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EXPLORING THE THERAPEUTIC MARVELS OF *TINOSPORA CORDIFOLIA*

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ABSTRACT: *Tinospora cordifolia* (Giloy), has been utilized across Ancient Indian and Ayurvedic medication for centuries due to its significant pharmacological properties. This comprehensive review explores the botanical, chemical, and therapeutic aspects of *T. cordifolia*, highlighting its widespread distribution, detailed plant description, and various vernacular names. The plant's cultivation preferences, climate and soil requirements, and propagation methods are examined. Additionally, the review delves into the plant's medicinal potential, particularly its antiviral and immunomodulatory properties, which acquired prominence during COVID-19. Active compounds such as glycosides, steroids, diterpenoid lactones, and alkaloids contribute to its pharmacological efficacy. *T. cordifolia* enhances the host immune system, promotes skin health, and offers anti-aging benefits. While generally safe, precautions for certain conditions like diabetes and pregnancy are advised. This review underscores *T. cordifolia's* role in modern herbal medicine and its potential for future pharmacological applications.

INTRODUCTION: Since ancient times, India has employed the medicinal herb *T. cordifolia* (Giloy) in both traditional and Ayurvedic treatments. The existence of various compounds with pharmacological significance, like glycosides, steroids, alkaloids, phenols, lactones diterpenoid and sesquiterpenoid, all sections of the plant are quite valuable [1]. After the COVID-19 pandemic commenced, the giloy plant gained popularity because of its immunomodulatory and antiviral properties [2]. Among the substances that have come out of the plant's leaves, root, stem and entire plant are alkaloids, steroids, diterpenoid lactones, aliphatics, and glycosides [3].

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T. cordifolia improves the host immune system by raising blood leukocyte and IGg levels and stimulating stem cell division. According to several traditional writings in Ayurvedic System of Medicine, including Ashtang Hridaya, Sushrut, Charak, and rest old treaty, Giloy has been employed in domestic systems of medicine [4]. The herbaceous shrub *T. cordifolia*, also known as "Amrita," "*Guduchi*," or "heart moon leaved," member of Menispermaceae family. It is valued for its curative effects in the Indian medical system [5].

Giloy leaf paste applied to the skin promotes skin regeneration and promotes wound healing. Giloy suppresses arma generation while keeping Kapha in balance. This herb stimulates the body's natural rejuvenating factor (Rasayana) and promotes wound healing. In addition, it can improve skin health as it promotes collagen production [6]. Blemishes, acne, fine lines, and wrinkles are reduced by Giloy botanicals' anti-aging properties.

Since, jiroy is a natural and safe herbal remedy, there are no significant side effects when taken. However, in some cases, using giloy can lead to constipation and low blood sugar levels. Therefore, if you have diabetes and are taking Ziroy for a long time, monitor your blood sugar regularly. Also, avoid jiroy if you are pregnant or nursing [7].

Botany:

Origin and Distribution: In Myanmar, India, and Sri Lanka, guduchi is a big, sprawling, smooth, perennial, deciduous vine featuring fleshy stems and a thin, papery bark. It is indigenous to India's tropical area, rising to a height of 500 meters with temperatures between 25 and 45 °C [8]. The Menispermeaceae family includes approximately 70 groups and 450 variety of plants, commonly found in torrid lower zone. They are typically shrubs that twine or climb. Small cymose flowers, lobed or alternate leaves, and hooked or reniform seeds are the norm. This family is an excellent origin of both alkaloids and terpenes. *Tinospora species* with roughly 15 species, Tinospora is one of the family's more significant genera. Important species for medicine include *T. uliginosa*, *T. crispa*, *T. malabarica T. tomentosa,* and *T. cordifolia* among others [9].

Guduchi, a renowned traditional Ayurvedic medicine, is commonly found in torrid regions of India, reaching elevations up to 1.2k meters. Its distribution spans from Assam to Kumaon in the north, ranging from Bihar, the Deccan region, the Konkan, West Bengal, Kerala, and Karnataka. *Tinospora cordifolia* is also present in China, Sri Lanka & Bangladesh [10].

Plant Description: *T. Cordifolia*, a considerable & hairless vine shrub that sheds its leaves, boasts a fibrous stem structure. In a cross-section scan, you'll spot yellowish wood with wedge-shaped vein bundles radiating outwards, featuring large vessels and narrow medullary rays in between. Its bark flaunts creamy white to grey tones, twisting elegantly spirally and dotted with lenticels resembling rosettes. The leaves are thin and heart-shaped. Positioned in the axils, the flowers form 2-9 cm long clusters on leafy branches, sporting a modest yellow hue while being unisexual. The male blossoms huddle together while their female counterparts prefer to stand alone. Seedlings take on a curved form with fleshy, single-seeded fruits coming into existence. Flowers bloom in the summertime whereas fruits make their appearance during winter [11].

Vernacular Name [12, 13]:

English: Indian Tinospora / Gulancha

Sanskrit: Tantrika, Chinnaruha, Vatsadaani, Madhuparni, Amrita, Guduchi, Chakralakshanika & Kundalini.

Hindi: Gulbel, Guduchi, Gurach, Giloya

Bengali: Giloe, Gulancha, Guluncha

Telugu: Madhuka, Iruluchi, Jivantika, Thippateega

Tamil: Amridavalli, Amudam, Asasi

Marathi: Giroli, Ambarvel, Gharol, Shindilakodi

Gujarati: Galo, Gulo, Gulwel

Kannada: Amrita balli, Madhupa

Latin: *Tinospora cordifolia* (willd.) Hook.F. & Thomson.

Cultivation: The plant is found in many places but prefers warm weather due to its rigidity. Planting usually happens between July & August, mainly in rainy seasons. Since it climbs, it desires uphold for proper growth. Rapid-augmenting species like Neem (*Azadirachta indica*), Jatropha (*Jatropha curcas*), and Moringa (*Moringa oleifera*) are cultivated to aid its growth.

Tinospora cordifolia, also known as Neem Giloy, a plant that grows with neem (*Azadirachta indica*) and provides superior benefits compared to giloy. *Tinospora cordifolia* desires medium-black or red soil for cultivation. *T. cordifolia* thrive in various soil types, sandy to clay loam. However, the soil must be well-drained, moist enough, and wealthy in biotic matter to support plant's build properly [14]. The plant thrives in multiple locations, yet it thrives in warm climates due to its sturdiness. Planting is typically done between July and August, particularly during rainy periods. Support is essential for its growth since it is a climber. Rapid-growing species like Neem (*Azadirachta indica*), Jatropha (*Jatropha curcas*), and Moringa (*Moringa*

oleifera) are commonly cultivated to promote development [15].

Climate and Soil: For the cultivation of *T. cordifolia*, medium dark or red soils are preferred. However, giloy can also be successfully grown in various soil types, including sandy and clay loam soils. The key requirements for optimal growth include well-drained soil that retains adequate moisture and is rich in organic matter. This plant thrives in tropical and subtropical climates and can be cultivated in light to medium sandy loam soils that are high in organic content and provide good drainage. It does not tolerate excessive rainfall or waterlogged conditions [16].

Propagation: The finest planting material for growing commercial crops is stem cuttings. From the mother plants, cuttings can be taken between June and July. Seeds can also be used to grow the plant. Seeds produce the same amount of medicine but take roughly twice as long to develop [17].

Select a sound stem cutting with at least one node from the parent plant. The spots on the stem known as nodes are where the leaves erupt. The lowest part of the stem cutting should be leaf-free. To promote root development, coat the cut end of the stem with rooting hormone powder. Make sure to bury the lower half of the stem cutting in soil when planting the stem cutting in a pot or directly in the ground.

The cutting with lots of water. Put the container or the planted cutting in an area that is warm, humid, and has some shade. Regularly water the cut, ensuring sure the soil is kept wet but not soggy. After a few weeks, the cutting should begin to produce new growth and create roots. The plant can be moved to its ultimate place after its roots have formed [18].

Planting: Planting procedures are usually carried out during monsoon between July and August. Stem cuttings, sourced from older stems containing nodes, are promptly transplanted into the field within 24 hours of detachment from the parent plant. Supporting structures like wooden posts or trellises are essential for its upward growth. The node-containing stem cuttings are shown right there in the field. For better yield, a spacing of 3 m 3 m is suggested [19].

Nutrient Management: Foods including proteins, fibre, carbs, vitamins, calcium, iron, and other necessary nutrients are abundant in Giloy. *T. cordifolia* (Giloy) is utilised as a nutraceutical in all of its components, including the leaves, stem, fruits, and roots. Giloy is rich in dietary fiber (15.8%), proteins (ranging from 4.5% to 11.5%), and carbohydrates (61.66%), while being low in fat (3.1%). Its nutritional worth is 292.54, with a caloric content measured per 100 mg. In addition to its medicinal properties, giloy is a source of essential elements such as calcium (0.131%), iron (0.28%), chromium (0.006%), and potassium (0.845%) [20].

Intercropping: As a robust twiner, it necessitates a host for support and rapidly envelops it. When draped over trees, stem cuttings with aerial roots start to grow and establish contact with underground roots [21].

Types of Intercropping [22]:

1. Row-intercropping involves cultivating multiple crops simultaneously, with at least one crop arranged in regular rows and others either interspersed within these rows or grown randomly alongside the primary crop.

2. Simultaneous cultivation of multiple crops without distinct row patterns is referred to as mixed intercropping. This method can be applied to pasture intercropping involving grasses and legumes.

3. Strip-intercropping: Simultaneously growing two or more crops in separate strips that are adequately spaced apart for autonomous farming operations, yet narrow enough to permit ergonomic human interaction.

4. Relay- Relay intercropping involves cultivating multiple crops simultaneously during distinct stages of their respective life cycles.

Weeds: Both in the field and the nursery, frequent weeding and hoeing is carried out as necessary [23].

Diseases and Pests: The therapeutic plants need to be grown without any pesticides or synthetic fertilizers. Use natural/organic manures like Vermi-Compost, Farmyard Manure (FYM), Green

Manure, and others depending on the species. Bio-insecticides can be created from Neem (kernel, seeds, leaves), Dhatura, Chitrakmool, cow's urine, etc [38].

Phytoconstituents and active components retrieved from *T. cordifolia*: Many key chemical ingredients have been identified as being present in *T. cordifolia*, including a variety of fatty acids, steroids, flavonoids, alkaloids, glycosides, tannins, phenols, polysaccharides, terpenoids and essential oils that have all been isolated during preliminary screening.

Active phytochemical substances such furano diterpene, columbin, clerodane furano diterpene, tinosporide, tinosporine, tinosporaside, cordifol, heptacosanol, cordifolide, & b-sitosterol are derived from these essential fundamental phytoconstituents of *T. cordifolia* [52].

Below Table Represents the Chemical and Active Phytoconstituents Present in *T. cordifolia:*

TABLE 1: ACTIVE PHYTOCONSTITUENTS PRESENT IN *T. CORDIFOLIA* AND ITS PLANT SOURCE

Chemicals/Constituents	Active phytoconstituents	Part of plant	Ref.
Alkaloids	Isoquinoline alkaloids: Magnoflorine, Tembetarine,	Stem	(50)
	Isocolumbin, Berberine, Palmatine. Quaternary ammonium	Root	(51)
	salt: Choline Clerodane diterpene: Tinosporin		(29)
	Protoberberine alkaloid: Tetrahydropalmatine		
Glycosides	Cardiac glycosides: Tinocordiside, Cordioside,	Stem	(50)
	Cordifolioside A, B, C, D & E, Tinocordifolioside		(51)
	Phenylpropanoid glycoside: Syringin, Syringin-type		(29)
	glycoside: Syringinapiosylglycoside, Iridoid glycoside:		
	Palmatosides F&C		
Diterpenoid lactones	Tinosporides, Columbin, [(5R,10R)-4R-8R-dihydroxy-	Whole plant	(50)
	2S3R:15,16-diepoxy-cleroda-13 (16), 14-dieno-17,12S:		(51)
	18,1S-dilactone], Jateorine, Furanolactone, Tinosporon,		(44
	Clerodane derivatives		
Steroids	Ecdysterone, Makisterone A,20 β-Hydroxy ecdysone,	Aerial part	(50)
	Giloinsterol, β-sitosterol, δ-sitosterol	Stem	(51)
Sesquiterpenoid	Tinocordifolin	Stem	(50), (51), (44)
Aliphatic compound	Heptacosanol, Octacosanol	Whole plant	(50), (51)
Miscellaneous	Cordifol, Cordifelone, Tinosporidine,	Whole plant	(50)
	Tinosporic acid, Giloin, Giloinin, Jatrorrhizine	Root	(51)

Ethnobotanical uses: The plant is used in a variety of ways, including as leaves, stems, and roots, and is highly valued for its adaptability and therapeutic properties. The plant has great therapeutic benefits in various parts [3].

Below Table Represents the Following Ethnobotanical outcomes Produced from *T. cordifolia*:

TABLE 2: ETHNOBOTANICAL PROPERTIES OF *T. CORDIFOLIA*

Parts	Uses	References
Leaves	Treatment of gout	(1)
Stem	Treat jaundice, skin diseases, managing hyperglycemia, vaginal and urethral	(1)
	fluids, minor fevers, and spleen swelling.	(3)
Stem& Root	Antivenom for serpent bites and therapies for scorpion envenomation.	(2)
Fruit	Ghee or honey are employed as a stimulant and for managing jaundice and	(4)
	rheumatism.	
Bark	Allergies, spasms, and leprosy-related conditions.	(1)

Pharmacological Activities: Giloy is known for its healing properties and has traditionally utilized to address various health issues [5]. In modern scientific studies, it has shown promising effects in managing diabetes by helping regulate blood sugar levels [6]. Furthermore, its anti-cancer properties have captured the attention of the scientific community, positioning it as a promising candidate for cancer treatment and prevention [7].

Below Table Represents Pharmacological Activities given by *T. cordifolia* was Treated with Different Diluents and Induced in Experimental Models:

TABLE 3: PHARMACOLOGICAL ACTIVITIES PRODUCED FROM *T. CORDIFOLIA*

Activity	Part of plant	Extract	Experimental model	Effect	Ref.
Anti-Diabetic activity	Leaves	Ethanolic extract	Streptozotocin-induced diabetes model	Lowering blood glucose levels, improving insulin sensitivity, and optimizing lipid metabolism.	(9), (10) (26), (27)
Anti-Cancer activity	Whole plant	Methylene chloride extract	PDX model	Reduction in tumor size and increased lifespan.	(8), (12) (25)
Immune-modulating activity	Whole plant	Aqueous extract	Edema rat model	Reduction in edematogenic agents. Modulating immune system, immune defense against pathogens and other harmful agents.	(8) (30)
Antioxidant activity	Whole plant	Ethanol extract	Mus musculus	Superior free radical scavenging activity.	(11) (43), (31)
Antimicrobial activity	Silver nanoparticles derived from stem.	-	Murine models	Enhance the effectiveness of antibiotic therapy against urinary pathogens	(11) (8) (37)
Antimalarial activity	Stem	Ethanolic extract	White swiss mice models	Reduced parasitemia and improved survival rates. Immune modulation, antioxidant effects, and action against malaria parasite.	(45) (36)
Analgesic activity	Leaves	Aqueous extract	Hot plate method	Increased the response time and decreased the number of writhes.	(46) (53)
Anti-inflammatory activity	Stem	Aqueous extract	Carrageenan induced paw edema model in rats	Significant anti-inflammatory activity	(47) (35)
Cardioprotective effect	Whole plant	Alcohol extract	Ischemia reperfusion models	Maintaining heart health and preventing cardiovascular diseases	(48) (24)
Allergic rhinitis	-	Aqueous extract	Double blind placebo-controlled trial.	Reduced the severity of allergic rhinitis symptoms	(49) (28)
Anti – bacterial activity	Leaves	Aqueous extract	-	*T. cordifolia* has killed bacteria at optimum level	(32) (33)

Phytochemistry: Glycosides, Polysaccharides, Phenolics, Alkaloids, Aliphatic compounds, Steroids, and Sesquiterpenoids are only a few various substances found in *T. cordifolia*. In particular, polysaccharides, terpenoids, and protoberberine alkaloids are thought to represent *T. cordifolia's* possible active components [1]. The plant contains a broad range of isolated constituents, like Tembetarine, cordifolisides A to E, giloin, tinosporine, columbin, Cordioside, crude giloininand, berberine, Ecdysterone, tinosporol, tinosporic acid, glucan polysaccharide, sitosterol, syringen, cordifol, Tinosporidine, syringine, amritosides, palmatosides C and F, palmarin, Magnoflorine, heptacosanol, jatrorrhizine, palmatine, gilenin, hydroxyecdysone, chasmanthin, tinosporide, bergenin, gilosterol, syringine apiosylglycoside, picrotene, tinosponone, makisterone A, Isocolumbin, tetrahydropalmaitine. These compounds contribute to the diverse chemical composition of plant [16].

Below are the Structures of Above-Mentioned Compound:

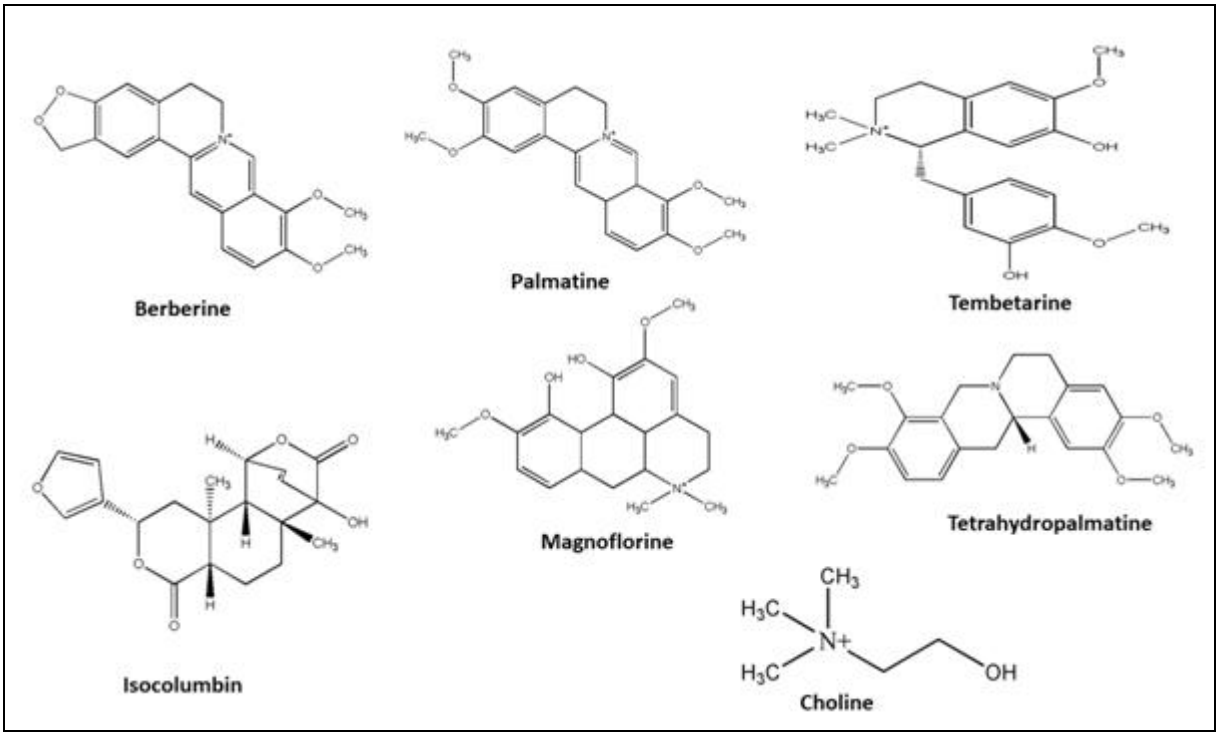

FIG. 1: CHEMICAL STRUCTURES OF ALKALOIDS PRESENT IN *T. CORDIFOLIA*

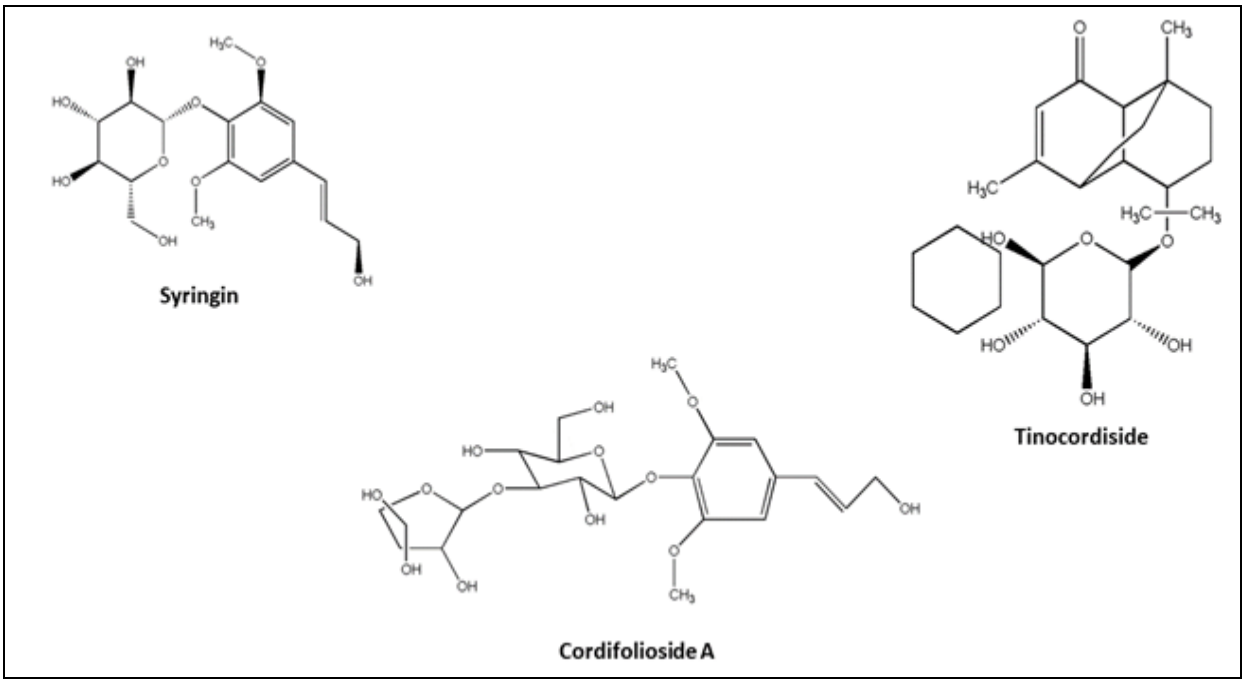

FIG. 2: CHEMICAL STRUCTURES OF GLYCOSIDES PRESENT IN *T. CORDIFOLIA*

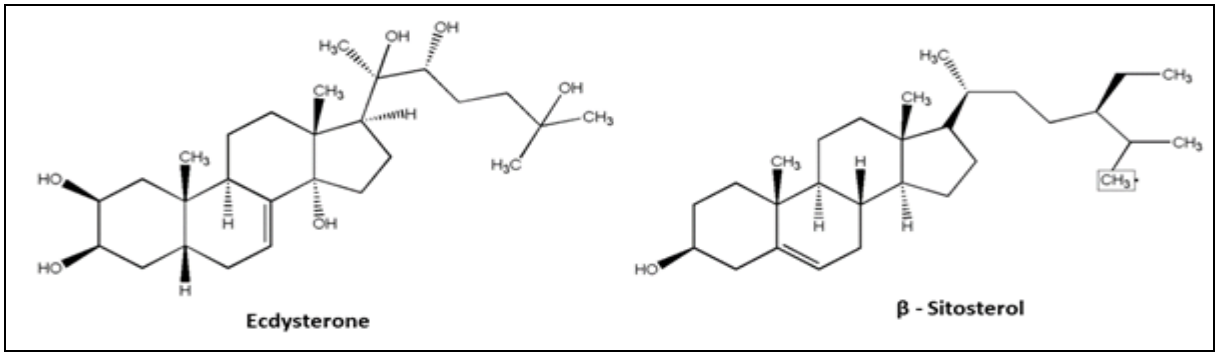

FIG. 3: CHEMICAL STRUCTURES OF STEROIDS PRESENT IN *T. CORDIFOLIA*

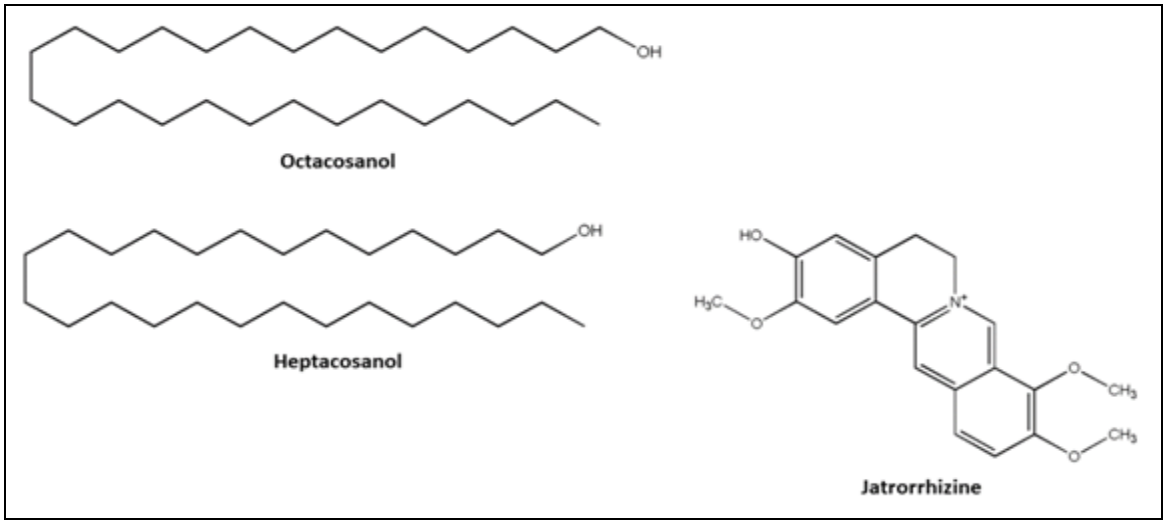

FIG. 4: CHEMICAL STRUCTURES OF ALIPHATIC COMPOUNDS AND MISCELLANEOUS PRESENT IN *T. CORDIFOLIA*

Economic Potential: Giloy is a vital therapeutic plant used in the Ayurved medical system. It's a key player in treating various ailments like general ill health, dyspepsia, urinary infections, fever, diabetes, jaundice, and dermatological conditions [1]. Dried stem costs between Rs. 15-20 per kilogram while the Giloy stem extract fetches Rs. 100 per kg [2]. A hect of *T. cordifolia* plant gives around 1500 kg of fresh woody stem initially but decreases to about 300 kg over two years [3]. The profits derived from cultivating this plant are exempt from taxes due to its agricultural nature. By following proper scientific cultivation methods and selecting quality planting materials, one can enjoy consistent benefits year after year.

While cultivating and marketing *T. cordifolia* (Giloy), the following things should be considered:

- The entrepreneur should have access to the agricultural land and any necessary infrastructure.
- Prices are determined using the current market rates.
- The production is dependent on using good cultivation techniques and quality.
- The scale of an enterprise determines how much money it will make.
- *T. cordifolia* farming yields tax-free profits. Additionally, a variety of government incentives are available, and the most recent rules should be reviewed.

The primary consideration is that the market for medicinal plants is inherently volatile, with economic conditions subject to periodic fluctuations [4].

TABLE 4: ECONOMICAL PRODUCT OF *T. CORDIFOLIA* AND THERE USES [5, 6, 34]

Product name	Uses
Shila Pravang	Early ejaculation and erectile dysfunction can be addressed using supplements to augment sexual vitality.
Guduchi Tablets	Can help with Common infections, immune diseases, Hepatic inflammation, Joint inflammation, and Antineoplastic properties.
Madhu Mehari	Relieving dryness of the mouth, numbness, debility, frequent urination, fatigue, excessive thirst, and maintaining blood sugar levels.
Safe Herbs	Addressing anaemia, vaginal discharge, and sexual debility.
Mussaffen	Act as a blooddetoxifierand assist in treating dermatological diseases
Rebuild	Free radical scavenger
Septilin	These supplementsassist in treatingupper respiratory system infections.
Tonplex	Boost defense and robustness.
Joint & Muscle Excellence Tablets	Helping purge joint toxins.
Natadadrol	Rich inPowerful muscle developmentproperties
Abhaibhubejhr	Antistress
Brave heart capsule	Lower lipid levels, particularly cholesterol and LDL cholesterol. They exhibit diuretic effects

Conservation of *T. cordifolia*: India is wealthy in floura particularly in therapeutic plant species used

by the local tribes to cure ailments [50]. Corresponding to the study conducted by WHO in 2016, estimated need for the therapeutic plants is US $14 billion per year and expected to cross US $5 trillion by year 2050. The Indian trade is approximately US $1 billion per annum [51]. According to the Red list report of ICUN 2000, many plant species are categorized as critically endangered & vulnerable. Unchecked commercialization, Population increase, urban expansion, and unregulated harvesting of forest plant species have resulted in overexploitation, habitat destruction, and the loss of plant biodiversity [39, 40].

T. cordifolia with a common name Guduchi belongs to family menispermaceae is glabrous, large, perennial deciduous, succulent spinner has unique morphological characteristics which include weak and fleshy stems, aerial roots arise from the stem are hair like, heart shaped leaves have smooth surface, yellowish flowers of the Guduchi plant blossom in rainy season & plant species have a pea shaped fruit which ripe in winter season [39, 40].

Guduchi is rich in alkaloids & terpenes. Guduchi has berberine which is a bioactive alkaloid, thus belongs to the protoberberine alkaloids. Berberine is used for the treatment of some major diseases like diabetes, hypertension, hyperlipidemia [42]. Guduchi has many medicinal properties i.e it acts as an immune modulator and behaves as bitter tonic, increases memory power, acts as a diuretic and is effective against renal obstruction like calculi & other renal disorders. Guduchi boosts memory power, develops intelligence and improves mental clarity. In Charak Samhita, which is the ancient & most potent book of ayurvedic medicine has described Guduchi as Medhya Rasayana i.e mental rejuvenative. Guduchi protects liver damage and is helpful in eye disorders. Debility, dyspepsia & urinary diseases are treated using steam of Guduchi plant. Guduchi possesses anti-pyretic properties & thus is used as a tonic against fevers, jaundice, cough, asthma, leucorrhoea, skin diseases, bits of poisonous insects & venomous snakes [50]. Conservation of these useful medicinal plant species is needed of the hour and thus is of utmost importance. Two basic situ methods can be adopted to conserve these species which are *in-situ* (on site) & *ex-situ* (off site). *In-situ* method includes preservation of species at natural rate through gradual evolutionary processes whereas *ex-situ* method includes conservation of species outside the native habitat. Tissue culture technology is included in *the ex-situ* conservation method which helps in getting the target at a furious rate [40].

Plant Tissue Culture Technology: Pathogen free plant is required for tissue culture. In green house conditions, the parent plant species were grown in pots containing equal proportions of soil and farmyard manure. i.e (1:1), thus the explant species of *T. cordifolia* must be passed through decontamination so as to develop healthy plant species. Fungal contamination is a major issue during tissue culture of *T. cordifolia*. Decontamination was performed by treating the plant species with a powdered mixture of Bavistin & neem powder for 45 minutes. Shoot tip, nodal leaf portion of *T. cordifolia* were used as an explanation for culture. The explant species were surface sterilized with (0.1% w/v) HgCl2 for 6 minutes and were washed thoroughly with sterile water about 5-6 times under aseptic conditions.

The inoculation of the nodal portion was performed in MS medium having 30 gms/l sucrose & 7.5 gms/l agar. The explant species were further subjected for shoot proliferation, MS medium supplemented with 0.3 mg/L BA and 0.7 mg/L NAA was utilized. After five weeks, the shoot segments were moved to MS medium containing varying concentrations of BA (0.4-1.3 mg/L) and IAA (0.3-1.2 mg/L) to induce root formation. After 4 weeks, the plant were enough mature to place insmall earthen pots containing a blend of farmyard manure, sterilized red soil, and vermiculite in a 1:1:1 ratio [40, 41].

The explant species after becoming mature were provided with artificial humidity of about 70-80% using polythene bags and further were transferred to the fields. These are done so that the plant species get acclimatized to the outside environment [40, 41].

Fungal contamination was reduced due to the decontamination treatment which was provided to the plant species. 1-2 leaves were observed in the nodal region after 3 weeks in the fields. The

survival rate was higher upto 90% as only 8 plants species could not survive out of 50 species which went through plant tissue culture [40, 41]. This medicinal plant species have many health benefits which will have an impact in the near future so the over exploitation of this species must be under control and thus sustainable usage for such resources will make the last longer.

CONCLUSION: *T. cordifolia* has been extensively researched in the domain of biological activity of various extracts, fractions, and compounds with the quantification of certain bioactive chemicals, according to literature evidence from many fields of study. Along with clinical and toxicological research, the potential mechanisms of action of crude extracts, formulations, and compounds were examined in *in-vitro* and *in-vivo* models. The antioxidant, anti-hyperglycemic, cardioprotective, immuno-modulatory, anti-cancer, and antibacterial characteristics of several components and extracts of *T. cordifolia* were emphasised in this study. It also act as a medicinal agents against various diseases. *T. cordifolia* is widely distributed in subtropical Asian countries. It has been utilised successfully in many Indian medical systems for a while, and its goods are used for better financial and therapeutic purpose. The numerous research on *T. cordifolia* shows that it is a excellent medicine and has not yet had any negative or hazardous side effects.

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CONFLICT OF INTEREST: Nil

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