Tinospora cordifolia (Giloy): A Comprehensive Review on Phytochemistry, Pharmacological Activities, Therapeutic Potential, and Safety Concern

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***Abstract*—Tinos Pora cordifolia (commonly known as Giloy or Guduchi) is a highly valued medicinal plant belonging to the family Menispermaceae, widely distributed across the Indian subcontinent and other Asian regions. Since ancient times, medicinal plants have served as an essential source of therapeutic agents, and T. cordifolia has gained significant attention due to its diverse pharmacological properties and extensive use in traditional systems of medicine such as Ayurveda, Unani, and Siddha. The plant is recognized for its rich phytochemical composition, including alkaloids, glycosides, steroids, flavonoids, tannins, lactones, and polysaccharides, which contribute to its broad spectrum of biological activities.**

Numerous studies have demonstrated that T. cordifolia exhibits a wide range of pharmacological effects, including anti-inflammatory, antioxidant, antidiabetic, antimicrobial, antiallergic, anticancer, anti-HIV, antipyretic, and immunomodulatory activities. The plant is extensively used in the management of various diseases such as diabetes, fever, skin disorders, gastrointestinal disturbances, urinary disorders, rheumatoid arthritis, and infectious diseases. Additionally, its immunomodulatory potential makes it particularly valuable in enhancing the body's defense mechanisms and may play a supportive role in the treatment of viral infections and immune-related disorders.

The stem of T. cordifolia, which is the most commonly used part, possesses properties such as bitterness, stomachic action, diuretic effects, and the ability to improve digestion and bile secretion. Furthermore, the plant has been reported to regulate blood sugar levels, improve liver function, reduce stress and anxiety, and promote skin regeneration by enhancing collagen production. Experimental studies, including both in vitro and in vivo investigations, have confirmed its antioxidant and antimicrobial potential, with increased activity observed at higher concentrations of extracts. Various extraction methods, particularly hydroalcoholic extraction, have been employed to isolate bioactive constituents, which are further formulated into dosage forms such as tablets, capsules, and liquid preparations to enhance stability and therapeutic efficacy.

Despite its numerous therapeutic benefits, certain limitations such as variability in absorption, lack of standardized formulations, and potential adverse effects in specific conditions have been reported, highlighting the need for further research and clinical validation. Nevertheless, T. cordifolia remains a promising natural source for drug development due to its efficacy, safety profile, and minimal side effects compared to synthetic drugs. This review emphasizes the phytochemical constituents, pharmacological activities, and therapeutic potential of T. cordifolia, supporting its role as a valuable medicinal plant in modern and traditional healthcare systems.

***Index Terms*—Tinospora cordifolia; Giloy; Guduchi; Phytochemistry; Pharmacological activity; Immunomodulatory activity; Safety profile**

I. INTRODUCTION

Tinospora Cordifolia (Guduchi) - Names & Details

Language/Region	Name
Latin	Tinospora cordifolia
English	Gulancha / Indian Tinospora / Heart-leaved Moonseed
Sanskrit	Guduchi, Amrita, Madhuparni
Hindi	Giloy, Guduchi
Bengali	Gulancha
Telugu	Thippateega
Marathi	Shindilakodi
Tamil	Seenthil Kodi
Malayalam	Chittamruthu
Kannada	Amruthaballi

Medicinal plants have played a fundamental role in the development of traditional healthcare systems across the world since ancient times. Systems such as Ayurveda, Unani, Siddha, and other indigenous medical practices rely heavily on plant-based formulations for the prevention and treatment of diseases. These systems are deeply rooted in cultural heritage and continue to be widely practiced, especially in developing countries. According to the World Health Organization (WHO), a large proportion of the global population depends primarily on traditional medicines derived from plants due to their accessibility, affordability, and relatively fewer adverse effects compared to synthetic drugs. Medicinal plants serve as a rich reservoir of bioactive compounds, which are responsible for their diverse pharmacological activities and have contributed significantly to the discovery of modern therapeutic agents.

Among the vast diversity of medicinal plants, Tinospora cordifolia (commonly known as Giloy, Guduchi, or Amrita) has gained remarkable importance due to its extensive use in traditional medicine and its wide spectrum of therapeutic applications. The name "Amrita," meaning "nectar of immortality," highlights its significance as a rejuvenating herb that promotes longevity and vitality. It belongs to the family Menispermaceae and is a large, deciduous, glabrous climbing shrub widely distributed throughout tropical and subtropical regions, including India, Sri Lanka, China, Myanmar, and Southeast Asia. The plant is characterized by its succulent stems, aerial roots, and heart-shaped (cordate) leaves, along with small greenish-yellow flowers, which are important for its botanical identification.

In classical Ayurvedic literature, including the Charaka Samhita and Sushruta Samhita, T. cordifolia is described as a "Rasayana" drug, indicating its role in rejuvenation, enhancement of immunity, and maintenance of overall health. It is also classified under "Medhya Rasayana," which implies its beneficial effects on cognitive function, memory, and mental clarity. Traditionally, the plant has been used to treat a wide range of diseases such as fever (jwara), diabetes, jaundice, rheumatoid arthritis, respiratory disorders, skin diseases, gastrointestinal disturbances, and urinary disorders. In addition, it is known for its adaptogenic properties, helping the body to cope with stress and improve general physiological function.

The pharmacological significance of T. cordifolia is mainly attributed to its rich and diverse phytochemical composition. Various bioactive constituents such as alkaloids, glycosides, flavonoids, steroids, terpenoids, polysaccharides, tannins, and lactones have been isolated from different parts of the plant, including the stem, root, and leaves. These phytoconstituents are responsible for a wide range of biological activities, including anti-inflammatory, antioxidant, antidiabetic, antimicrobial, hepatoprotective, cardioprotective, antiallergic, anticancer, and immunomodulatory effects. The presence of these compounds makes T. cordifolia a versatile medicinal plant with multiple therapeutic applications.

Particularly noteworthy is the immunomodulatory activity of T. cordifolia, which enhances both innate and adaptive immune responses. Scientific studies have demonstrated that the plant influences key biological pathways such as cytokine production, NF-κB signaling, apoptosis, and phagocytosis, thereby improving the body's defense mechanisms against infections and diseases. It has also been reported to reduce oxidative stress by scavenging free radicals and enhancing antioxidant enzyme activity, which plays a crucial role in preventing cellular damage and chronic diseases.

Furthermore, T. cordifolia has shown promising effects in the management of metabolic disorders, especially diabetes, through its hypoglycemic activity. It helps regulate blood glucose levels and improves insulin sensitivity, making it beneficial in the treatment of type II diabetes [5]. Additionally, its hepatoprotective properties contribute to liver health by protecting against toxins and improving liver function. The plant also exhibits antimicrobial activity against a wide range of bacterial and fungal pathogens, further supporting its use in infectious diseases.

In recent years, there has been a significant increase in scientific interest in T. cordifolia, driven by the global shift toward natural and plant-based therapies. Its importance became particularly evident during the COVID-19 pandemic, where it was widely used as an immunity booster and supportive treatment in traditional medicine systems. Moreover, advancements in pharmaceutical sciences have enabled the development of various formulations of Giloy, including powders (churna), decoctions (kadha), fresh juice (swarasa), capsules, syrups, and advanced drug delivery systems such as nanoparticles and phytosomes, which enhance its stability, bioavailability, and therapeutic efficacy.

Despite its extensive traditional use and promising pharmacological profile, certain challenges remain that limit its widespread acceptance in modern medicine. These include lack of standardization of herbal formulations, variability in the concentration of active constituents, and limited clinical evidence supporting its efficacy and safety in humans. Additionally, most of the existing studies are based on in vitro and animal models, emphasizing the need for well-designed clinical trials to validate its therapeutic potential.

In conclusion, Tinospora cordifolia represents a highly valuable medicinal plant with immense potential in both traditional and modern healthcare systems. Its wide range of pharmacological activities, coupled with its safety profile and natural origin, makes it an important candidate for future drug development. By integrating traditional knowledge with modern scientific research, T. cordifolia can serve as a bridge between ancient healing practices and contemporary medicine, offering new opportunities for the development of effective and safe therapeutic agents.

II. PLANT DESCRIPTION

Phytochemistry and Nutritional Composition of Tinospora cordifolia

Tinospora cordifolia is a well-known medicinal plant possessing a rich diversity of phytochemical constituents along with significant nutritional value. Various parts of the plant, including leaves, stems, roots, and fruits, contribute to its therapeutic efficacy. The presence of multiple classes of bioactive compounds such as alkaloids, glycosides, steroids, flavonoids, phenolics, terpenoids, and polysaccharides plays a crucial role in its wide range of pharmacological activities.

1. Nutritional Composition

The leaves of T. cordifolia are considered nutritionally important and are widely used as functional food components. Studies have shown that dried giloy leaves are rich in essential nutrients such as:

Calcium and phosphorus – important for bone strength
Iron – supports blood formation
Proteins (approximately 11%) – required for body growth and repair
Crude fiber – aids digestion
Ash content – indicates the presence of essential minerals

Due to the presence of both macronutrients and micronutrients, giloy leaves are increasingly utilized in dietary supplements and nutraceutical formulations.

2. Major Phytochemical Constituents

Phytochemical investigations reveal that Tinospora cordifolia contains a wide spectrum of biologically active compounds. These include:

Alkaloids
Glycosides
Steroids
Flavonoids
Phenolic compounds
Tannins
Terpenoids and diterpenoids
Polysaccharides
Essential oils and fatty acids

These phytoconstituents are responsible for the plant's medicinal properties and have been isolated through preliminary phytochemical screening.

3. Important Bioactive Compounds

Several specific active compounds have been identified from different parts of the plant. These include:

β-sitosterol
Columbin
Tinosporine, tinosporide, tinosporaside
Cordifolide and cordifol
Clerodane furano diterpenes
Heptacosanol

These compounds exhibit various biological activities such as anti-inflammatory, antioxidant, immunomodulatory, and antimicrobial effects, contributing to the therapeutic importance of the plant.

4. Solvent Extraction and Phytochemical Analysis

Different extraction techniques are employed to isolate phytoconstituents from T. cordifolia. The plant material can be extracted using a variety of solvents, including:

Aqueous extract
Methanolic extract
Ethanolic extract
Hydro-alcoholic extract
n-Hexane extract
Chloroform extract

Ethyl acetate extract
This extraction methods help in obtaining different classes of phytochemicals based on their polarity. Subsequently, various analytical techniques are used to identify and characterize the compounds present in the extracts.

5. Biological Significance of Phytochemicals
The phytochemical constituents of T. cordifolia play a vital role in its pharmacological actions. These compounds are known to:
Enhance immune response (immunomodulatory activity)
Reduce inflammation and oxidative stress
Exhibit antimicrobial and antiviral effects
Provide neuroprotective and anticancer benefits
The synergistic effect of these compounds makes T. cordifolia an important medicinal plant in both traditional and modern healthcare systems.

Plant Description of Tinospora cordifolia
Tinospora cordifolia is a large, deciduous, glabrous, and perennial climbing plant that is widely distributed across India, particularly in tropical regions, extending up to an altitude of approximately 1200 meters above sea level. In addition to India, this plant is also found in several neighboring countries, including China, Sri Lanka, Bangladesh, Pakistan, and Myanmar. The species generally thrives in warm climatic conditions, which are favorable for its growth and development.
The cultivation of Tinospora species is influenced by soil characteristics. The plant grows well in medium-black or red soils and can adapt to a variety of soil types ranging from sandy to clay loam. However, optimal growth is observed in soils that are well-drained, adequately moist, and rich in organic matter. These conditions ensure proper root development and overall plant health, thereby enhancing its medicinal value.
Tinospora cordifolia is commonly referred to by various names such as Guduchi, Giloy, Amrita, and heart-leaved moonseed. In traditional belief, it is often regarded as a divine plant and is associated with the concept of “Amrita,” meaning the nectar of immortality, symbolizing its rejuvenating and life-enhancing properties.
Within the genus Tinospora, several species exhibit similar morphological characteristics but differ in certain botanical aspects. One such species is Tinospora crispa, a comparatively smaller herbaceous climber that is woody and glabrous in nature. It is commonly known as Faridbel and is widely distributed in both tropical and temperate regions of India. Another related species, Tinospora sinensis (also referred to as T. malabarica), is a large deciduous climber characterized by a shining, light-colored stem and larger, orbicular-cordate leaves compared to T. cordifolia. This species also exhibits dioecious flowers and produces aerial roots from its branches.
Overall, the genus Tinospora comprises multiple species with significant medicinal importance, among which T. cordifolia holds a prominent position due to its extensive use in traditional medicine and its well-documented therapeutic properties

III. MORPHOLOGY

The morphological characterization of Tinospora cordifolia plays a crucial role in its proper identification, classification, and pharmacognostic evaluation. This plant is a large, deciduous, perennial climbing shrub belonging to the family Menispermaceae, widely distributed across tropical and subtropical regions. It commonly grows over large trees, forming extensive networks of coiling branches and aerial roots. The plant exhibits a unique combination of structural features that distinguish it from other medicinal species, making it easily recognizable in its natural habitat.
The external morphology of T. cordifolia includes well-developed stems, leaves, roots, flowers, and fruits, each contributing to its overall botanical identity. The stem is succulent and acts as the primary storage site for bioactive constituents, while the aerial roots provide mechanical support and additional absorption. The leaves are broad and cordate with characteristic venation patterns, aiding in taxonomic identification. The reproductive structures, including flowers and fruits, further contribute to its classification and propagation.
From a pharmacogenetic perspective, the study of morphology is essential not only for authentication of the crude drug but also for detecting adulteration and ensuring quality control of herbal formulations. The presence of distinctive features such as lenticels on the stem, reticulate venation in leaves, and specialized root structures provides reliable diagnostic markers. Moreover, variations in morphological characteristics

may occur due to environmental factors such as climate, soil conditions, and geographical distribution. Thus, a detailed understanding of the morphology of Tinospora cordifolia is fundamental for its correct identification, cultivation, and utilization in traditional as well aedicinal systems. The following section describes the morphological features of different plant parts in detail.

1. Stem

The stem is succulent, fleshy, and climbing in nature.
It is long, cylindrical, and filiform, with a smooth surface.
The outer surface appears whitish to creamy with spiral markings and lenticels.
The stem gives rise to numerous aerial roots.
The internal wood is soft, porous, and white, which turns yellow upon exposure to air.

2. Leaves

Leaves are simple, alternate, and exstipulate.
They are long petioled (about 12–15 cm).
The shape is cordate (heart-shaped) with a deeply notched base.
The lamina is membranous, ovate, and 10–20 cm long.
Leaves show reticulate venation and are often glabrous or slightly pubescent.

3. Roots (Aerial Roots)

The plant produces long, thread-like aerial roots arising from branches.
These roots show tetra- to penta-arch structure.
The cortex is divided into:
Outer thick-walled region
Inner parenchymatous zone

4. Flowers

Flowers are small, greenish-yellow, and unisexual.
They are arranged in raceme type inflorescence.
Male flowers occur in clusters, while female flowers are solitary.
Each flower has 6 sepals arranged in two whorls and 6 smaller petals.
Flowering occurs mainly during spring to early summer (March–June).

5. Fruits and Seeds

Fruits are fleshy drupelets, usually orange to red in color.
They occur in clusters of 1–3 fruits.
Fruits develop mainly during the winter season.
Seeds are curved in shape, with a well-developed and ornamented endocarp, which is important for identification.

IV. BENEFITS OF GILOY FOR HEALTH

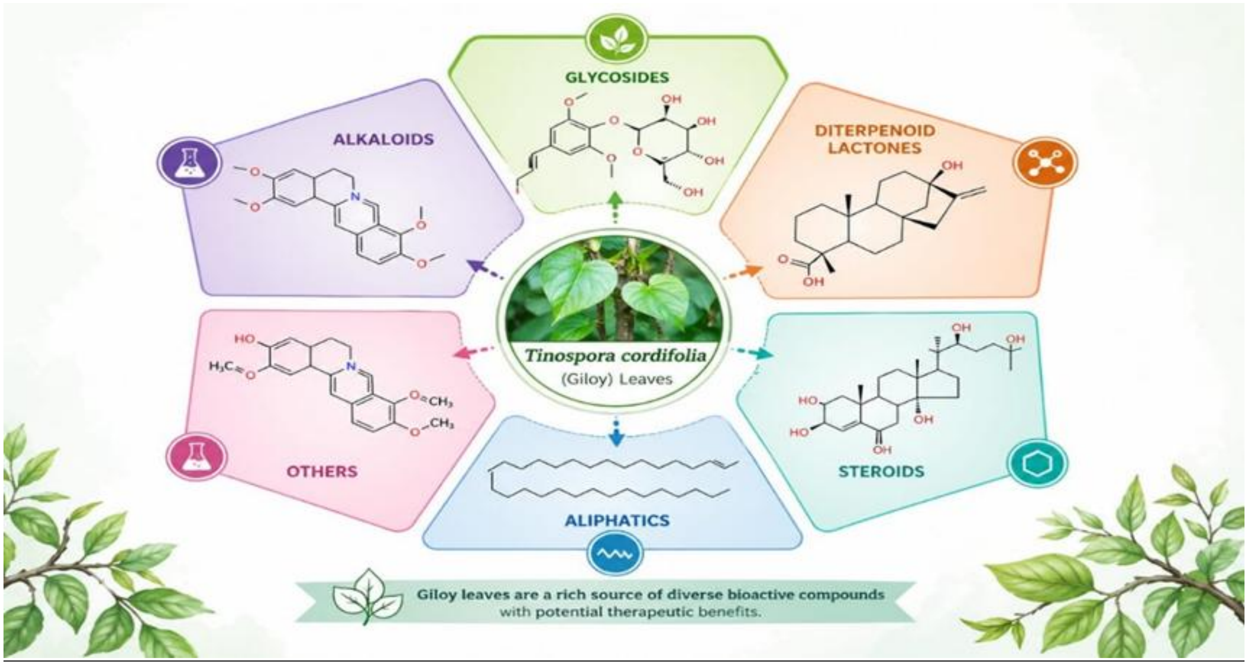
V. PHYTOCHEMISTRY

Tinospora cordifolia (Giloy) is recognized not only for its therapeutic properties but also for its significant nutritional value. The plant, particularly its leaves, serves as a rich source of essential nutrients and bioactive compounds that contribute to its pharmacological potential. Various studies have reported that dehydrated leaves of T. cordifolia contain appreciable amounts of macronutrients and micronutrients, including calcium, protein, iron, crude fiber, and ash content, indicating its potential use as a functional food ingredient [1].

All parts of the plant, such as leaves, stems, roots, and fruits, are utilized in traditional medicine as well as in dietary preparations. Among these, the leaves are considered especially valuable due to their higher concentration of nutrients and health-promoting components. The presence of essential nutrients supports metabolic functions and enhances the overall nutritional profile of the plant, making it beneficial for both medicinal and dietary purposes [2,3].

In addition to its nutritional composition, T. cordifolia is rich in a wide range of phytochemical constituents. These include important classes of bioactive compounds such as alkaloids, glycosides, diterpenoids, steroids, flavonoids, and polysaccharides. These phytoconstituents are responsible for the diverse biological activities exhibited by the plant, including antioxidant, anti-inflammatory, immunomodulatory, and antimicrobial effects. The synergistic action of these compounds plays a crucial role in the therapeutic efficacy of Giloy [1].

The presence of these phytochemicals highlights the importance of T. cordifolia as a valuable medicinal plant with dual benefits nutritional as well as pharmacological. Therefore, it has gained increasing attention in recent years for its potential application in the development of functional foods, nutraceuticals, and herbal formulations aimed at improving health and preventing diseases.



VI. PHARMACOLOGICAL ACTION

In the last two decades, Tinospora cordifolia has been extensively investigated by researchers worldwide due to its remarkable pharmacological and therapeutic significance. Numerous scientific studies and experimental reports have confirmed that this plant exhibits a wide range of biological activities, making it an important medicinal herb in both traditional and modern medicine systems. The major pharmacological properties reported include anti-diabetic, anti-inflammatory, antioxidant, immunomodulatory, anticancer, anti-microbial, and anti-allergic activities.

Among these, its anti-diabetic potential is one of the most widely studied and well-documented effects, particularly in the management of type 2 diabetes mellitus (T2D). Traditional medicinal systems in Asia and Africa have long used this plant for controlling blood sugar levels, and modern pharmacological research strongly supports this traditional claim.

The wide spectrum of pharmacological activities of Tinospora cordifolia is mainly attributed to its rich phytochemical profile. The plant contains several biologically active constituents such as alkaloids, phenolic compounds, diterpenoids, glycosides, aliphatic compounds, and steroids, all of which contribute individually and synergistically to its therapeutic actions. These compounds are responsible for regulating different biochemical and physiological pathways involved in disease progression.

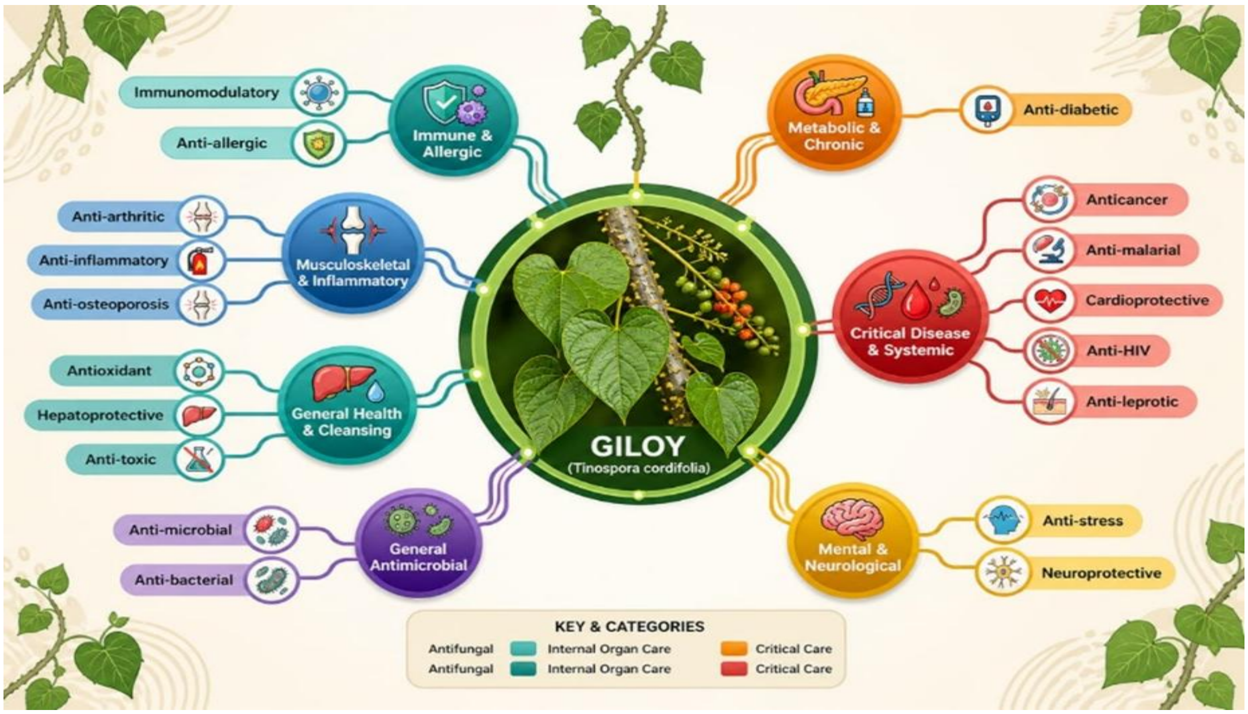
Most of the pharmacological evidence is based on studies using crude extracts as well as isolated bioactive compounds. Among the important phytochemicals, alkaloids such as palmatine, jatrorrhizine, and magnoflorine have shown strong insulin-mimicking and insulin-releasing properties in both in vitro and in vivo experimental models. These compounds help in improving glucose uptake and enhancing insulin activity, thereby contributing to better glycemic control.

Further experimental findings indicate that isolated constituents of Tinospora cordifolia produce a clear insulin-associated hypoglycemic response, supporting its traditional use in diabetes management. In diabetic animal models, administration of plant extracts has shown a significant reduction in elevated blood glucose levels, confirming its anti-hyperglycemic effect.

Additionally, this plant exhibits a multi-target mode of action, affecting several organs and tissues involved in glucose metabolism. These include the liver, adipose tissue (fat), pancreatic β-cells, intestinal mucosa (L-cells), and skeletal muscles, which collectively contribute to maintaining glucose homeostasis. This multi-organ action makes it more effective compared to single-target synthetic drugs.

The pharmacological effects are also supported by both extra-pancreatic and intra-pancreatic mechanisms. Extra-pancreatic actions include improved glucose uptake in peripheral tissues, inhibition of intestinal glucose absorption, and regulation of hepatic glucose production. Intra-pancreatic effects involve stimulation and possible regeneration of pancreatic β-cells, leading to improved insulin secretion and function.

Overall, the therapeutic potential of Tinospora cordifolia is not limited to diabetes alone. Its broad pharmacological profile suggests its usefulness in several other pathological conditions such as metabolic disorders, infections, immune dysfunction, oxidative stress-related diseases, and inflammatory conditions. This wide range of activities highlights its importance as a promising natural source for drug development and future pharmacological research.



1.Anti-Diabetic

The anti-diabetic properties of Tinospora cordifolia have been strongly supported by numerous pharmacological studies. Various bioactive compounds such as alkaloids, tannins, cardiac glycosides, flavonoids, saponins, and steroids play a significant role in regulating blood glucose levels.

Traditionally, this plant has been extensively used across Asia and Africa for managing type 2 diabetes. The alkaloid-rich fraction obtained from its stem particularly compounds like palmatine, jatrorrhizine, and magnoflorine has demonstrated both insulin-like and insulin-stimulating effects in laboratory (in vitro) as well as animal (in vivo) studies. These isolated alkaloids contribute to lowering blood glucose by enhancing insulin-related responses.

Experimental studies on diabetic models have shown that extracts of this plant effectively reduce elevated glucose levels, indicating strong anti-hyperglycemic activity. Its mechanism of action is multi-targeted, affecting several organs and tissues including the liver, adipose tissue, pancreatic β-cells, intestinal mucosa (L-cells), and muscle

2. Immunomodulatory Activity

The immunomodulatory potential of Tinospora cordifolia, particularly its leaves, is attributed to a diverse range of bioactive phytoconstituents that actively regulate and strengthen the immune system. These include alkaloids (such as palmatine, magnoflorine, and tetrahydropalmatine), glycosides (tinocordiside and clerodane derivatives), steroids (β-sitosterol), diterpenoid lactones (columbin and tinosporon), and polysaccharides like RR1. Together, these compounds contribute to both innate and adaptive immune responses by enhancing immune cell activity and modulating inflammatory mediators.

At the cellular level, giloy leaf extract stimulates various immune cells including macrophages, natural killer (NK) cells, B lymphocytes, and T lymphocytes. This activation leads to increased production of cytokines and improved immune signaling. Studies indicate that these bioactive compounds enhance phagocytosis, which is a primary defense mechanism of the body, along with increasing nitric oxide (NO) and reactive oxygen species (ROS) generation in immune cells. These molecules play a crucial role in destroying pathogens and infected cells. Additionally, the extract promotes lymphocyte proliferation and differentiation, resulting in increased total white blood cell count, bone marrow cellularity, and enhanced humoral immunity through elevated immunoglobulin (IgG) levels.

The immunomodulatory activity is also closely associated with the regulation of inflammatory pathways. Giloy leaf extract exhibits significant anti-inflammatory effects by inhibiting pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. One of the key mechanisms involves suppression of the NF-κB signaling pathway, which is a central regulator of inflammation. By inhibiting this pathway, giloy reduces the production of inflammatory mediators like prostaglandin E2 (PGE2) and nitric oxide. Furthermore, it inhibits enzymes such as cyclooxygenase (COX-2) and lipoxygenase (LOX), which are involved in the synthesis of inflammatory compounds. This dual inhibition contributes to reduced inflammation and tissue damage.

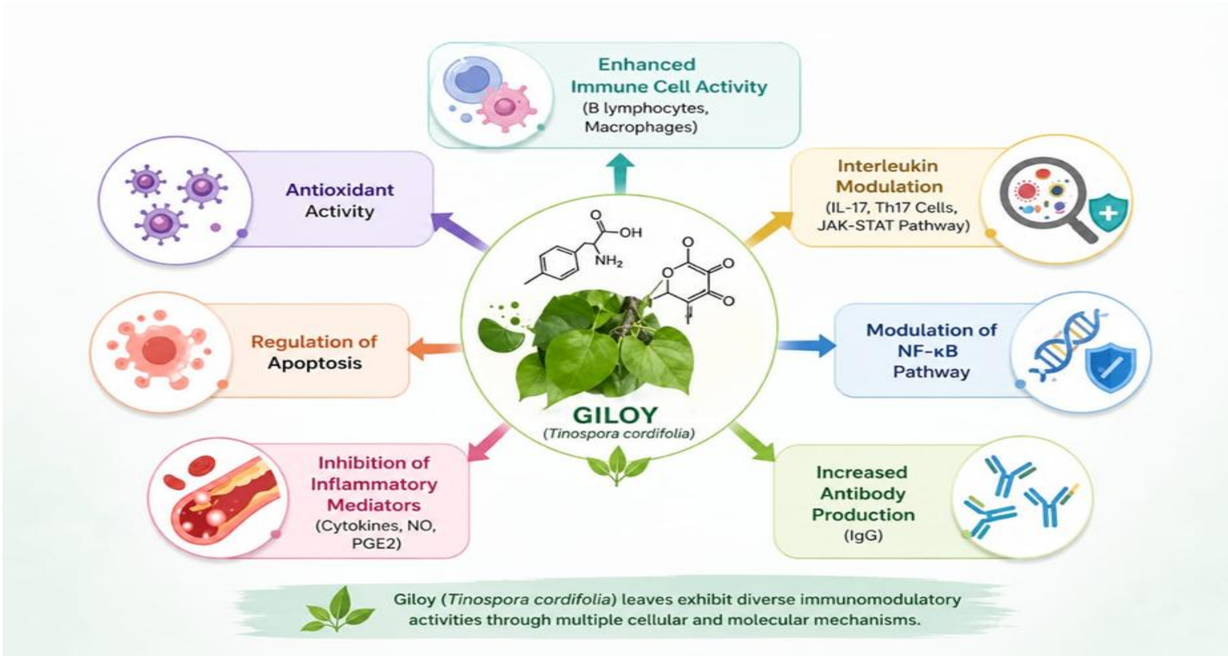
Another important aspect of its immunomodulatory function is its role in apoptosis regulation. Giloy leaf constituents such as magnoflorine, palmatine, and cordifolioside-A have demonstrated the ability to induce programmed cell death in abnormal or cancerous cells. This process involves activation of caspase enzymes, suppression of anti-apoptotic genes like Bcl-2, and upregulation of pro-apoptotic genes such as Bax. Additionally, giloy extract can arrest the cell cycle at the G1 phase, thereby preventing uncontrolled cell proliferation. Enhanced nitric oxide production further contributes to cytotoxic effects against tumor cells.

The antioxidant properties of giloy leaves also play a significant role in immune modulation. The presence of polyphenolic compounds such as tannins and flavonoids enables the extract to neutralize free radicals and reduce oxidative stress. Experimental studies have shown that giloy leaf extract effectively scavenges DPPH, hydroxyl, and nitric oxide radicals, thereby protecting cellular components from oxidative damage. It also enhances antioxidant enzymes like superoxide dismutase, catalase, and glutathione peroxidase while reducing lipid peroxidation markers such as malondialdehyde. This antioxidant defense is crucial in maintaining immune cell integrity and function.

Moreover, giloy influences interleukin modulation, particularly involving IL-17 and Th17 cells through the JAK-STAT signaling pathway. These pathways are essential in immune regulation and inflammatory responses. Giloy extract has been reported to reduce IL-17-producing cells, which are often associated with autoimmune and chronic inflammatory diseases. At the same time, it enhances macrophage activity and promotes a balanced immune response, including stimulation of Th1-type immunity through polysaccharides like RR1.

In addition to its benefits, it is important to consider safety aspects. While giloy is generally regarded as safe in traditional use, excessive consumption may lead to adverse effects such as gastrointestinal discomfort, hypoglycemia, allergic reactions, or potential liver toxicity in sensitive individuals. Therefore, controlled usage is recommended.

Overall, the immunomodulatory activity of giloy leaves is multifaceted, involving enhancement of immune cell function, regulation of cytokine production, suppression of inflammatory pathways, antioxidant protection, and modulation of apoptosis. These combined effects make it a promising natural therapeutic agent for managing immune-related disorders, inflammation, and infections. Further research is needed to fully understand its molecular mechanisms and to identify specific bioactive compounds responsible for these effects, which could contribute to the development of novel immunotherapeutic drugs.



3.Anti-Cancer Activity

Cancer is recognized as one of the leading causes of mortality worldwide, ranking second among life-threatening diseases. The anticancer potential of Tinospora cordifolia has been extensively investigated against a variety of tumor types, and numerous studies highlight its ability to inhibit cancer progression through multiple biological mechanisms.

One of the key mechanisms underlying its anticancer effect is the regulation of the cell cycle and induction of apoptosis. Extracts of this plant have been shown to arrest cancer cells at critical phases such as G0/G1 and G2/M. This effect is achieved by downregulating important regulatory proteins like cyclin D1, which controls the transition from G1 to S phase, and Bcl-xL, an anti-apoptotic protein that helps cancer cells survive. By suppressing these proteins, the extract prevents uncontrolled cell proliferation and promotes programmed cell death, thereby demonstrating strong anti-proliferative activity.

In vitro studies further support its cytotoxic potential, showing increased levels of lactate dehydrogenase (LDH), which indicates cellular damage, along with reduced cell viability. Additionally, enhanced activity of detoxifying enzymes such as glutathione S-transferase has been observed, suggesting improved cellular defense mechanisms. A polysaccharide isolated from this plant has also shown the ability to reduce the metastatic potential of melanoma cells (B16–F10), indicating its role in preventing cancer spread.

Different extracts of the plant exhibit activity against multiple cancer cell lines. For instance, aqueous extracts have demonstrated potent cytotoxic effects against human colon cancer cell lines (Colo-205 and HCT-116) as well as lung cancer cell lines (A-549 and NCI–H322). Similarly, methanolic extracts of the stem have shown significant activity against human breast cancer cells (MDA-MB-231), highlighting its broad-spectrum anticancer potential.

Apart from direct anticancer effects, the plant also exhibits radioprotective properties. Studies in male Swiss albino mice have shown that its extract can protect reproductive tissues from the harmful effects of sublethal gamma radiation. Furthermore, specific compounds such as diterpenoids have demonstrated chemopreventive effects in chemically induced liver cancer (hepatocellular carcinoma) models. These effects are associated with modulation of antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and glutathione peroxidase (GPx), along with regulation of liver function markers such as SGOT, SGPT, and LDH. These biochemical changes collectively support its protective and anti-tumor roles.

In vivo studies have also reported antiangiogenic activity, which refers to the inhibition of new blood vessel formation required for tumor growth. This activity is associated with modulation of cytokines and growth factors such as IL-1β, IL-6, TNF-α, GM-CSF, and vascular endothelial growth factor (VEGF). Certain phytoconstituents including 20β-hydroxyecdysterone, cordioside, and columbin have shown significant tumor regression and increased survival rates in mice models of Ehrlich ascites carcinoma.

Moreover, extracts of this plant have demonstrated anticarcinogenic and antimutagenic properties in experimental studies, indicating their potential to prevent the initiation and progression of cancer at the genetic level. These findings suggest that the plant not only targets existing cancer cells but may also help in reducing mutation rates and cancer risk.

One of the major challenges in conventional cancer therapy is the toxicity associated with chemotherapeutic drugs. Although several plant-derived anticancer agents such as vinblastine, vincristine, paclitaxel, and irinotecan are already in use, there is a growing interest in identifying safer alternatives. In this context, phytochemicals isolated from this plant, including alkaloids and terpenoids like magnoflorine, palmatine, tinocordiside, and cordifolioside A, have shown promising anticancer activity with potentially lower toxicity.

Overall, both in vitro and in vivo studies strongly support the anticancer potential of this plant. However, more detailed and targeted research is required to fully understand its mechanisms of action, identify specific active compounds, and evaluate its clinical efficacy. Such studies could pave the way for the development of novel, plant-based chemotherapeutic agents with improved safety and effectiveness.

4.Cardioprotective

Various experimental studies have shown that Tinospora cordifolia possesses significant protective effects on the heart. In animal models, the root extract at a dose 200 mg/kg demonstrated strong protection against isoprenaline-induced cardiac damage in streptozotocin-induced diabetic rats.

The alcoholic extract of T. cordifolia has also been found to produce dose-dependent cardioprotective effects in ischemia–reperfusion-induced myocardial infarction. This protection was associated with a reduction in infarct size and decreased levels of serum lipid peroxidation. The mechanism behind this effect is believed to involve antioxidant activity, protection of Mg^{2+}-dependent Ca^{2+}-ATPase, prevention of free radical–mediated inhibition of Na^{+}/K^{+}-ATPase, and calcium channel blocking action.

In addition, the alcoholic extract has shown beneficial effects in controlling calcium chloride-induced cardiac arrhythmias in experimental animals. The stem extract also contributes indirectly to heart health by improving lipid metabolism in streptozotocin-induced diabetic conditions.

Prolonged administration of the root extract at doses of 2.5 and 5.0 g/kg body weight for six weeks significantly reduced serum and tissue levels of total cholesterol, phospholipids, and free fatty acids in alloxan-induced diabetic rats. Furthermore, the methanolic stem extract was effective in normalizing altered levels of cardiac enzymes such as creatine kinase and lactate dehydrogenase, along with antioxidant markers including superoxide dismutase, catalase, and glutathione in cadmium-induced toxicity models, indicating its strong cardioprotective potential.

Another study demonstrated that methanolic extract reduced myocardial damage caused by isoprenaline in Wistar rats, suggesting its role in strengthening myocardial cell membranes and supporting overall cardiac function.

Overall, Tinospora cordifolia exhibits notable cardioprotective activity through antioxidant, enzyme-regulating, and membrane-stabilizing mechanisms. However, further research is necessary to better understand the exact molecular pathways involved in preventing cardiac dysfunction, hypertrophy, and related heart disorders.

5. Anti-Oxidant Activity

Antioxidants are essential for maintaining normal physiological functions, as they protect cells from damage caused by reactive oxygen species (ROS) and minimize the harmful effects of free radicals. Tinospora cordifolia has been widely studied for its strong antioxidant potential. Phytoconstituents such as flavonols and phenolic compounds isolated from this plant have demonstrated significant free radical scavenging activity, particularly when evaluated using the DPPH assay.

The plant has also been shown to enhance intracellular antioxidant defense by increasing glutathione levels and upregulating the expression of the gamma-glutamylcysteine ligase gene. These effects contribute to its ability to neutralize free radicals effectively. Additionally, T. cordifolia helps regulate oxidative stress by improving enzymatic antioxidant systems, thereby controlling ROS generation and restoring oxidative balance.

In experimental studies, ethanolic extracts of T. cordifolia exhibited notable antioxidant effects in alloxan-induced diabetic rats. This was reflected by improvements in key antioxidant markers, including reduced lipid peroxidation and increased activity of catalase, superoxide dismutase, and glutathione.

Further investigations have revealed that T. cordifolia is effective in preventing iron-induced lipid damage, inhibiting lipid peroxidation, and modulating enzyme systems involved in carcinogen metabolism. It also reduces free radical formation under conditions such as oxygen-glucose deprivation and shows nitric oxide scavenging activity.

Overall, these findings highlight the strong antioxidant capability of Tinospora cordifolia, which plays a crucial role in protecting cells from oxidative stress and related damage.

6.Anti-Allergic Activity

Tinospora cordifolia has long been used in traditional medicine for managing respiratory conditions such as asthma and chronic cough. Its extracts have demonstrated significant anti-allergic potential in both experimental and clinical settings.

Studies have shown that the aqueous extract of T. cordifolia can reduce mast cell–mediated allergic responses through antihistaminic action. This effect contributes to the alleviation of common symptoms associated with allergic rhinitis, including sneezing, nasal discharge, nasal blockage, and itching.

Experimental investigations, both in vivo and in vitro, further support its anti-allergic properties. The stem extract was found to suppress histamine-induced reactions, such as cutaneous anaphylaxis in animal models and contraction of guinea pig ileum. Additionally, it inhibited the release of pro-inflammatory mediators like tumor necrosis factor-alpha from activated mast cells and reduced intracellular calcium levels, which play a crucial role in allergic responses.

These findings indicate that T. cordifolia effectively modulates key mechanisms involved in allergic reactions, particularly those mediated by mast cells and histamine release.

Overall, Tinospora cordifolia shows promising potential as a natural therapeutic agent for both acute and chronic allergic conditions, offering effectiveness with minimal side effects compared to conventional anti-allergic medications.

7.Anti-Inflammatory Activity

Tinospora cordifolia (Giloy) has been widely reported to exhibit significant anti-inflammatory activity, which is mainly attributed to its diverse bioactive constituents such as alkaloids, glycosides, diterpenoid lactones, and steroids. These compounds act through modulation of key inflammatory signaling pathways and suppression of pro-inflammatory mediators.

Inflammation is typically initiated by external stimuli such as lipopolysaccharides (LPS), which activate immune cells like macrophages via Toll-like receptor 4 (TLR4). Activation of TLR4 triggers downstream signaling cascades involving IκB kinase (IKK), leading to the activation and nuclear translocation of nuclear factor-kappa B (NF-κB). NF-κB is a critical transcription factor responsible for the expression of various pro-inflammatory genes, including cytokines and enzymes.

Bioactive compounds of T. cordifolia have been shown to inhibit this pathway at multiple levels. Specifically, they suppress the activation of TLR4-mediated signaling and inhibit the phosphorylation of IKK, thereby preventing the activation of NF-κB (p65/p50). As a result, the transcription of pro-inflammatory genes is significantly reduced.

Furthermore, T. cordifolia extracts have been reported to decrease the production of key pro-inflammatory cytokines such as interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α). In addition, they inhibit the synthesis of inflammatory mediators like nitric oxide (NO) and prostaglandin E_2 (PGE_2), which play crucial roles in the propagation of inflammation.

Another important mechanism involves the downregulation of cyclooxygenase-2 (COX-2), an enzyme responsible for prostaglandin synthesis during inflammatory responses. By inhibiting COX-2 expression, T. cordifolia further contributes to the reduction of inflammation.

Overall, the anti-inflammatory effect of T. cordifolia is mediated through the suppression of the TLR4/NF-κB signaling pathway, leading to decreased production of inflammatory cytokines, mediators, and enzymes.

These combined actions result in a significant attenuation of inflammatory responses.

8. Other Pharmacological Activity

Apart from the major pharmacological properties, Tinospora cordifolia has also demonstrated beneficial effects in managing a variety of conditions such as leprosy, ulcers, depression, diarrhea, asthma, and infertility. These diverse therapeutic actions are attributed to its rich composition of bioactive compounds.

Studies have shown that methanolic leaf extracts of T. cordifolia can inhibit thrombin-induced platelet activation, indicating its potential role in preventing abnormal blood clot formation. Additionally, the plant has exhibited activity against HIV/AIDS by enhancing immune responses. It stimulates immune cells such as B lymphocytes, macrophages, and polymorphonuclear leukocytes, along with improving hemoglobin levels. Certain extracts, particularly n-hexane and n-butanol fractions, have demonstrated moderate cytotoxic effects on peripheral blood mononuclear cells and inhibitory action against HIV-1 reverse transcriptase. Improvements in clinical parameters, including reduced eosinophil count and increased hemoglobin levels, have also been observed in affected individuals.

The plant also possesses notable anti-toxic properties. Aqueous root extracts have shown protective effects against toxin-induced kidney damage, particularly in cases of aflatoxin exposure, by reducing oxidative stress and neutralizing free radicals. This protection is associated with decreased levels of thiobarbituric acid reactive substances and enhanced activity of antioxidant enzymes such as superoxide dismutase, glutathione S-transferase, and glutathione peroxidase.

Furthermore, combined administration of stem and root extracts has demonstrated protective effects against heavy metal toxicity, such as lead-induced damage. Improvements were observed in hematological parameters, including red blood cell count and hemoglobin levels.

Overall, the wide range of pharmacological activities exhibited by Tinospora cordifolia highlights its importance as a versatile medicinal plant. Its diverse phytoconstituents present in different parts of the plant contribute to its longstanding use in traditional medicine for treating various diseases and health disorders.

VII. SAFETY & TOXICITY

Tinospora cordifolia, commonly referred to as Giloy, is an important herb in Ayurvedic medicine and is widely valued for its therapeutic potential. Traditionally, it has been used for its antipyretic, anti-inflammatory, and liver-protective properties. However, recent scientific findings have raised concerns regarding its safety, particularly the risk of liver toxicity associated with excessive or prolonged intake of giloy leaf powder.

Although giloy has long been considered beneficial, emerging evidence suggests that high or continuous consumption may result in hepatotoxicity (liver damage). Experimental studies, including in vitro and animal models, indicate that exposure to giloy extracts can increase lipid peroxidation, elevate lactate dehydrogenase levels, and reduce glutathione-S-transferase activity. These biochemical changes are markers of oxidative stress and cellular injury in the liver.

At the same time, certain phytochemicals present in giloy such as alkaloids (berberine, palmatine, and jatrorrhizine) and compounds like sinapic acid are known for their hepatoprotective effects. For example, berberine has been reported to reduce inflammation by inhibiting TNF-α-mediated pathways and lowering nitrosative stress through suppression of iNOS activity.

In addition to its effects on the liver, Tinospora cordifolia exhibits a wide range of pharmacological activities, including anticancer, antimicrobial, antioxidant, and anti-inflammatory actions. These effects are attributed to its rich phytochemical composition, which includes polyphenols, alkaloids, terpenoids, steroids, and glycosides.

Overall, giloy is generally regarded as safe when consumed within recommended limits (up to approximately 2000 mg/kg in experimental studies). However, like other herbal or pharmaceutical substances, improper dosage or prolonged use may lead to adverse effects, including liver toxicity. Therefore, cautious and regulated use is essential

VIII. FUTURE PROSPECTS

Tinospora cordifolia leaves have shown increasing evidence of immunomodulatory potential; however, there remains a considerable gap in understanding the exact mechanisms responsible for these effects. The detailed molecular pathways and cellular interactions governing antioxidant activity, regulation of inflammation, modulation of Th17 cells, inhibition of the NF-κB pathway, interleukin balance, as well as immunosuppressive and leukocyte-enhancing actions are still not fully elucidated. Bridging this gap between observed biological effects and their underlying mechanisms is essential to unlock the complete therapeutic value of giloy leaves.

Future research should therefore focus on key signaling pathways such as NF-κB, which has already been associated with the biological activity of giloy. A deeper and clearer understanding of these pathways is necessary, particularly the molecular interactions between bioactive constituents of giloy leaves and these signaling systems, to support the development of targeted therapeutic strategies. In addition, extensive investigations are required to determine how giloy leaf compounds interact with various immune cells, including Th17 cells, macrophages, and natural killer cells. Understanding their influence on activation, differentiation, and functional responses of these cells will be crucial for advancing clinical applications.

Further studies should also explore the synergistic potential of giloy leaves when combined with commonly consumed nutrient-rich foods containing vitamins, minerals, and antioxidants. Such research could contribute to dietary recommendations aimed at improving immune health and aid in the development of nutraceutical products. Moreover, the role of food matrices should be examined to identify ingredients that enhance the bioavailability of giloy's bioactive compounds, enabling optimized formulation strategies for maximum therapeutic benefit.

Comparative analysis of the immunomodulatory effects of giloy leaves with established immunomodulatory drugs and other natural compounds is also necessary. This would help clarify its unique mechanisms of action and identify possible synergistic combinations for improved therapeutic outcomes. By integrating existing findings with comprehensive mechanistic research, the medicinal potential of giloy leaves can be more effectively realized.

In the future, researchers should also emphasize the establishment of standardized protocols for giloy leaf preparations to ensure consistent quality, safety, and efficacy. Additionally, further efforts are required to address regulatory challenges associated with giloy-based products to facilitate their successful commercialization and broader clinical application.

IX. CONCULSION

Tinospora cordifolia (Giloy) is a widely recognized medicinal plant in traditional systems of medicine, particularly Ayurveda, where it is valued for its broad therapeutic applications. The present review highlights its rich phytochemical diversity, including alkaloids, glycosides, flavonoids, diterpenoids, steroids, and polysaccharides, which collectively contribute to its extensive pharmacological profile.

Scientific investigations have confirmed that T. cordifolia exhibits multiple biological activities such as antioxidant, anti-inflammatory, immunomodulatory, anti-diabetic, hepatoprotective, cardioprotective, neuroprotective, anticancer, antimicrobial, anti-arthritic, and anti-osteoporotic effects. These effects are mediated through several molecular mechanisms, including modulation of NF-κB signaling, regulation of cytokines (TNF-α, ILs), enhancement of antioxidant enzymes, suppression of oxidative stress, and control of apoptosis and cell cycle progression.

A key strength of T. cordifolia lies in its immunomodulatory action, where it enhances both innate and adaptive immune responses by stimulating macrophages, lymphocytes, and natural killer cells while maintaining cytokine balance. Additionally, its hypoglycemic, hepatoprotective, and neuroprotective properties further support its therapeutic relevance in chronic metabolic and degenerative diseases.

Despite its wide pharmacological potential, emerging evidence also indicates possible safety concerns, particularly hepatotoxicity associated with excessive or prolonged use. This highlights the importance of dosage regulation, standardization of formulations, and further toxicological evaluation to ensure safe clinical application.

Overall, Tinospora cordifolia represents a promising natural source for drug development. However, further well-designed clinical studies and mechanistic investigations are required to fully validate its efficacy, safety, and molecular targets. Integration of traditional knowledge with modern scientific validation will be crucial for translating this medicinal plant into evidence-based therapeutic applications

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