* is a medicinal herb which is commonly known as Giloy belong to family menispermaceae. It can also be found in places like Africa, China, South-East Asia, Indo-Malaya region and Australia. Traditionally, people use this herb as prominent food materials due to their higher nutraceutical value and various healing properties. For phytochemical investigation, extraction of whole plant is preferable whereas most of the phytochemical are found to be present in leaves. Various potent phytochemicals are found in this herb such as tinosponone, tinocordiside, tinosporaside, cordifoliside, β-sitosterol, mekisterone A, *etc*. which are belong to class of alkaloids, sesquiterpenoids, glycosides, steroids, volatile oil, *etc*. Owing to the presence of these potent compounds, it exhibits wide range of large number of pharmacological activities such as antiviral, antibacterial, antifungal, antioxidant, antidiabetic, anticancer activities, *etc*. In past two years, SARS-CoV-2 infections has taken life of millions of people across the globe and there were no any vaccine or proper antiviral medicine available to defend this deadly pandemic, hence people were mostly relying on herbal plant therapy. Giloy is one such magical herb which exhibit healing properties in SARS-CoV-2 infected patients. Moreover, *in-silico* studies have been carried out to determine the binding affinity as well as inhibiting potential of various phytoconstituents of giloy. In this review work, we compiled all the updated information about *T. cordifolia* as well as emphasizing more on SARS-CoV-2 inhibiting potential.

Keywords: *Tinospora cordifolia,* Giloy, Phytochemistry, Ethnomedicine, Pharmacology, SARS-CoV-2 inhibition.

INTRODUCTION

Medicinal plants or medicinal herbs possess therapeutic properties or exert beneficial pharmacological effects on human. According to archaeological evidence, approximately 60,000 years ago people started using herbal medicine. Medicinal plants are used widely by the traditional medical practitioners in their day-to-day practice because of their effectiveness, easy availability and low cost. It is essential to study about medicinal plants to promote the uses of herbal medicine as well as it can be use in newer drug development. The natural herbal preparation was first used by Chinese as medicines [1]. Many countries of the world including Bangladesh, India, Pakistan and still use traditional forms of medicine [2]. According to the Food and Agriculture organization estimation, in 2002 over 50,000 medicinal plants are used across the world and about 80% of the world population rely on traditional herbal medicine for primary health care. Plant based medicines are still being used by people as it has very minimal side effects and has better compatibility with human body [3].

Tinospora cordifolia (Willd.) Miers ex Hook. F. & Thoms. a large deciduous climbing shrub; an essential herb in ayurvedic medicine belongs to the moonseed family Menispermaceae. It is found throughout India, Sri Lanka, Bangladesh and China ascending to an altitude of 300 meters [4]. The plant is commonly known as Giloe [5] in Hindi (Fig. 1), which is a Hindu

Fig. 1. *Tinospora cordifolia* plant. (Photo credit: Shahnaz Alom; Picture taken on 15th May, 2022; place: Titabar, Jorhat, Assam, India)

mythical term refers to keeping celestial being eternally young. Other synonyms are Amrita (means nectar in Sanskrit), Guduchi (Sanskrit), Gurcha, Giloy (Hindi), Heartleaf moonseed, *Tinospora* (English), Gulancha (Bengali), Amarlata (Assamese), Gilo (Punjabi) [5,6]. Because of the numerous therapeutic properties giloy is used in traditional medicine to treat the diseases such as diabetes, jaundice, diarrhoea, leprosy, helminthiasis, skin disease, anemia, inflammation, urinary disorder, antiperiodic, *etc*. [7,8].

Though all parts of this plant are useful but the stem is more beneficial as it contains starch commonly known as "Guduchi-satva", which is highly nutritive and used to treat many diseases such as chronic fever, increase energy and appetite and relieves burning sensation [9]. The root of giloy is used as emetic. Different part of this plant contains different chemical constituents such as glycosides, essential oils, diterpenoid lactones, phenolic, sesquiterpenoid, steroids and polysaccharides which shows different pharmacological activities [10]. Giloy is useful in the treatment of heart disease, rheumatoid arthritis, increase immunity, leprosy, *etc*. [9]. *T. cordifolia* is a well-known medicinal plant and if we do further research on this plant it may leads to an excellent outcome in modern medicine.

An exhaustive literature survey has been carried out from January to May 2022 by systematic study of available original research journal as well as review journal available in PubMed, ResearchGate, PubMed Central database, Google Scholar, Mendeley, Crossref, cite factor, *etc*. we tried to incorporate more recent and updated information regarding *T. cordifolia.* Various information regarding taxonomical and vernacular classification, habitat, distribution, traditional uses, phytochemistry and pharmacological properties along with specific focus on study of this plant in inhibition of SARS-CoV-2.

Taxonomical classification		Vernacular name	
Kingdom	Plantae	English	Giloy
Division	Magnoliophyta	Hindi	Gulancha
Class	Magnoliopsida	Sanskrit	Guduchi, Amrita
Order	Ranunculales	Telugu	Tippateege
Family	Menispermaceae	Malayalam	Amrytu, Chittamritam
Genus	*Tinospora*	Gujarati	Gulvel
Species	*Tinospora cordifolia*	Urdu	Gilo, Satgilo

Botanical description: *T. cordifolia* is a large deciduous climbing shrub which spreads widely. Family of these plant is menispermaceae consist of its about 70 genus and 450 species and generaly found in the tropical low land regions [9,11]. *T. cordifolia* is an everlasting deciduous twiner with succulent stem. The outer bark is thin and brown to grayish in colour. Long thread like aerial used to grow from branches and stems. Leaves are plain, alternate or lobed, cordate entire and membranous and long with approximately 15 cm long which is round, heart shaped, twisted partially, curved convexly and half way round and flowers are green colour but mature leaves are yellowish green to yellow colour [12]. Leaves are bitter in taste and they have uncertain odor. Lamina of the leaves are 10-20 cm long and 8-15 cm broad. They are rich in phosphorous, calcium and proteins. The pea shaped fruits are fleshy and single seeded which are the collection of one to three. These are shining, duplets and become red when fully growth. The fruit has smooth texture and it is ovoid in shape [11,13]. The colour of the fruit is scarlet or orange red. Flowers are grown in summer and fruits are during winter. Male flowers always exist in groups and female flowers exist in solitary. Sepals and petals are six in number. Inner sepals are larger than outer sepals. Petals are smaller than sepals which are membranous and free [9]. Seeds are white and hook shaped and bean shaped. Embryo are also in curved shaped automatically. Roots are fleshy, thread like, squared, which are arise from the mature branches. Microscopic examination of aerial root is distinguished by tetra to penta-arch primary structure. The aerial roots which are dried, creamy white or light grey brown in colour, bitter in taste and odorless. Starch is here all over the parenchyma of the aerial root [14,15].

Distribution: *T. cordifolia* is distributed throughout the tropical region of India covering approx. 1200 m above sea level, which is destined from Kumaon (Northen India) to Assam (Eastearn India). It can be also found in places like Africa, China, South-East Asia, Indo Malaya region and Australia. It is a fairly common including the deciduous and dry forests. All over the world, out of 40 different species, few species are used for the medicinal treatment that is *T. Bakis*, *T. Cordifolia*, *T. Crispa*, *T. malabarika*, *Tinospora Rumpi*, *etc*. [4].

Extraction: The extraction of phytoconstituents is one of the most important steps for isolation of various compounds from plants. In the extraction process, selection of phytoconstituents is the most important step to extract the desired product in a large quantity. Through HPTLC analysis, the presence of cordifoliaside-A was extracted in NBTC stem (ethanolic extract) [16]. Under observation for 7-10 days, the stems of *T. cordifolia* were dried and pulverized by an electric grinder. Methanol was used to exact the dried sample and then the ratio 70:30 at 40 ºC of acetone for 16 h in Soxhlet apparatus. After that using a rotary vacuum evaporator, was residue was dried under reduced pressure [17]. The extract of stem was partitioned to $CHCl_3$ and aqueous extract. The $CHCl_3$ solution was dried and evaporated up to get a brownish viscous residue (8 g). Then, it was placed on a silica gel column and eluted with $CHCl_3$ and enriched with methanol to afford fine fractions. Fraction three with $CHCl_3$:CH_3OH in the ratio 10:1 was subjected to silica gel

column chromatography to give a single compound (2.8 g). The isolated compound after spectroscopic analysis confirmed the presence of high content of the alkaloid palmatine [18].

Phytochemistry: Since the mankind's beginning, medicinal plant possesses an important role as therapeutic agent and medicaments for various ailments. Owing to presence of large number of phytoconstituents such as alkaloid, steroids, aliphatic compound, glycosides, polysaccharides, volatile oils, *etc*. it exhibits wide range of large number of pharmacological activities such as antiviral, antibacterial, antifungal, antioxidant, antidiabetic, anticancer activity, etc. The traditional and complementary use of *T. cordifolia* is often seen in curing chronic disease, infectious skin diseases, fever, cancer, gastrointestinal disturbances, tuberculosis, bronchitis, syphilis, malaria, asthma, dyspepsia, gout and jaundice. It increases the platelets count in blood and the juice is considered as diuretic, tonic, antiperiodic and antidote to snake bite.

Several workers [19,20] have carried different research on evaluation and screening of phytochemicals that has been found in stem and root extract of *T. cordifolia.* Almost all parts of this plant having important phytoconstituents but greater number of phytoconstituents can be found in stem and root extract. A schematic depiction of various classes of phytoconstituents present in giloy is shown in Fig. 2.

Alkaloids: Most potent and pharmacologically important alkaloids that has been isolated is tinosporine A (**1**) due to which this plant show many activities [21]. Apart from this alkaloidal compounds, others important alkaloids that can be extracted from *T. cordifolia* are magnoflorine (**2**), choline (**3**), jatrorrhizine (**4**), palmatine (**5**), tembetarine (**6**) and berberine (**7**) [5] (Fig. 3).

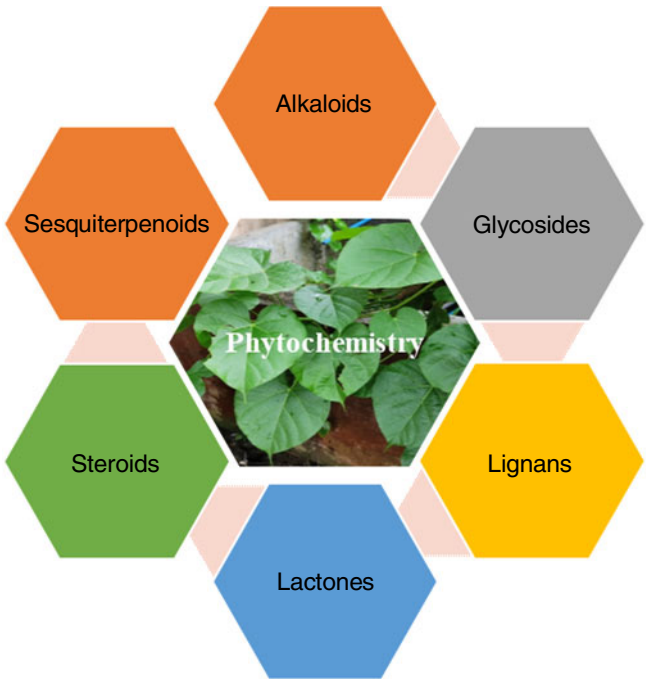

Fig. 2. Schematic depiction of various class of phytoconstituents present in giloy

Glycosides: Glycosides contain glycon and aglycone parts whereas the pharmacological activities are actually shown by aglycon parts. Some important glycosides are tinosporide (**8**), tinosporaside (**9**), tinocordiside (**10**), cordioside (**11**), cordifolioside A (**12**), cordifoliside B (**13**), cordifoliside A (**14**), cordifoliside C (**15**), cordifoliside D (**16**), tinocordifolin (**17**) [22-24]. Apart from these, other important glycoside are also

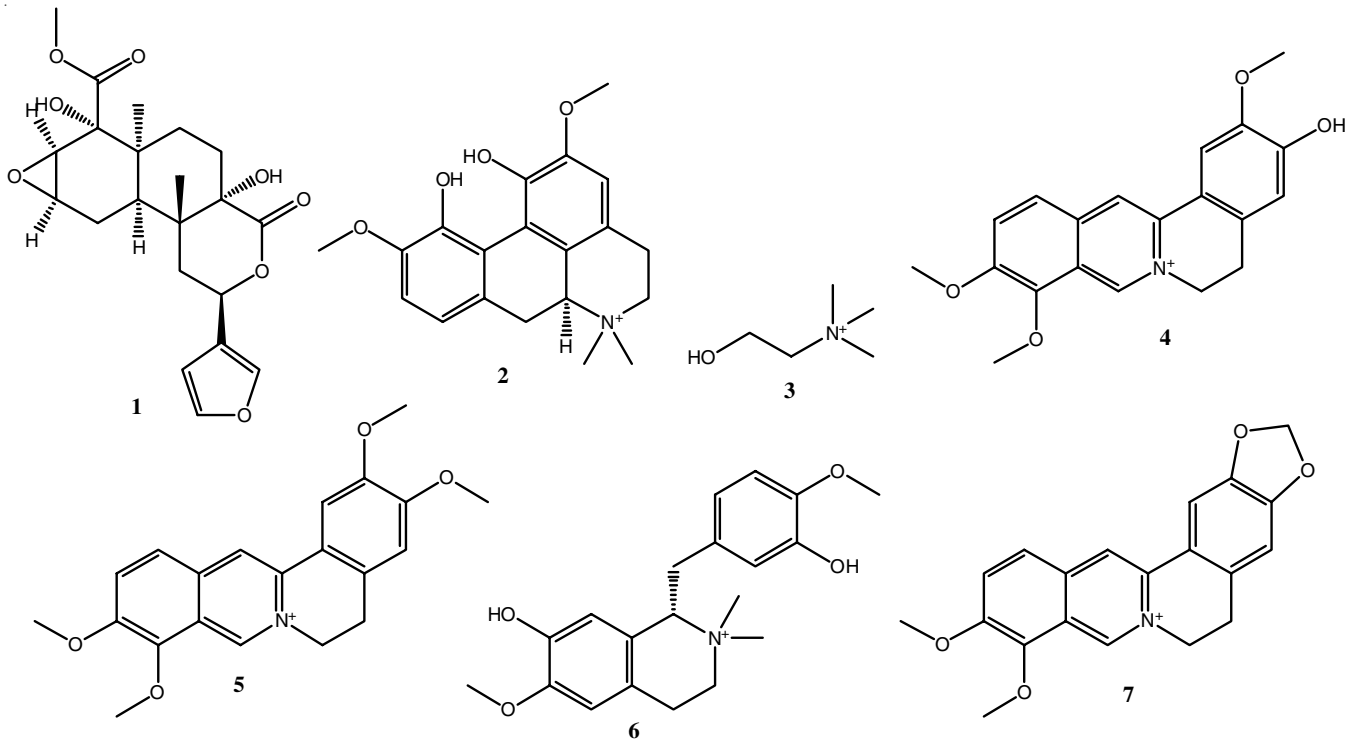

Fig. 3. Structures of alkaloidal drugs present in giloy

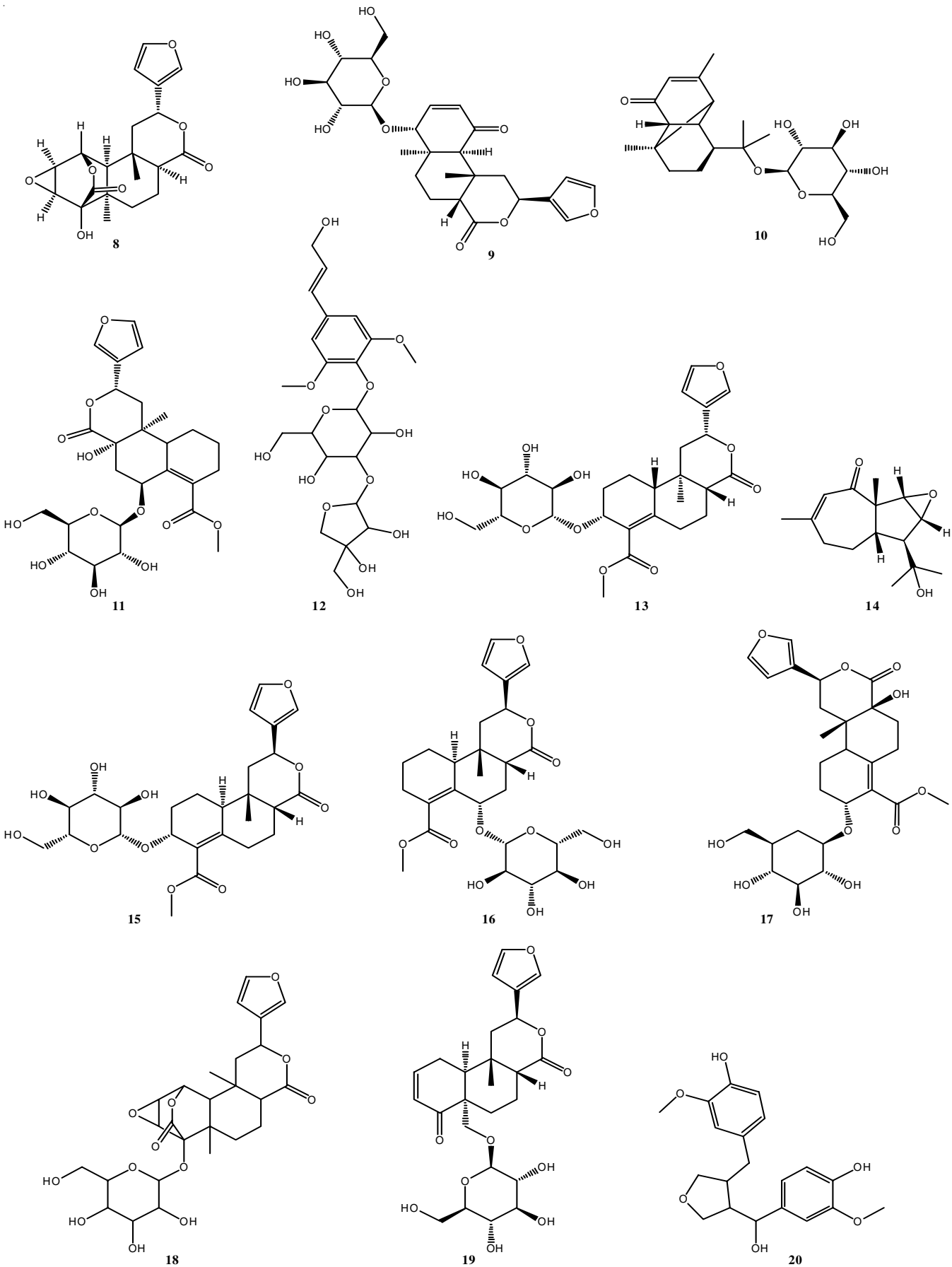

Fig. 4. Structures of glycosides present in giloy

found in the stems of *T. cordifolia* are palmatosides E (**18**) and palmatosides [25] (Fig. 4).

Lignans: Lignans are the polyphenolic compounds which are mainly found in plants. They are mostly found in the plant based foods such as grains, legumes, vegetable and fruits. Sharma *et al*. [26] isolated one important lignan in *T. cordifolia*, which was (3,4-dihydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxybenzyl)tetrahydrofuran (**20**) (Fig. 4).

Lactones: Some therapeutically important diterpenoids furanolactone *viz*. tinosporine (**1**), cordifolide A (**21**), β-sitosterol (**22**), columbin (**23**), tinosponone (**24**) were also isolated in whole plant of *T. cordifolia* [26,27] (Fig. 5).

Steroids: *T. cordifolia* shoot contain few steroidal compounds for which plant exhibits activity like inhibition of osteoporosis induced by glucocorticoids. Some important steroids *viz*. β-sitosterol (**25**), β-hydroxyecdysone (**26**) and makisterone A (**27**) were also isolated [28-30] (Fig. 6).

Sesquiterpenoid aliphatic compound: Few sesquiterpenoid aliphatic compound such as 1-heptacosanol (**28**) and 1-octacosanol (**29**) were found by few researchers [31]. Structure of these compounds are shown in Fig. 6.

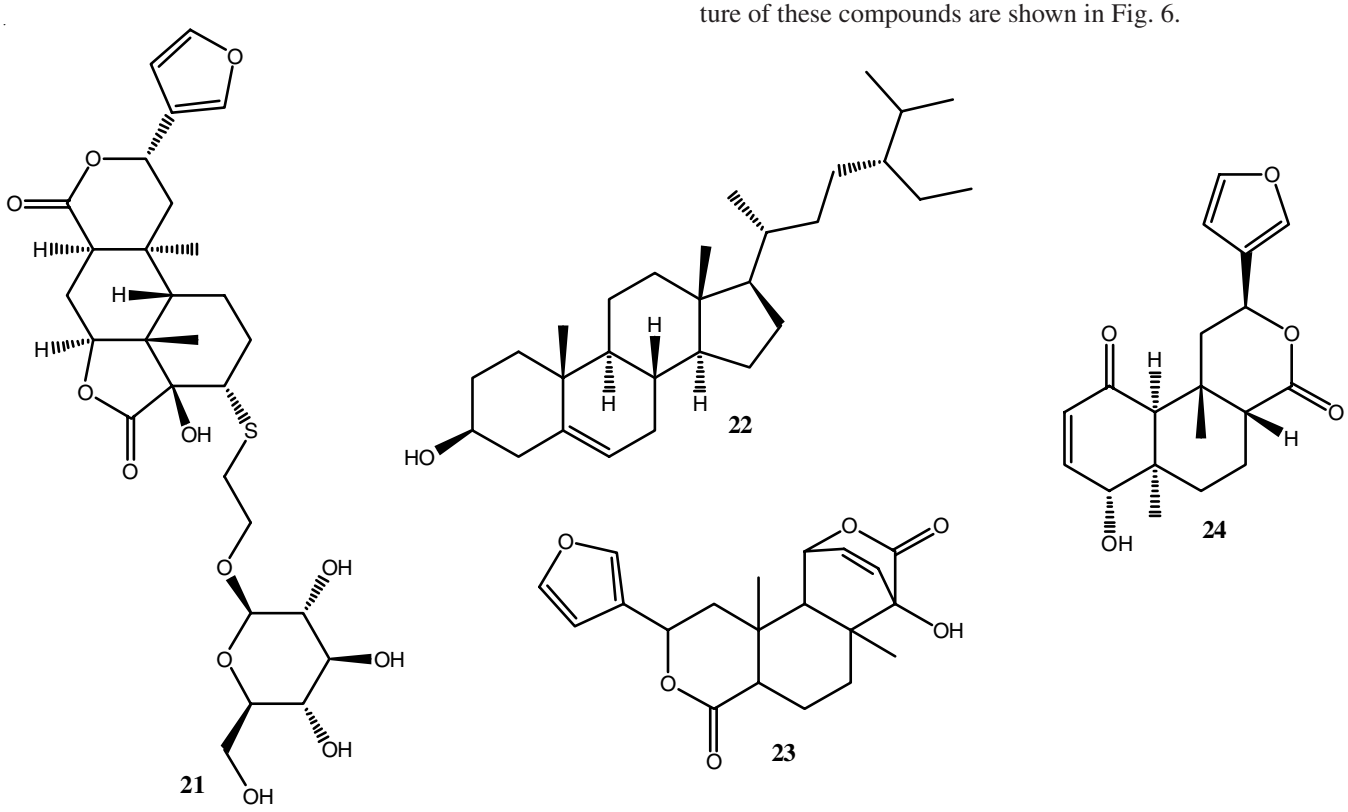

Fig. 5. Structures of various lactones present in giloy

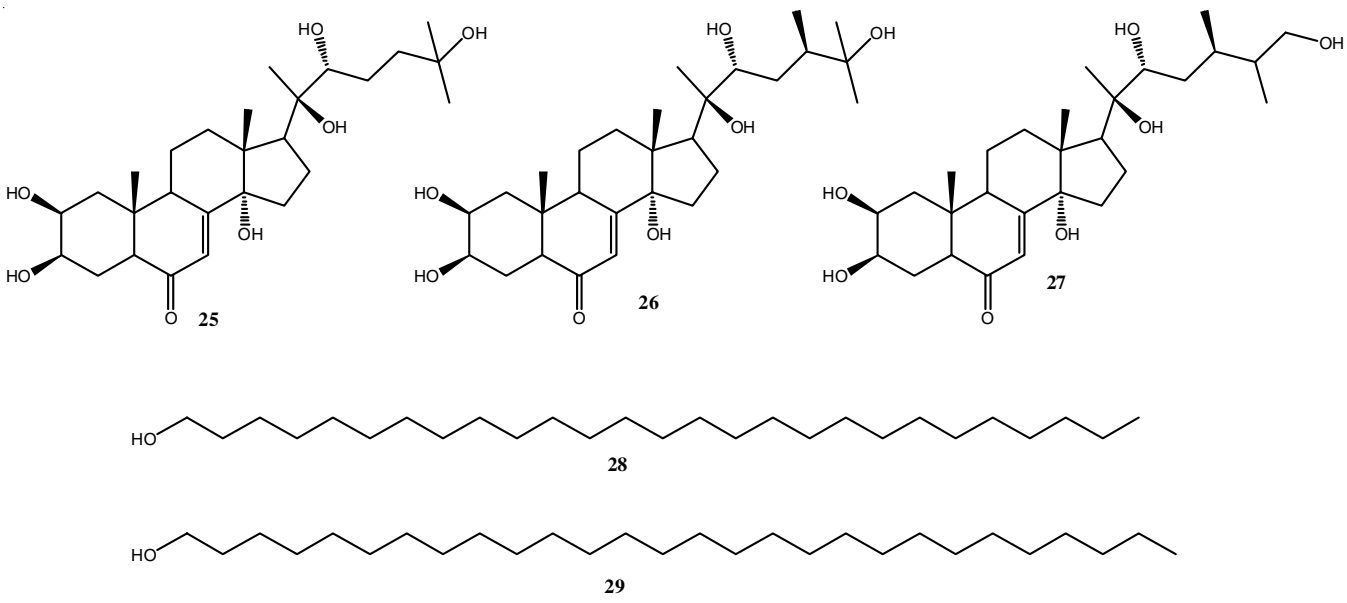

Fig. 6. Structures of steroidal drugs present in giloy

Traditional uses: Traditionally in Bhava Prakash [32], *T. cordifolia* is mentioned as a bitter tonic, astringent, diuretic and potent aphrodisiac and curative against skin infection, jaundice, diabetes and chronic diarrhoea and dysentery. According to Ayurveda, *T. cordifolia* is mentioned as "rasayana" which means circulation of "rasa"-the nutrient. According to Charka, rasayana is used in increasing the life period, anti-aging, increasing memory power and intelligence, immunity booster and protect human body from disease [3,5,10].

Since ancient times, *T. cordifolia* is used as a culinary and treatment for different diseases by the tribes of Khedbrahma region of Northern Gujarat state, India. These tribals use the powder prepared from stem bark and roots of *T. cordifolia* for cancer treatment [32]. For the treatment of diarrhoea and dysentery, they use the decoction prepared from the root part and for the periodic fever, decoction of stem part of *T. cordifolia* are used [1]. The tribal people of Dahanu forest region in Maharastra state of India, namely Agaris, Dhodias, Bhils, Khakaris, Dublas, Rimoshis, Thakurs, Vagharis, Vardaris, Varlis, *etc*. spread the stem decoction with cold or hot water (about 3-4 gm) in morning in an empty stomach as a tonic in general debility [33]. The local people of Patiyala, Punjab state of India uses the leaf juice of allied species of *T. cordifolia i.e. T. sinensis* for the treatment of ear pain [34].

Pharmacological activities: Due to the presence of numerous phytoconstituents, various pharmacological activities of *T. cordifolia* have been widely reported by the researchers. A schematic representation of various pharmacological properties of *T. cordifolia* are shown in Fig. 7. In sub-sections, the pharmacological activities exhibited by *T. cordifolia* is discussed as follows:

Anti-toxin: By alternating various hormones and mineral levels *T. cordifolia* shows a protective effect on different organs. *T. cordifolia* reverses the toxicity of aflatoxin in kidney by increasing the hormone level and activities of enzymes which ultimately leads to decrease the reactive oxygen species [35]. When the extract of *T. cordifolia* is given orally then it decreases the toxic effects of lead nitrate in mice liver [36]. *T. cordifolia* overcomes the cyclophosphamide induced toxicity by considerably raising the level of GSH, cytokines and gradually declining the level of tumor necrosis factor in urinary bladder and prevent the damage of hepatic cells which confirms the anti-toxin activity of *T. cordifolia* [37].

Anti-arthritic: In India and China, *T. cordifolia* has been used as traditional medicine against different illness since time

Fig. 7. Overall representation of various pharmacological properties of *T. cordifolia*

immemorial. An ethanolic extract of *T. cor*difolia exhibited the anti-arthritic activity using Freund's complete adjuvant and Bovine type II collagen method [38].

Memory enhancer: *T. cordifolia* is also known as learning and memory enhancer. In double-blind placebo-controlled study, it was found that pure aqueous extract of *T. cordifolia* can enhanced the learning and memory [39]. In normal rat models, *T. cordifolia* is found to increase learning and memory power and also reverse the memory deficit produced by cyclosporin. Nandkumar *et al*. [40] found that in Hebb William maze, the aqueous and alcoholic extracts of *T. cordifolia* reduces the learning scores but enhance memory and learning capacity.

Anti-stress and CNS depressant activity: According to several studies [41], *T. cordifolia* is useful in keeping human brain healthy and also useful in stress management. Mainly the root part of *T. cordifolia* shows the anti-stress activity [42]. In mice, different parts of *T. cordifolia* plant also exhibited the anti-stress activities [43,44]. Moreover, using different solvents extracts (*e.g*. ethanol, aqueous and petroleum ether) of root, leaf and stem of *T. cordifolia* showed a potential decreased in the locomotor activity in rodents, which was evaluated by using actophotometer [4].

Antioxidant activity: *T. cordifolia* exhibits the antioxidant potential by scavenging free radicals and other reactive species in its different extracts. It reduces the regulation of lipid peroxidation process and regulates catalase and glutathione which are anti-oxidant enzymes [39,45,46]. It was also reported that by raising the GSH level and reducing the expression of nitric oxide synthase gene, the antioxidant activity also exhibited [47,48]. Another study [49] reported that the aqueous, ethanolic and methanolic extract of *T. cordifolia* also shows the potential antioxidant activity. It was found that in alloxan induced diabetic rats, an ethanolic extract of *T. cordifolia* decreases the superoxide dismutase, glutathione peroxidase and increases catalase activity and erythrocytes membrane lipid peroxidase [25]. This plant has a polysaccharide compound known as "arabinogalactan", which shows a protection against free radicals in rat model [16,50].

Hepatoprotective activity: Different extracts of *T. cordifolia* have hepatoprotective activity, which acts against CCl_4 induced liver damage in rats. The ethanolic extract of *T. cordifolia* reduces the serum enzyme such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), *etc*. [51]. Moreover, various phytoconstituents like alkaloids, terpenoids, steroids, *etc*. present in *T. cordifolia* are responsible for the hepatoprotective activity [52], when evaluated by using bile duct ligation induced jaundice in rats [53].

Immunomodulatory activity: Some isolated chemicals of *T. cordifolia* like cordifolioside A and syringin has immunomodulatory activities [54]. When macrophage cell is exposed to *T. cordifolia* then it increases the production of various enzymes which acts as antimicrobial agent and enhances the immunity [55]. Aqueous extract of this plant stimulates the production and activation of cytokine and immune effector cell [56]. Moreover, the phytoconstituents like steroids, alkaloids are responsible for the immunomodulatory activities [57]. The alcoholic extract of *T. cordifolia* increases the white blood cell count and bone marrow cells indicating a stimulatory effect on the haemopoietic system and shows immunomodulatory action [58]. By increasing the phagocytic property of macrophage, splenocytes and nitric acid production, it shows the immuneprotective activity [56]. Furthermore, G1-4A, a polysaccharide compound increases the differentiation and proliferation of T cell and B cell, which ultimately enhanced immunity [59].

Anticancer activity: The radio-protective property of this plant can increase the body weight as well as the weight of the tissues. As stated by researchers, *T. cordifolia* can protect the harmful activities of γ-radiation in mice model. The methanolic extract of this plant have potential anticancer activity by inducing the death of cancerous cells [60]. The hydroalcoholic root extract of *T. cordifolia* can increases the level of glutathione (GSH) and other metabolizing enzyme of liver and also reduced the level of malonaldehyde production, which leads to decrease in free radical formation and act as an antioxidant for cell [61]. Various secondary metabolites isolated from *T. cordifolia* were tested in different types of tumor cells and found that yangambin and palmatine is used in the treatment of KB cells, whereas tinocordiside is used to treat oral cancerous cell and colon cancer cell [62].

Antimicrobial activity: The antimicrobial activity of methanolic extract of *T. cordifolia* was evaluated against *E. coli*, *S. typhi*, *S. paratyphi*, *K. pneumonia*, *P. vulgaris*, *etc*. and exibited some prominent antimicrobial activities [45]. Silver nanoparticles formulated from *T. cordifolia* stem shows potent antibacterial activity against *P. aeruginosa* strain [63]. A potent active compound isolated from the stem of *T. cordifolia* shows significant antifungal activity against *T. rubrum* and *T. simii* and antibacterial activity against *B. subtilis* and *E. faecalis* [64]. The leaves and stem extract of this plant is useful against urinary tract infection caused by *P. aeruginosa* and *K. pneumoniae* [65]. *T. cordifolia* can decrease the resistance of many anti-biotics used in urinary tract infection [66].

Antiallergic activity: Along with other activities, *T. cordifolia* also possess some potent antiallergic effects. Allergic effects like nasal pruritus, nasal discharge, nasal obstruction, sneezing, *etc*. can be treated by using *T. cordifolia* [5].

Analgesic activity: Due to the presence of flavonoids, alkaloids, glycosides, terpenoids and steroids, *T. cordifolia* shows significant analgesic activity [53]. The analgesic activity of *T. cordifolia* was evaluated by using hot plate and abdominal writhing method and shows the significant analgesic activity in albino rat models. Since, the plant shows positive results of the analgesic activity of *T. cordifolia*, which involves central as well as peripheral analgesic mechanism [67]. The mechanism behind the analgesic activity of *T. cordifolia* is mediated through the inhibition of prostaglandin synthesis and potentiation of analgesic effect of morphine on opioid receptors [42,68]. The petroleum ether extract of *T. cordifolia* increases the anti-nociceptive activity by elevating the levels of monoamines such as dopamine, noradrenaline and serotonin [52].

Antipyretic activity: Ashok *et al*. [69] determined the antipyretic activity of *T. cordifolia* in albino rats by using yeast induced pyrexia model.

Antidiabetic activity: *T. cordifolia* exhibited antidiabetic properties and is useful in managing the type-2 diabetes mellitus. Specially, the stem part is useful in the curing diabetes. As per studies [70], it has an efficacy of 40-80% compared to insulin due to the presence of cardiac glycoside, saponins, alkaloids (jatrorrhizine, magnoflorine, palmatine), tannins, *etc*. The ethyl acetate, dichloromethane, hexane and chloroform extract of *T. cordifolia* was evaluated against *in vitro* α-glucosidase inhibition activity and found that *T. cordifolia* have significant α-glucosidase inhibition activity [71]. The aqueous extract of *T. cordifolia* decreases the undesirable abnormalities in the liver including lipid peroxidation, GSH levels, protein carbonyl group and enzymatic antioxidants, which is caused by fructose [72]. A study shows that when *T. cordifolia* was administered into a diabetic pregnant rat in daily diet showed a positive effect by eliminating the relative incidence of disease and any kind of birth defects [73]. It conciliates its antidiabetic potential through promoting insulin secretion, inhibiting gluconeogenesis and glycogenolysis and thereby regulating blood glucose. In alloxan-induced diabetic model the root extract of *T. cordifolia* showed an anti-hyperglycemic effect by decreasing its excess glucose level in urine as well as in normal [74].

Anti-inflammatory activity: Patgiri *et al.* [75] found that *T. cordifolia* showed potent elevation in pain threshold or time of reaction after 30, 60 and 90 min of administration, in doses of 200 mg/kg and 100mg/kg associated with 5 mg/kg of diclofenac. At the same above doses, *T. cordifolia* showed 40.5% and 36.63% inhibition of paw edema after 3 h of administration. *T. cordifolia* decoction showed the potent anti-inflammatory activity against carrageenan induced hind paw edema in rat models [54]. The mechanism behind the anti-inflammatory action of *T. cordifolia* showed by potentiating noradrenaline by uptake blocking effect, inhibition of noradrenaline metabolism by COMT and increasing 5-HT activity by MAO inhibition [55].

Antimalarial activity: The stem ethanolic extract of *T. cordifolia* exhibited the antimalarial activity. The combination of *T. cordifolia* (Wild.) Hook.f. & Thomas and *Cissampelos pareira* L. shows *in-vivo* inhibition of propagation *Plasmodium berghei*, a rodent parasite in mice [76].

Diuretic activity: In a study, *T. cordifolia* was found to have diuretic effect [77]. *T. cordifolia* is used in various ayurvedic formulation to treat different urinary problems [32]. In diabetes induced rat kidney, it was found that *T. cordifolia* extract shows a significant alteration of gluconeogenic enzyme and morphological activity [78].

Anti-HIV activity: The roots extract of *T. cordifolia* have anti-HIV potential. It helps in managing the HIV by reducing eosinophil count and increasing the CD4 T-cells count in HIV positive patients. The extract improves the bactericidal and phagocytic activity intracellularly. Furthermore, it also stimulates the peritoneal macrophage, B-lymphocyte, polymorphonuclear leucocytes, level of hemoglobin and macrophages [16,79,80].

Anti-ulcer activity: The ethanolic extract of the roots of *T. cordifolia* also showed anti-ulcer activity. In restrain stress which induced ulceration model, the extract shows significant protective effects. Due to its significant protective effects the anti-ulcer activity of *T. cordifolia* can be compare with the standard drug diazepam [79].

Anti-aging activity: *T. cordifolia* has also been found to possess the free radical scavenging properties against reactive nitrogen and oxygen by making less expression of iNOS gene [81]. *T. cordifolia* shows significant decreases of thiobarbituric acid reactive substance and increase in superoxide dismutase, reduced glutathione catalase, monoamine oxidase activities such as MAO-B and MAO-A are elevated by the *T. cordifolia* extract, which leads to antidepressant activity [82].

Anti-convulsant activity: The ethanolic extract of *T. cordifolia* plant shows the good anti-convulsant activity. The percentage inhibition of convulsion of ethanolic extract was 61.1%, when compared with standard drug [40].

Hypolipidemic activity: In diabetic patient, an increase level of serum lipid can cause coronary heart disease which can be prevented by using hypolipidemic agent [83]. The aqueous extract of roots of *T. cordifolia* showed a greater hypolipidemic activity [25].

Anti-osteoporotic effects: The anti-osteoporotic effects of *T. cordifolia* has an impact on the bone matrix mineralization, proliferation and differentiation on the *in-vivo* osteoblast model. The growth of the osteoblast can be stimulated by alcoholic extract of *T. cordifolia* through increasing the differentiation of cells into osteoblastic lineage and the mineralization of bone-like matrix [84,85]. The β-ecdysone which is extracted from *T. cordifolia* has been reported to induce a significant increase in the thickness of joint cartilage and also induce the osteogenic differentiation in the mesenchymal stem cells of mouse [86].

Anti-Parkinsonism activity: In 1-methyl-4-phenyl-1,2,3,6-tetra hydropyridine (MPTP)- intoxicated Parkinsonian mouse model, the aqueous extract of *T. cordifolia* shows potent anti-inflammatory activity. This indicates that by suppressing neuro-inflammation in MPTP-induced Parkinsonian mouse model, *T. cordifolia* can protect dopaminergic neurons [87].

Anti-amoebic activity: *T. cordifolia* has anti-amoebic effect against *Entamoeba histolytica*. The inhibition of the enzymes such as protease, RNase, aldolase, alkaline phosphatase, DNase activities, *etc*. can contribute into the anti-amoebic effect of *T. cordifolia* extracts [87].

Post-menopausal syndrome: The drug named minofil contain *T. cordifolia* along with other plant drugs which is used in women's post-menopausal syndrome. Minofil gives more prominent activity in post-menopausal syndrome without any side effects [88].

Urinary calculi and uremia: For dissolution of urinary calculi, *T. cordifolia* water extract was evaluated and found some positive response. It was reported that *T. cordifolia* can act against uremia. In dogs, the water extract produced marked but temporary fall in blood pressure, along with bradycardia and increased the ventricular contraction and the extract produce diuresis in rats. In uremic dogs and patients, it helps to decrease the blood urea levels [25].

SARS-CoV-2 inhibiting activity: Based on the emerging demand of searching some potent medication against SARS-

CoV-2, mainly researchers investigated the numerous phytoconstituents of *T. cordifolia* against main protease (M^{pro}) of SARS-CoV-2 virus [89]. The main focus of virus resides on the virus and nucleocapsid(n) proteins, RNA dependent RNA polymerase and receptor motif on human ACE2 and its related functional proteins such as TMPRSS2 [90]. Aqueous extract of *T. cordifolia* could serve as prophylaxis if it administrated for few days [91]. It is also reported to induce immunomodulatory effect in human immuno-deficiency virus positive patients [92-95]. Tinocordiside, a phytoconstituent of *T. cordifolia* shows the potent inhibition against SARS-CoV-2 [96]. Due to the presence of cordifolioside A, phytoecdysteroid, magnoflorine; *T. cordifolia* possess immunomodulatory and anti-inflammatory effects, it increases the phagocytic property of neutrophils which in turn helps in inhibiting SARS-CoV-2 virus [54,97]. Ecdysone, have beneficial effects on renin-angiotensin system, which may be useful in inhibiting SARS-CoV-2 since both virus and renin-angiotensin system involved ACE-2 receptors [98]. *T. cordifolia* shows beneficial effects against SARS-CoV-2 spike protein induced phenotype disease in a humanized zebrafish model [23]. The main active phytoconstituents of *T. cordifolia* such as β-sitosterol, berberine, coline, octacosanol, tetrahydropalmatine were investigated against $3CL^{pro}$ protein of SARS-CoV-2 and found that among all the phytoconstituents, berberine can significantly control replication of virus by potent $3CL^{pro}$ protein inhibition [90].

Conclusion

Tinospora cordifolia also known as Giloy, sometime consider as the magical herbs due to its diverse phytochemicals content and enormous pharmacological activities. Different bioactive compound belongs to class of alkaloids, sesquiterpenoids, glycosides, steroids, volatile oils, *etc*. Among which compound such as tinosporine, tinosponone, β-sitosterol, mekisterone, tinocordiside, cordifoliside, *etc*. make this herb medicinally important one. Screening of various activities have been done by various authors *in-vitro* as well as *in-vivo* also, in which they found very effective results. Antioxidants, anticancer, antiviral, antimicrobial properties are quite important properties of this herb. Moreover, SARS-CoV-2 inhibitory properties are being investigated through *in-silico* studies and its gives good inhibition results. Although *in-vivo* experiment need to be done to confirm their efficacy against the deadly viruses. Thus, based on various researches, *T. cordifolia* is considered as an excellent drug and can be used to cure many more diseases for mankind.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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