**REVIEW ARTICLE**

**Tinospora cordifolia** (Giloy): Phytochemistry, Ethnopharmacology, Clinical Application and Conservation Strategies

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**Abstract:** *Tinospora cordifolia* (Giloy) is a medicinal plant used in folk and Ayurvedic medicines throughout India since ancient times. All the parts of the plant are immensely useful due to the presence of different compounds of pharmaceutical importance belonging to various groups as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, and phenolics. These compounds possess pharmacological properties, which make it anti-diabetic, antipyretic, anti-inflammatory, anti-oxidant, hepato-protective, and immuno-modulatory. However, due to the increasing population, there is an inadequate supply of drugs. Therefore, this review focuses on phytochemistry, ethnopharmacology, clinical application and its conservation strategies so that the plant can be conserved for future generations and utilized as alternative medicine as well as to design various pharmacologically important drugs.

**Keywords:** *Tinospora cordifolia*, Ayurveda, phytochemistry, ethnopharmacology, steroids, conservation strategies.

1. **INTRODUCTION**

*Tinospora cordifolia* (Giloy) is a deciduous shrub of the Menispermaceae family [1, 2], which is mainly found in Asian, African and Australian continents at an altitude of 300 to 1200 m above the sea level [3, 4]. The term Giloy/Giloy in Hindi [5] refers to a Hindu mythological term meaning the heavenly magic that can save the planetary beings from ageing and be young. In India, Giloy is known by many names like Gilo in Punjabi and Kashmiri, Guduchi in Sanskrit, Seendal in Tamil, Amarlata in Assamese and many more. The Sanskrit name, Guduchi, means protecting the entire body while the term amrita means the ability to maintain longevity and youthfulness. The name changes with the country and its language also. They are called as Xin ye qing in Chinese; Tinofolin in French; Moonseed, or Indigenous and its language also. They are called as Xin ye qing in Chinese; Tinofolin in French; Moonseed, or

The stem of Giloy is threadlike with fleshy aerial roots arising from the branches. The stem varies in thickness (0.6 to 5.0 cm), with the young stems being smooth and green having swellings at nodes. However, the old stems become light brown with sticky swellings due to circular lenticels [7]. The color of its bark varies from creamy white to gray, having enlarged rosette-like lenticels. Its leaves are thin and heart-shaped. The shrub bears small yellow or greenish-yellow flowers that show axillary and terminal racemose panicles (Fig. 1). The male flowers are assembled while the female flowers blossomed in a solitary manner during summer. During winters, fleshy fruits with a single curved seed are produced. The drupes are red and glossy, pea-sized and oval in shape [8].

These plant parts are extensively used in a wide spectrum of therapeutic activities. They contain a surplus quantity of flavonoids, glycosides, saponins and other pharmaceutical compounds which are known for their antioxidant activity. Different chemical constituents such as giloin, columbin, chasmanthin, palmatine, isocolumbin, tembetarine, syringing, ecodysterone, cordiside, tincordisofolin, tincordisofioloside, cordisoloside A, palmarin, tinosporin and tinosporic acid have been isolated from different parts of Giloy [9]. It is known to possess anti-cancer [10], anti-ulcer [11], memory enhancer [12], anti-depressant [13], anti-schizophrenic [14], anti-fertility [15], chemo-preventive [16], hypolipidemic [17], neuroprotective [18], blood purifier [19], anti-pyretic [20], anti-hepatitis [21], anti-microbial, anti-inflammatory, anti-periodic, anti-spasmodic, anti-arthritis, analgesic and...
Fig. (1). Each scale represents 1 cm (A) Flower of *T. cordifolia* (x 12 cm), (B) Fruit (Berry) (x 1 cm) and (C) Leaf (x 20 cm length), Stem (x 60 cm). *(A higher resolution/colour version of this figure is available in the electronic copy of the article).*

diuretic [9, 22] properties which provide new life to the whole body, thus referring to as a rejuvenating herb.

Table 1. Various Giloy-based products available in the market with their pharmaceutical properties.

<table>
<thead>
<tr>
<th>Pharmaceutical Products</th>
<th>Targeted Ailment</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Tinospora cordifolia</em> pellets</td>
<td></td>
</tr>
<tr>
<td>Gudachyadi churna</td>
<td>Diabetes and fever</td>
</tr>
<tr>
<td>Guduchi Taila</td>
<td>Liver infection and diabetes</td>
</tr>
<tr>
<td>Abhaihubbujhr</td>
<td>Anti-stress</td>
</tr>
<tr>
<td>Safe herb</td>
<td>Anemia and sexual disabilities</td>
</tr>
<tr>
<td>Brave heart capsule</td>
<td>Cholesterol, diuretic</td>
</tr>
<tr>
<td>Cirrholyiv capsule</td>
<td>Hepatoprotective</td>
</tr>
<tr>
<td>Cirrholyiv-ds syrup</td>
<td>Hepatoprotective</td>
</tr>
<tr>
<td>Mussafen</td>
<td>Blood purifier and anti-allergic</td>
</tr>
<tr>
<td>Madhu Mehari</td>
<td>Diabetes, fatigue, urinary problem</td>
</tr>
<tr>
<td>Tomplex</td>
<td>Increase immunity</td>
</tr>
<tr>
<td>Rebuild</td>
<td>Anti-stress and antioxidant</td>
</tr>
<tr>
<td>Sanjivani vati</td>
<td>Chronic fever and gastro-enteritis</td>
</tr>
<tr>
<td>Guduchi satvva</td>
<td>Burning sensation and liver disease</td>
</tr>
<tr>
<td>Guduchi ghriti</td>
<td>Gout</td>
</tr>
<tr>
<td>Amritaguggulu</td>
<td>Osteo-arthritis, gout</td>
</tr>
<tr>
<td>Punchniima churana</td>
<td>Diabetes, poison, ascites, arthritis</td>
</tr>
<tr>
<td>Ilogen Excel</td>
<td>Anaemia, diabetes</td>
</tr>
<tr>
<td>Trasina</td>
<td>Antioxidant</td>
</tr>
<tr>
<td>Dihar</td>
<td>Antioxidant, diabetes, cholesterol</td>
</tr>
</tbody>
</table>

Source: [23-24].

Due to high medicinal properties, it has been enlisted amongst highly traded medicinal plants as well as amongst highly important medicinal plants of agro-climatic zone eight (Rajasthan, Uttar Pradesh and Madhya Pradesh) by National Medicinal Plant Board (NMPB), New Delhi, India [23]. There were various products with their pharmaceutical properties available in the market [23, 24] (Table 1). However, due to the overexploitation of Giloy by people as well as pharma companies, there is an acute scarcity of the plant. Hence, this review will provide insights on the plant distribution, chemical constituents and their pharmaceutical applications as well as growth constraints and conservation strategies so that the plant could be preserved for the future generation.

2. PHYTOCHEMISTRY

Different chemical compounds (*e.g.* alkaloids, glycosides, steroids *etc.*) have been extracted from Giloy (Table 2). The leaves contain a fairly rich amount of protein (11.2%) along with minerals, namely calcium and phosphorus [25, 26]. Berberine and jatrorrhizine have been reported in the callus and cell suspension cultures of stem extract of Giloy [27]. Arabinogalactan compound had been obtained from the dried stems. Further, four new glucoside compounds, namely amritosides A, B, C and D have been obtained from stems of Giloy and the structural characterization was done by spectroscopic studies [28]. Further, the purified polysaccharide revealed polyclonal mitogenic property against B-cells, however, macrophages were not required for their proliferation [29]. Ahmad *et al.* [30] identified four new compounds, viz., tinosporafuranol, tinosporafurandiol, tinosporaclerodanol, and tinosporaclerodanoid compounds from the stem bark of *T. cordifolia* Miers (Menispermaceae) (Table 2) [31-55].

The major alkaloids isolated from Giloy include aporphine, berberine, choline, isocolumbine, jatrorrhizine, magnoflorine, tembetaryne, tinosporin, tinosporic acid, palmitene, and tetrahydropalmatine. These compounds show pharmacological properties like anti-cancer, anti-diabetes, anti-inflammation and anti-viral [6]. Van Kiem, Van Minh, Dat,
Hang, Nam, Cuong, Huong and Van Lau [56] isolated four new compounds from the methanol extract of Giloy among which two are aporphine alkaloids namely tinocoroside A and tinoscorside B, while the other two are tinocorside C and tinoscorside D. Pan, Terrazas, Lezama-Davila, Rege, Gallucci, Satoskar and Kinghorn [57] further isolated a new sulfur-containing compound (cordifolide A) along with cordifolides B-C, and tinosposide from Giloy. Later, Sivasubramanian, Gadeppali Narasimha, Rathnasamy and Campos [58] extracted tinocordin along with tinosporide, 8-hydroxycolumbin from Giloy using chloroform. The essential oil from the leaf of the plant contains compounds like 2-hexenal, 1-hexanol, 4-hexen-1-ol, isobutyl phthalate, myristic acid, linalool, 2,4-pentadienal, 1-penten-3-ol, 2-penten-1-ol, and 2-phenylo ethanol [59]. The signaling mechanism of the novel compound, (1, 4)-alpha-D-glucan (RR1), isolated from Giloy, was investigated to reveal its immunostimulating properties [60]. All these compounds have a significant role in pharmacological applications.

3. ETHNOPHARMACOLOGY

The pharmacology of Ayurveda is based on mechanisms of biophysics, observation, inference and intuition. The mode of action of any substance depends on five mechanisms of action, namely, i) Rasa (taste perception by the chemical receptors on the tongue), ii) Guna (ten pairs of a mirror image or opposite attributes of a substance), iii) Vipaka (tissue metabolism and digestion in the intestine by neutral (madhura), acidic (amla) or alkaline (katu) medium), iv) Virya (explained by potency; hot (ushna) or cold (sheeta)) and v) Prabhav (specialized receptors-based action). All these are biophysical in nature. The six tastes in Ayurveda are sweet (madhura), sour (amla), salty (lavana), bitter (tikta), pungent (katu) and astringent (kasaya). However, in modern sensory science, the quality attribute describes the sensations of taste compounds into five tastes: sweet, sour, salty, bitter, and umami [61].

Different extracts of Giloy possess pharmacological activities, including immunotherapeutic properties [62]. The aqueous extract of the stem has been reported to contain immunologically active arabinogalactan polysaccharide [29] along with other bioactive compounds. The aqueous extract was further tested for its immunostimulant [63] and immunomodulant properties along with in vivo production of antibodies [64]. Further, the aqueous extract of stems is effective against hyperlipidemia [65] and shows antibacterial and immunomodulatory properties as well [55]. On the other hand, the aqueous extract of roots possesses hypoglycemic activity [66]. These pharmacological activities of Giloy are due to the biologically active phytochemicals prevailing in different parts of the plant (Table 2). These compounds are responsible for treating ailments like leprosy, asthma, gout, and chronic diseases like diabetes as mentioned in the classical texts of Ayurveda (e.g., Charak, Sushruta and Ashtanga Sangraha) as well as other critiques like Bhava Prakash and Dhanvantari Nighantu besides folk and tribal medicine across India, as shown in Table 3 [9, 67]. Further, for the treatment of diseases and infections, several patents have been filed by various inventors for the various uses and formulation of T. cordifolia, as shown in Table 4 [68-82].

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### Table 2. Chemical constituents present in different parts of Tinospora cordifolia and their clinical application.

<table>
<thead>
<tr>
<th>Type of Chemical</th>
<th>Active Chemicals</th>
<th>Plant Part</th>
<th>Clinical Application</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alkaloids</strong></td>
<td>Aporphine Alkaloids, Berberine, Choline, Isocolumbin, Jatrorrhizine, Magnoflorine, Palmetine, Tembetarine, Tetrahydropalmatine, Tinosporin,</td>
<td>Stem, Root</td>
<td>Anti-viral, anti-tumor, anti-diabetes, anti-inflammatory, neurological, immunomodulatory, and psychotropic conditions</td>
<td>[31-36]</td>
</tr>
<tr>
<td><strong>Diterpenoid Lactones</strong></td>
<td>Clerodane derivatives ([5R,10R]-4R,8R-dihydroxy-2S-3R-15,16-diepoxy-cleroda-13 (16), 14-dieno 17,12S:18,1S-dilactone), Columbin, Furanolactone, Jatrorrhizone, Tinosporan, Tinosporides</td>
<td>Whole Plant</td>
<td>Vasorelaxant, inhibitors of Ca++ influx, anti-inflammatory, anti-microbial, anti-hypertensive, and anti-viral</td>
<td>[37-41]</td>
</tr>
<tr>
<td><strong>Glycosides</strong></td>
<td>Cordioside, Cordifolioside A, B, C, D and E, Furanoid diterpene glucoside, 18-norclerodane glucoside, Palmitosides, Pregnane glycoside, Tinoscorside, Tinocorolactol, Syringin, Syringinapiosyl glycoside</td>
<td>Stem</td>
<td>Treats dementia, motor and cognitive deficits, neuron loss in spine and hypothalamus, immunomodulator</td>
<td>[42-46]</td>
</tr>
<tr>
<td><strong>Steroids</strong></td>
<td>Ecdysterone, Giloinsterol, 20β-hydroxyecdysone, Makisterone A, β-sitosterol, 6-sitosterol</td>
<td>Shoot</td>
<td>Treats IgA neuropathy or Berger's disease, glucocorticoid-induced osteoporosis in early inflammatory arthritis</td>
<td>[47-49]</td>
</tr>
<tr>
<td><strong>Sesquiterpenoid</strong></td>
<td>Tinocordifolin</td>
<td>Stem</td>
<td>Anti-septic</td>
<td>[50]</td>
</tr>
<tr>
<td><strong>Aliphatic compounds</strong></td>
<td>Heptacosanol, Nonacosan-15-one Dichloromethane, Octacosanol</td>
<td>Whole plant</td>
<td>Anti-nociceptive and anti-inflammatory. Protection against 6-hydroxydopamine induced parkinsonisms in rats</td>
<td>[51-53]</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>Cordifol, Cordifelone, Giloin, Giloinin, Jatrorrhizine, 3, (a,4-di-hydroxy-3-methoxy-benzyl)-4-(4-compounds hydroxy-3-methoxy-benzyl)-tetrahydrofuran, Tinosporidine, Tinosporic acid, N-transferuloyltyramine</td>
<td>Root, Whole Plant</td>
<td>Anti-HIV, protease inhibitors for HIV</td>
<td>[54, 55]</td>
</tr>
</tbody>
</table>
Table 3. Applications of Giloy in folk and tribal medicine in different parts of India [9, 67].

<table>
<thead>
<tr>
<th>Tribals in India</th>
<th>Diseases</th>
<th>Mode of Application of Giloy</th>
<th>Common Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baiga tribes of Naugarh and Chakia blocks of Varanasi, U.P.</td>
<td>Fever</td>
<td>Pills prepared from the paste of stems Giloy and the roots of Bharkatiya (Solanum surattense).</td>
<td>Guduchi</td>
</tr>
<tr>
<td>Tribals of Mumbai and nearby areas as well as fishermen along the sea coast</td>
<td>Fever, jaundice, chronic diarrhea, periodic fever</td>
<td>Whole plant</td>
<td>Gulvel</td>
</tr>
<tr>
<td>The tribals of Khedbrahma region in north Gujarat</td>
<td>Cancer</td>
<td>Powdered form of root and stem bark of Giloy consumed with milk for cancer</td>
<td>Garo, Galac</td>
</tr>
<tr>
<td></td>
<td>- Dyentery and diarrrhea</td>
<td>Decotion of root for diarrhea and dysentery</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>- Periodic fever</td>
<td>Decotion of old stems for periodic fever</td>
<td>-</td>
</tr>
<tr>
<td>Tribals of Jammu and kashmir (J&amp;K) and Bigwada (Rajasthan)</td>
<td>Fever</td>
<td>Decotion of stem consumed orally</td>
<td>Amrita, Gilo</td>
</tr>
<tr>
<td>Inhabitants of Bhuvneshwar (Rajsthan)</td>
<td>Fever</td>
<td>Warm juice obtained from the root of Giloy consumed orally</td>
<td>Guluchi</td>
</tr>
<tr>
<td>Inhabitants of Banka (Bihar)</td>
<td>Balashosha (Emaciation in children)</td>
<td>Shirt dyed by soaking in the juice of Giloy worn by children for Balashosha</td>
<td>Giloy</td>
</tr>
<tr>
<td></td>
<td>- Daha (burning)</td>
<td>Paste or juice of Amrita Giloy leaves and seed powder of Brassica campestris used for dha</td>
<td>-</td>
</tr>
<tr>
<td>Local people of Patiala (Punjab)</td>
<td>Fever</td>
<td>Juice of Giloy leaves along with honey consumed orally</td>
<td>Gilo</td>
</tr>
<tr>
<td>The Muslim tribes of Rajouri, Jammu (Tawsi) comprising Gujars and Backwals</td>
<td>Bone fracture</td>
<td>Whole plant</td>
<td>Amrita, Gilo</td>
</tr>
<tr>
<td>Tribal races namey Agaris, Bhils, Dhodias, Dublas, Khakaris, Rimoshis, Thakurs, Vagharis and Varlis in Dhanu forest of Maharashtra</td>
<td>General weakness</td>
<td>A tonic of decoction of Giloy stem (about 3-4 g) with cold and hot water in morning in an empty stomach</td>
<td>Gulvel</td>
</tr>
<tr>
<td>People of Dhurala (Haryana)</td>
<td>Kasa (cough)</td>
<td>Powder of Haritiki (Terminalia chebula), Giloy and Ajwain (Trachyspermum ammi) in equal quantity is consumed orally once a day early in the morning with salt</td>
<td>Amrita</td>
</tr>
<tr>
<td>Local people of Patiala (Punjab)</td>
<td>Karna shula (pain in ear)</td>
<td>Two drops of juice of Giloy leaves or allied species (T. sinensis) put in the affected ear</td>
<td>Gilo</td>
</tr>
<tr>
<td>Local women of Arjunpura (Rajasthan)</td>
<td>Raktapradara (leukorrhea)</td>
<td>Paste of Giloy and 5 seeds of Krishnamarich (Piper nigrum) consumed orally in the morning every day</td>
<td>Guduchi</td>
</tr>
<tr>
<td>The inhabitants of Badala (UP)</td>
<td>Swasa (Asthma)</td>
<td>Juice of stem consumed orally with honey</td>
<td>Giloy</td>
</tr>
<tr>
<td>People of Dehrabara Kolaras, Sivpurri of M.P.</td>
<td>Twak-rogia (Skin disease)</td>
<td>Decotion of stem consumed orally</td>
<td>Gurcha</td>
</tr>
<tr>
<td>Mundas of Chhota Nagpur</td>
<td>Fracture</td>
<td>Paste of whole plant used as plaster</td>
<td>Gulvel</td>
</tr>
<tr>
<td>In certain parts of India</td>
<td>Poisonous insects and snake bites</td>
<td>Paste of Giloy applied at the part bitten part as well as orally consumed at an interval of half an hour</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Eye disorders</td>
<td>Drops of Giloy root decoction used in eyes</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 4. Patents for the treatment of diseases and infections on recently explored studies on Tinospora cordifolia.

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Use of parts of T. cordifolia in the treatment of cancer</td>
<td>WO991008750A1</td>
<td>[68]</td>
</tr>
<tr>
<td>2</td>
<td>An ayurvedic formulation for hepatoprotective activity and also as drug therapy for flu, TB and AIDS</td>
<td>US5529778A</td>
<td>[69]</td>
</tr>
<tr>
<td>3</td>
<td>A formulation containing Tinospora cordifolia for alleviating symptoms associated with arthritis</td>
<td>US5683698A</td>
<td>[70]</td>
</tr>
<tr>
<td>4</td>
<td>Polyherbal composition for the treatment of hepatitis B</td>
<td>US613631A</td>
<td>[71]</td>
</tr>
</tbody>
</table>

(Table 4 Contd....)
4. APPLICATIONS

4.1. Anti-diabetic

The stem of Giloy has been used in the traditional folk medicine of India for regulating the blood glucose level [83]. Its mode of action against diabetic occurs by reducing Oxidative Stress (OS), inhibiting gluconeogenesis and glycogenolysis while enhancing the secretion of insulin that ultimately regulates the blood glucose [83]. The major phytochemicals of Giloy responsible for controlling diabetes include alkaloids, flavonoids, glycosides, saponins, steroids and tannins. Patel and Mishra [35] used the stem of *Tinospora cordifolia* and evaluated the three alkaloids palmatine, jatrorrhizine and patelilin; their effects on hepatic gluconeogenesis in rat liver [35]. The formulations of Giloy with ginger [84] and *Picrorhiza kurroa*, *Tinospora cordifolia*, *Vitis vinifera*, *Boerhavia diffusa* and *Withania somnifera* are effective in removing free radicals generated during various infections (e.g., during aflatoxicosis) [33]. The extract exerts protective action by reducing Thiobarbituric Acid Reactive Substances (TBARS) and increasing the GSH and antioxidant enzymes like catalase (CAT), GPx, SOD, Glutathione Reductase (GR) and glutathione S-transferase (GST) in the kidney. Further, the oral intake of Giloy extracts prevents the incidence of lead nitrate induced liver damage [84]. The stem and leaf extracts of Giloy have also been reported to exhibit hepatoprotective action against aflatoxin-induced toxicity in the kidneys (nephrotoxicity) [33]. Giloy extracts are effective in removing free radicals generated during various infections (e.g., during aflatoxicosis) [33]. The extract exerts protective action by reducing Thiobarbituric Acid Reactive Substances (TBARS) and increasing the GSH and antioxidant enzymes like catalase (CAT), GPx, SOD, Glutathione Reductase (GR) and glutathione S-transferase (GST) in the kidney. Further, the oral intake of Giloy extracts prevents the incidence of lead nitrate induced liver damage [84]. The stem and leaf extracts of Giloy have also been reported to exhibit hepatoprotective function in Swiss albino male mice against the lead nitrate induced toxicity [85]. The lead toxicity in mice causes a decrease of SOD and CAT, while an increase of Acid Phosphatase (ACP), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP) and Aspartate Aminotransferase (AST) levels. This was reversed by the synergetic use of leaf and stem extracts of Giloy [84]. The aqueous extract of leaves and stems acts against the lead toxicity by acting on the hematological values [85].

4.2. Anti-toxic

The alkaloid compounds of Giloy show protective action against aflatoxin-induced toxicity in the kidneys (nephrotoxicity) [33]. Giloy extracts are effective in removing free radicals generated during various infections (e.g., during aflatoxicosis) [33]. The extract exerts protective action by reducing Thiobarbituric Acid Reactive Substances (TBARS) and increasing the GSH and antioxidant enzymes like catalase (CAT), GPx, SOD, Glutathione Reductase (GR) and glutathione S-transferase (GST) in the kidney. Further, the oral intake of Giloy extracts prevents the incidence of lead nitrate induced liver damage [84]. The stem and leaf extracts of Giloy have also been reported to exhibit hepatoprotective function in Swiss albino male mice against the lead nitrate induced toxicity [85]. The lead toxicity in mice causes a decrease of SOD and CAT, while an increase of Acid Phosphatase (ACP), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP) and Aspartate Aminotransferase (AST) levels. This was reversed by the synergetic use of leaf and stem extracts of Giloy [84]. The aqueous extract of leaves and stems acts against the lead toxicity by acting on the hematological values [85].

4.3. Anti-arthritic/Anti-osteoporotic

The formulations of Giloy with ginger has been found effective in rheumatoid arthritis treatment [86]. It affects the in vitro differentiation, mineralization and proliferation of bone matrix and hence has the potential to treat osteoporosis. Alcoholic extract of Giloy is reported to enhance the osteo-
blastosis along with the mineralization of bone matrix [87]. Ecdysteroid compounds isolated from Giloy have protein anabolic and antiosteoporotic effects in mammals as β-Ecdysone (Ecd) that enhances the thickening of joint cartilage and osteogenic differentiation in mouse mesenchymal stem cells as well as decreases osteoporosis in animal models [88]. Further 20-OH-β-Ecd isolated from Giloy exerts antiosteoporotic effects [87], thereby exhibiting the potential of Giloy to treat osteoporosis and osteoarthritis [89].

4.4. Anti-HIV

The root extract of Giloy is effective against the recurrent resistance of HIV [90]. The anti-HIV effects of root extract were reported to decrease the eosinophil count while increasing the counts of B-lymphocytes, macrophages and polymorphonuclear leucocytes along with an increase in hemoglobin level, thereby, establishing its vital role in the management of the disease [90, 91]. In a study by Kalikar, Thawani, Varadpande, Sontakke, Singh and Khiyani [90], the effectiveness of Tinospora cordifolia extract (TCE) was assessed in HIV positive patients. The patients were divided into two groups and were given either TCE extract or placebo for 6 months. Participants who received TCE showed a significant reduction in haemoglobin and eosinophil count after 6 months. About 60% of them also reported a decrease in symptoms. This shows the improvement in the immune system because of Giloy.

4.5. Anti-cancer/Anti-tumour

The effect of the root extract of Giloy studied in male Swiss albino mice models has revealed a significant increase in tissue and body weight, an increase in tubular diameter along with the inhibition of the harmful effects of gamma radiation. With pre-irradiating mice studies, the root extract had a profound radiation-induced enhancement in lipid peroxidation, further leading to the decline of GSH concentration [92]. In addition, the pre-treatment of HeLa cells by TCE (dichloromethane extract of Tinospora cordifolia) declined the cell viability with the increase in LDH and decrease in GST activity [93]. The clerodane furano diterpene glycoside (TC-2) present in the aqueous-alcoholic stem extract of Giloy has the potential to cure colon cancer, which functions by the induction of apoptosis and autophagy in HCT116 cells mediated by mitochondria [94].

The effect of Tinospora cordifolia along with Zingiber officinale (ginger) on breast cancer, has been studied by Javir and Joshi [95]. A combination of the two was tested in the MCF-7 breast cancer cell line. They arrested the cell cycle at G0/G1 phase (71% cells), which leads to cell cycle arrest preventing them from entering the G2/M phase, probably through inactivation of cyclin D1. Synergistic effect of T. cordifolia (TC) along with Zingiber officinale (ZO) was found to be effective against cancer, which showed higher inhibition of cell proliferation as compared to individual dosage of TC and ZO. This synergistic effect is possible because of the combined activity of berberine, palmatine, β-sitosterol, curcumin, etc. In cancer cell lines MMP9, VEGF is involved in cell proliferation, invasion and migration. In MCF-7 cell lines, MMP2, MMP9 and ALOX 5 genes were found to be the major targets of TC+ZO for anticancer activity through network analysis. It was also found that TC+ZO downregulated MMP9 gene by 5 folds and upregulated ER-α gene by 3.5 folds as an expression of ER-α reduces cell proliferation and loss of ER-α gene results in augment of breast cancer invasion and metastasis [95].

4.6. Anti-microbial Activity

The methanolic extracts of Giloy are effective against various strains of Staphylococcus, Salmonella, Pseudomonas, Enterobacter and Escherichia coli [96-98]. Further, the extract has improved phagocytic property and intracellular bacterial capacities of neutrophils in mice [99-100] and acted as immunostimulant on macrophages [101]. In addition, the methanolic extracts of stem of Giloy possess enhanced phagocytic activity as revealed by polymorphonuclear cells in bovine subclinical mastitis [55, 102]. Further, Sarkar, Padhi, Vasanthakumar, Verma and Deep [103] evaluated the antimicrobial activity of Giloy satva by the paper disc diffusion method. The activity was tested against both gram-positive and gram-negative bacteria like E. coli, S. aureus, C. albicans, K. pneumoniae, P. vulgaris and B. subtilis. The test drug was compared with the known concentration of standard drugs – Ofloxacin and Miconazole. Giloy was found significantly effective except in the case of B. subtilis and C. albicans. Thus, the potential of Giloy can be used in treating diseased conditions like flu.

4.7. Anti-oxidant Activity

The methanolic stem extracts of Giloy showed antioxidant activity when administered orally with the increase in lipid peroxide of erythrocytes membrane and catalase activity while the decrease of SOD and GPx activities in aflatoxin-induced diabetic rats [104]. Giloy extract is regarded as an inhibitor of an enzyme, aldose reductase, as well as the actions of various anti-oxidants [105], which reduces the chemical toxicity caused by free radicals [106]. The plant extract has profound free radical scavenging activities against Superoxide Anion (O), Hydroxyl Radicals (OH), nitric oxide (NO) radicals, and peroxynitrite anion (ONOO) [18], as well as reduces the toxic side effects of an anticancer drug, Cyclophosphamide (CP), in mice due to the formation of free radicals [107]. The protective effects of Giloy have been reported even with high anti-oxidant and enzyme levels in the fetal milieu [108]. Besides this, Giloy plays an important role in removing free radicals produced during aflatoxicosis and protects the kidneys against the aflatoxin-induced toxicity due to the action of alkaloid compounds [33]. This further leads to the increment of TBARS substances in the brain while the decrease of their levels in the heart of diabetic rats [109].

4.8. Anti-stress Activity and Mental Disorders

The ethanolic extract of Giloy possesses an anti-stress activity. The use of ethanolic extract with a dose of 100 mg/kg was found to be equivalent to a dose of diazepam at 2.5 mg/kg in all the parameters studied [110]. The herbal psychotropic preparation BR-16A containing Giloy showed a possible nootropic action of BR-16A involving cholinergic and GABAergic modulation in mice [111]. Mishra, Manchanda, Gupta, Kaur, Saini, Sharma and Kaur [112]
studied the effect of 50% ethanolic extract of *T. cordifolia* stem (TCE) to improve the anxiety-like behavior induced in acute sleep-deprived rats. They reported that the petroleum ether extract of *T. cordifolia* can reverse the depression-like condition in mice. Reduction in the monoamine oxidase activities in the brain was also observed, thereby increasing the levels of brain monoamines.

### 4.9. Anti-ulcer Activity

Poor dietary habits, stress, *Helicobacter pylori* infection and genetic factors have made peptic ulcers as one of the most prevalent gastrointestinal diseases. The root extract of Giloy exerts a protective action against ulceration caused by restraint stress. The anti-ulcer activity of the extract was comparable to that of diazepam [113]. In a study conducted by Kaur, Singh and Kumar [114], the anti-diarrheal and anti-ulcer activity of ethanolic and aqueous extracts of *T. cordifolia* in rats was studied. The ulcers were induced by pylorus ligation and using ethanol in rats. The rats were divided into different groups. Each group received different pre-treatment with either rantidine, ethanolic extract or aqueous extract. Pylorus ligation caused gastric damage with high ulcer index in experimental control rats. However, depending on the dose, the rats treated with various extracts showed a significant reduction in ulcer index. Factors like gastric volume, total and free acidity were also decreased and the gastric pH increased. The group with ethanol-induced ulcer also showed a significant decrease in gastric damage represented by lower ulcer index in the case of pre-treated rats. Pre-treatment with aqueous and ethanol extract decreased the lipid peroxidation and increased the level of catalase and GSH [114].

### 4.10 Effect on the Immune System

A polysaccharide G1-4A having B-cell mitogenic activity has been isolated from the stem of the *Tinospora* [115]. G1-4A has also been reported to inhibit the activity of *Mycobacterium tuberculosis* by stimulation of macrophages. Bala, Pratap, Verma, Singh and Padwad [116] prepared different extracts from the stem of the plant and studied the immunomodulatory activity against human cancer cell lines KB, CHOK-1, HT-29, SiHa and murine primary cells. They isolated 8 molecules from *T. cordifolia* and characterized them based on NMR and mass spectrometry. The extract was found more active towards KB and SiHa cell lines than pure molecules, which showed specific activity. In addition, a study by Gupta, Rajan and Kulkarni [117] revealed that treatment of G1-4A activates murine macrophages through the classical pathway in TLR4 dependent manner. It also promotes the expression of pro-inflammatory cytokines such as TNF-α, IL-1β, IFN-γ, IL-12 and IL-6 in RAW 264.7 cells.

## 5. CONSERVATION STRATEGIES OF PLANT

The plant is a climber and requires proper support for its growth. Therefore, Giloy is usually grown with Neem, Jatropha or Drumstick tree to provide proper support for its growth. Giloy growing on Neem tree is referred to as a NEEM GILOY and mimics the chemical and therapeutic properties as neem [118]. Giloy can grow from sandy to clay loam soils; however, the optimum growth is observed in medium black or red soil with enough moisture and organic matter. The plant growth is favored warm and temperate climate. The plantation is usually done during the rainy season from July to August. Giloy plant can be replicated through seeds as well as vegetative propagations as cutting, grafting or layering. However, these methods are not feasible for large scale propagation of the plant. The difficulties with clonal propagation lie with low seed viability, poor setting and germination of seeds. The vegetative propagation is also not feasible due to low productivity and weather dependent growth conditions. Further, the plants have become more prone due to habitat fragmentation and invasive weeds. These conditions have put the plant under the endangered category. Therefore, various recent techniques as *in vitro* multiplication of nodal explants have been developed for propagation [119-121]. Further, the tissue culture technique and other biotechnological approaches could be applied for its large-scale production and conservation of the plant.

## CONCLUSION

The importance of Giloy in therapeutics for the amelioration of various diseases like cancer, diabetes and heart diseases have been highlighted in this article, which are also validated by modern pharmacotherapeutics. However, most pharmacological tests were performed with crude extracts of the plants. The specific compounds responsible for the specific bioactivities have not been investigated. Further, the studies should be conducted to reveal the interaction of the active compounds with the living systems and their structural and functional relationships. Therefore, future studies should focus on the pharmacological and biological activities of the plant extracts and analyses of bioactive chemicals responsible for the action. Based on these findings, the future dosage could be formulated for curing various immune-related chronic diseases. This can be achieved with future study trials involving *in vitro* and *in vivo* pharmacokinetics, bioavailability, and toxicological studies and subsequent clinical trials to check their efficacy. In addition, the future prospects need immense and in-depth investigation of the plant tissue culture using recent biotechnological approaches, including genomics and proteomics, thereby enabling effective disease targeting. The plant is an incredible source that can offer much to the scientific world of medicine; therefore, it needs proper awareness and conservation approach.

## AUTHOR CONTRIBUTIONS

P.K. conceived and designed the manuscript; M.K., D.K.M., H.B, B.S. and P.K. wrote the manuscript; P.R., V.B. help in the writing of the manuscript; P.K. finalize the manuscript and critically reviewed the manuscript for submission.

## CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

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**Tinospora cordifolia triggers autophagy and apoptosis in HCT-116 colon cancer cells. J. Ethnopharmacol., 2018, 21, 295-310.**

http://dx.doi.org/10.1016/j.jep.2017.09.034 PMID: 28962889


[Baldwin, A.S. Control of oncogenesis and cancer therapy resistance by the transcription factor NF-kappaB. *J. Clin. Invest.,* 2001, 107(3), 241-246. doi:10.1172/JCI111991 PMID: 11160144](http://dx.doi.org/10.1172/JCI111991)


[Rani, J.; Ranji, J.; Shankar, S.A.; Shankar, S.G.; Vijayalaksmi, G.S.; Deepa, K.; Sidhu, H.S. Enhanced phagocytosis and antibody


