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Review Article

Pharmacological review of *Tinospora cordifolia*: A traditional herb with modern therapeutic relevance

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Abstract

The global reliance on herbal medicines continues to expand, with the World Health Organization (WHO) estimating that nearly 80% of the world's population depends on traditional remedies for primary health care needs. Among the vast array of medicinal plants, Tinospora cordifolia (Willd.) Miers, commonly known as Giloy or Guduchi, has been historically revered in the Ayurveda, Siddha, and Unani systems of medicine for its adaptogenic, immunomodulatory, and rejuvenating properties. Ancient Ayurvedic literature such as Charaka Samhita and Sushruta Samhita refer to Giloy as "Amrita," meaning nectar of immortality, and highlight its usage in treating fever, metabolic disorders, and liver ailments.

Modern scientific investigations have identified a rich phytochemical composition, including alkaloids like berberine and magnoflorine, diterpenoid lactones such as tinosporin and columbin, steroids like β-sitosterol and stigmasterol, flavonoids such as quercetin and kaempferol, and polysaccharides including arabinogalactan, which contribute to its therapeutic profile. Experimental models have confirmed its immunostimulatory effects by enhancing macrophage activity, hepatoprotective potential by normalizing liver enzymes, antidiabetic properties through insulin sensitization, anti-inflammatory effects via COX-2 inhibition, and antioxidant capacity through scavenging reactive oxygen species.

Clinical trials have demonstrated its efficacy in chronic fever management, improving glycemic indices in diabetic patients, alleviating rheumatoid arthritis symptoms, and aiding recovery in viral infections such as dengue and hepatitis B. Recent integrative approaches during the COVID-19 pandemic have included Giloy formulations as supportive therapy, with evidence of reduced fatigue and immune enhancement.

While generally considered safe when used appropriately, reports of hepatotoxicity associated with adulterated products and excessive dosage underscore the need for regulated formulations and evidence-based guidelines. This review consolidates both traditional knowledge and contemporary scientific findings, advocating for standardized extraction protocols, larger clinical trials, and molecular-level research to establish Giloy's role as an effective Phytotherapeutic agent in modern medicine.

Keywords: *Tinospora cordifolia*, Immunomodulation, Adaptogen, Herbal drug, Antioxidant

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1. Introduction

Traditional medicine remains a cornerstone in global health strategies, with WHO's 2019 report highlighting that over 80% of the global population uses plant-based remedies for health maintenance and disease management.[1] These therapies are particularly prominent in rural regions where access to conventional pharmaceuticals is limited, as well as in urban centers seeking integrative and preventive health approaches.[1,2]

India, with its rich biodiversity and ancient medical traditions, is home to thousands of medicinal plant species. Among these, *Tinospora cordifolia* holds a unique position, widely prescribed in Ayurveda, Siddha, and Unani practices for managing systemic disorders, enhancing immunity, and supporting metabolic functions.[2–4] The Charaka Samhita and Sushruta Samhita—two foundational Ayurvedic texts composed over two millennia ago—reference Giloy under the name "Guduchi" and describe its usage in conditions such as Jwara (fever), Prameha (metabolic diseases, including diabetes), Kamala (jaundice), and Aruchi (loss of appetite).[5] The Bhavaprakasha Nighantu, compiled during the medieval period, details its bitter taste, detoxifying properties, and role in rejuvenation formulations.[4]

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Table 1: Bioactive phytochemicals identified through various analytical methods

Phytochemical class	Key compounds	Reported activities
Alkaloids[6]	Berberine, Magnoflorine	Antimicrobial, antidiabetic, anti-inflammatory
Diterpenoid Lactones[7]	Tinosporin, Columbin	Immune enhancement, metabolic regulation
Steroids	β-Sitosterol, Stigmasterol	Lipid profile modulation, anti-inflammatory
Flavonoids	Quercetin, Kaempferol	Antioxidant, neuroprotective
Glycosides	Cordioside, Tinoscordin	Hepatoprotective, antioxidative
Polysaccharides	Arabinogalactan	Immune modulation, macrophage activation

The classification of Giloy as "Amrita," or nectar of immortality, reflects its long-standing cultural and therapeutic importance. Traditional preparations such as Guduchi Satva (powdered starch), Guduchi Ghrita (medicated ghee), and Amritarishta (fermented decoction) are prescribed in various formulations for enhancing physical resilience and improving quality of life.[3,5]

2. Phytochemical and Phytochemistry Insight of *Tinospora cordifolia*

Modern pharmacological research has provided a molecular explanation for the plant's extensive therapeutic applications. Analytical methods such as High-Performance Liquid Chromatography (HPLC), Gas Chromatography-Mass Spectrometry (GC-MS), and Nuclear Magnetic Resonance (NMR) spectroscopy have identified key bioactive constituents given in **Table 1**. These constituents collectively underpin the diverse health benefits attributed to Giloy in both traditional and modern contexts.[6]

3. Modern Clinical Evidence

Over the past five decades, clinical research has extensively explored the therapeutic potential of this plant, with both controlled trials and observational studies providing significant evidence. It has been shown to manage chronic fever through immune stimulation and temperature regulation,[8] and to reduce fasting blood glucose and glycosylated hemoglobin in patients with type 2 diabetes mellitus.[9] In autoimmune disorders such as rheumatoid arthritis, it alleviates symptoms by modulating inflammatory cytokines.[10] Clinical findings also highlight its hepatoprotective role in hepatitis B by normalizing liver enzymes and reducing oxidative stress. Furthermore, in viral infections like dengue, it enhances recovery by improving platelet counts and mitigating inflammation. More recently, during global health crises such as the COVID-19 pandemic, it has been recognized for providing immune support, enhancing resilience, and reducing fatigue.[11]

4. Safety and Regulatory Concerns

While the safety profile of Giloy is favorable when used in standardized dosages, concerns about hepatotoxicity linked to adulterated or improperly processed formulations have been reported. Some studies highlight gastrointestinal discomfort and allergic reactions as potential side effects in vulnerable populations.[12] Hence, strict quality control, dosage standardization, and monitoring are imperative for its safe clinical application.

5. Need for Standardization and Future Research

In order to facilitate global acceptance and regulatory approval, the following areas need further research and development

1. **Standardization:** Defining biomarkers for potency and purity to ensure consistency across batches.
2. **Pharmacokinetics:** Understanding absorption, metabolism, distribution, and excretion of bioactive compounds.
3. **Molecular mechanisms:** Using omics technologies and in silico modeling to map therapeutic pathways.[6]
4. **Clinical trials:** Conducting large-scale, multicenter, randomized controlled trials to validate traditional claims.[11]
5. **Formulation development:** Enhancing bioavailability through advanced delivery systems like nanoparticles.

6. Botanical Description

Tinospora cordifolia Miers, commonly known as Giloy or Guduchi, is a perennial climbing shrub belonging to the family Menispermaceae that is widely distributed across tropical and subtropical regions of the Indian subcontinent and neighboring countries.[3,5] It has been extensively used in traditional medicine systems such as Ayurveda, Siddha, and Unani for thousands of years for its rejuvenating and immune-enhancing properties.[4]

6.1. Morphology

1. **Habit:** It is a climbing, deciduous perennial shrub that can grow up to 5–15 meters in length, often wrapping around host trees such as neem, mango, and peepal for support.[3,5]
2. **Stem:** The stem is succulent, cylindrical, and characterized by longitudinal grooves. In its juvenile state, it is green, turning brown as it matures. Aerial roots emerge from the stem, aiding in attachment to surrounding structures.
3. **Leaves:** The leaves are heart-shaped (cordate), 5–15 cm in length, alternate, simple, and glabrous with prominent venation patterns aiding in identification.[5]

4. **Flowers:** The flowers are small, greenish-yellow, and unisexual. The plant is dioecious, meaning male and female flowers are found on separate plants.[6]
5. **Fruits:** The fruits are small, ovoid drupes that turn red when ripe and are used in various medicinal formulations.[6]
6. **Root system:** The roots are thin, fibrous, extensively branched, and aid in nutrient absorption and anchorage.[5]

7. Organoleptic Properties

1. **Taste:** Bitter (Tikta), which is associated with therapeutic potency in traditional systems.[4]
2. **Odor:** Distinct and medicinal.[4]
3. **Texture:** Fresh stems are fibrous and succulent, while dried stems are harder and brittle.

8. Identification Tests

1. **Phenolic test:** The stem turns red upon treatment with ferric chloride, indicating the presence of phenolic compounds.[6]
2. **Latex reaction:** Milky latex exudes from the stem and coagulates upon air exposure, confirming authenticity.[6]

9. Geographical Distribution

Tinospora cordifolia is naturally found across India, as well as in Sri Lanka, Bangladesh, and Myanmar, thriving in tropical and subtropical climates.[3,5] Its distribution pattern is as follows in India it is common in Uttar Pradesh, Madhya Pradesh, Maharashtra, Rajasthan, Tamil Nadu, Kerala, and Assam[3] and in neighboring regions it is found in Sri Lanka, Bangladesh, and Myanmar, where it grows abundantly in humid forests.[3]

1. **Climate:** Prefers well-drained soils with moderate rainfall and humidity.[5]
2. **Traditional belief:** Plants growing on neem trees are considered superior in medicinal value due to synergistic effects between the two botanicals.[5,7]

10. Phytochemistry

The therapeutic potential of Tinospora cordifolia is attributed to its rich composition of bioactive compounds, which have been extensively analyzed using techniques such as High-Performance Liquid Chromatography (HPLC), Gas Chromatography-Mass Spectrometry (GC-MS), and Nuclear Magnetic Resonance (NMR).[6]

10.1. Alkaloids

1. **Berberine:** Known for its antimicrobial, antidiabetic, and anti-inflammatory properties.[6]
2. **Magnoflorine:** Demonstrates neuroprotective and anti-inflammatory effects.

10.2. Diterpenoid lactones

1. **Tinosporin:** Enhances immune responses and reduces inflammation.[7]
2. **Columbin:** Regulates glucose metabolism and is beneficial in diabetes management.[7]

10.3. Steroids

1. **β-Sitosterol:** Helps modulate lipid profiles and possesses anti-inflammatory activity.
2. **Stigmasterol:** Reduces cholesterol levels and oxidative stress.

10.4. Glycosides

1. **Tinoscordin:** Acts as an antioxidant and supports liver function.
2. **Cordioside:** Protects cells from damage and controls inflammation.

10.5. Flavonoids

1. **Quercetin:** Neutralizes free radicals and prevents lipid peroxidation, protecting cells from oxidative damage.
2. **Kaempferol:** Enhances anti-inflammatory pathways and supports cardiovascular health.

10.6. Polysaccharides

10.6.1. Arabinogalactan

Stimulates macrophage activity and enhances immune defense mechanisms.

10.7. Other constituents

The plant also contains tannins, saponins, and essential oils, which contribute to its antimicrobial and antioxidant properties.[6]

11. Pharmacological Action

The pharmacological effects of Tinospora cordifolia are mediated through multiple biochemical pathways influenced by its diverse phytoconstituents.

11.1. Immunomodulatory effects

The polysaccharides, particularly arabinogalactan, activate macrophages and natural killer (NK) cells, resulting in enhanced innate immunity. This leads to increased production of cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), helping the body fight infections.

11.2. Anti-inflammatory mechanisms

Giloy inhibits cyclooxygenase-2 (COX-2) and nuclear factor-kappa B (NF-κB) signaling pathways, thereby reducing inflammatory mediator synthesis, including prostaglandins and leukotrienes. This mechanism is particularly useful in reducing joint pain, swelling, and tissue inflammation.[13]

11.3. Antioxidant defense

The flavonoids such as quercetin and kaempferol scavenge reactive oxygen species (ROS), preventing oxidative damage to lipids, proteins, and DNA. The activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD) and catalase is also enhanced, helping in the management of oxidative stress-related conditions.[14]

11.4. Antidiabetic effects

Active compounds like berberine improve insulin receptor signaling and increase the expression of glucose transporter proteins (GLUT4), resulting in better glucose uptake and regulation. The regeneration of pancreatic β-cells also contributes to improved glycemic control.

11.5. Hepatoprotective mechanisms

By reducing oxidative stress and promoting hepatocyte regeneration, Giloy normalizes liver enzymes such as serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic-pyruvic transaminase (SGPT), while also stabilizing bilirubin levels, thus supporting liver health.

11.6. Neuroprotective effects

The suppression of neuroinflammatory pathways and oxidative stress prevents neuronal degeneration. Clinical observations suggest improvements in memory, learning, and mood regulation in neurodegenerative disorders.

11.7. Cardioprotective effects

The plant's steroidal compounds, particularly β-sitosterol, reduce lipid accumulation and oxidative stress in cardiac tissues. Animal studies have shown a reduction in infarct size and improved myocardial function under ischemic conditions.

12. Pharmacological Activities of Giloy

Tinospora cordifolia has been extensively studied for its wide-ranging therapeutic properties. Experimental, clinical, and observational studies highlight its diverse pharmacological activities, many of which are supported by its rich phytochemical composition.

12.1. Immunomodulatory activity

Giloy enhances immune function by stimulating macrophage activation and increasing white blood cell count. Studies have shown that it upregulates cytokine production, including IL-1, IL-6, and TNF-α, thereby strengthening both innate and adaptive immunity.[15] It also increases antibody formation in animal models, providing defense against infections.

12.2. Antidiabetic activity

In type 2 diabetes models, administration of Giloy extract resulted in improved fasting blood glucose levels and better glycemic control.[16] It modulates insulin signaling pathways, increases glucose transporter expression, and enhances pancreatic β-cell function, contributing to long-term management of hyperglycemia.[16]

12.3. Hepatoprotective activity

Giloy protects the liver from toxins, including carbon tetrachloride (CCl4) and drug-induced hepatotoxicity, by enhancing antioxidant defenses and reducing lipid peroxidation. Clinical studies showed normalization of liver enzymes such as SGOT and SGPT in patients with liver dysfunction.[17]

12.4. Anti-inflammatory activity

The plant's bioactive compounds suppress inflammation by inhibiting key enzymes and signaling pathways involved in the inflammatory process. Experimental models demonstrated reductions in paw edema, joint swelling, and pain severity in arthritis-induced animals.[13,18]

12.5. Antioxidant activity

Giloy's flavonoids and polysaccharides neutralize reactive oxygen species, prevent lipid peroxidation, and enhance the activity of antioxidant enzymes like SOD and catalase. These mechanisms contribute to cellular protection against oxidative stress, a common factor in chronic diseases.[14,19]

12.6. Neuroprotective activity

The plant's neuroprotective potential has been investigated in models of neurodegeneration, such as Alzheimer's disease. Improvements in cognitive function, memory retention, and neuronal survival were observed, largely due to its antioxidant and anti-inflammatory properties.[20]

12.7 Cardioprotective activity

Studies demonstrated that β-sitosterol and stigmasterol improve lipid profiles and reduce oxidative stress in cardiac tissues. Animal models of ischemia-reperfusion injury showed decreased infarct sizes and improved cardiac output after Giloy supplementation.[21]

12.8 Anticancer activity

Giloy's constituents have been found to inhibit tumor cell proliferation, enhance apoptosis, and reduce angiogenesis in various cancer models. Its radioprotective properties also make it useful in oncology for supporting conventional therapies.[13,22]

12.9. Antimicrobial activity

The antimicrobial potential of Giloy is well-documented. Berberine and other alkaloids interfere with bacterial cell walls, reducing pathogen load in infections such as malaria, typhoid, and viral illnesses. In vitro studies confirmed its action against Staphylococcus aureus, Escherichia coli, and other pathogens.[6]

13. Clinical Evidence

Several clinical trials and observational studies have validated the therapeutic claims of Giloy, with evidence ranging from immune enhancement to metabolic regulation.

13.1. Chronic fever management

A clinical trial involving patients with recurrent febrile conditions reported that administration of Guduchi extract led to a significant reduction in fever episodes and associated fatigue.[8] The immunomodulatory action, particularly the enhancement of macrophage activity, contributed to faster recovery.[8]

13.2. Diabetes mellitus

A randomized controlled trial involving 60 patients with type 2 diabetes reported a 25% reduction in fasting blood glucose and improved glycosylated hemoglobin (HbA1c) after 12 weeks of Giloy extract supplementation.[9] Patients also reported better energy levels and reduced medication dependence.[9]

13.3. Rheumatoid arthritis

In a study of patients suffering from rheumatoid arthritis, Guduchi supplementation resulted in decreased joint pain, stiffness, and swelling over a 3-month period. Levels of C-reactive protein (CRP) were significantly reduced, correlating with symptomatic improvement.[10,18]

13.4. Liver health in Hepatitis B

Patients with viral hepatitis receiving Giloy-based formulations showed normalization of liver enzymes (SGOT and SGPT) and improved bilirubin levels. The antioxidant effects of flavonoids and hepatocyte regeneration were considered key mechanisms.

13.5. Allergic rhinitis

A double-blind, placebo-controlled study revealed that individuals with allergic rhinitis showed significant improvement in nasal congestion, sneezing, and eye irritation after daily intake of Giloy extract for 8 weeks.

13.6. Viral illnesses

In a study conducted during the dengue epidemic, Giloy extract was associated with improved platelet counts and faster recovery times. Similarly, hepatitis patients demonstrated better liver function and reduced inflammation markers after using Giloy supplements.

13.7. COVID-19 adjunct therapy

During the COVID-19 pandemic, integrative protocols including Guduchi were used to support immune function. Patients reported reduced fatigue, enhanced energy, and fewer secondary infections when Giloy was used alongside conventional care.[11]

14. Safety and Toxicology

Giloy is widely considered safe when used within therapeutic dosage ranges. However, excessive consumption or use of adulterated products has been linked to adverse effects.

14.1. Reported side effects

Mild gastrointestinal disturbances such as nausea, diarrhea, and constipation have been reported in a minority of cases.[12] Allergic reactions, including skin rashes and itching, have been observed in sensitive individuals.[12]

14.2. Hepatotoxicity concerns

A few case reports noted liver toxicity in patients using unregulated or adulterated formulations containing high concentrations of bioactive alkaloids. These highlight the need for standardized extraction and strict quality control protocols.

14.3. Safety in vulnerable populations

Although generally safe, caution is advised when administering Giloy to pregnant women, lactating mothers, and individuals with autoimmune disorders, as its immunostimulatory action may aggravate underlying conditions.[12]

14.4. Toxicological evaluations

Animal studies following OECD guidelines demonstrated no significant toxicity at therapeutic doses, with normal hematological and biochemical parameters observed over 28 days of repeated dosing.

15. Formulations and Dosage

Giloy is available in multiple forms, with dosage tailored to the condition being treated.

15.1. Common preparations

1. **Guduchi satva:** Powdered starch used for metabolic disorders and fever.[3]
2. **Guduchi ghrita:** Medicated ghee prepared with herbal extracts for skin diseases and liver disorders.[3]
3. **Amritarishta:** Fermented preparation used in chronic fever and malarial conditions.[3]
4. **Guduchi churna:** Powdered extract for digestive and metabolic disorders.[3]
5. **Ayush kwath:** Herbal decoction used as an immunity booster during pandemics.[11]
6. **Tablets/Capsules:** Standardized extracts (300–600 mg/day) used for diabetes and inflammatory conditions.[9]

15.2. Recommended dosage

1. **Chronic conditions:** 300–500 mg twice daily after meals with lukewarm water or milk.[3]
2. **Acute fever:** 20–30 ml juice extract twice daily for 5–7 days.[8]
3. **Liver disorders:** 10–15 ml extract twice daily along with diet regulation.
4. **Immune support:** 300 mg standardized extract once daily for long-term use.[11]

15.3. Formulation considerations

Standardization, purity, and bioavailability are crucial for achieving therapeutic outcomes. Extracts with defined marker compounds such as berberine and tinosporin ensure consistent efficacy.

15.4. Future prospects

Despite substantial evidence supporting Giloy's therapeutic potential, further research is required to facilitate its integration into mainstream medical practice. One of the foremost needs is the standardization and quality control of formulations, where defining phytochemical markers for potency and ensuring batch-to-batch consistency will enhance credibility and therapeutic reliability. Another critical area involves pharmacokinetic and bioavailability studies, where understanding how the body absorbs, metabolizes, and excretes Giloy's bioactive compounds will aid in developing formulations with improved efficacy. Progress in molecular research, where omics-based technologies and computational modeling can help elucidate specific pathways of action, may further enable applications in personalized medicine.[6] At the clinical level, large-scale multicenter randomized controlled trials, where robust data can establish safety and standardized therapeutic guidelines, remain an essential requirement.[11] Finally, innovations in advanced delivery systems, where approaches like nanoparticle-based formulations may enhance absorption, reduce dosing frequency, and improve patient adherence, represent a promising translational frontier.

16. Conclusion

Tinospora cordifolia (Giloy) is highly revered in traditional Indian medical systems and has gained increasing recognition in modern scientific research for its broad therapeutic potential. Classical Ayurvedic texts such as the *Charaka Samhita* and *Bhavaprakasha Nighantu* describe it as a rejuvenating and immune-enhancing herb, while contemporary pharmacological studies have validated its multifaceted activities, including immunomodulatory, antioxidant, hepatoprotective, antidiabetic, anti-inflammatory, and neuroprotective effects.[5,13]

The pharmacological efficacy of Giloy is attributed to its diverse phytochemical repertoire, comprising alkaloids such as berberine and magnoflorine,[6] diterpenoid lactones including tinosporin and columbin,[7] steroids like β-sitosterol and stigmasterol, flavonoids such as quercetin and kaempferol, along with various glycosides and polysaccharides such as arabinogalactan. These bioactive compounds exert their effects through well-characterized biochemical and molecular pathways, providing mechanistic insights into its therapeutic roles.

Clinical evidence further strengthens these findings, with controlled studies reporting efficacy in managing recurrent fever,[8] lowering fasting blood glucose and glycosylated hemoglobin in type 2 diabetes,[9] reducing joint inflammation in rheumatoid arthritis,[10] improving hepatic function in hepatitis B patients, and enhancing immune resilience during viral infections and pandemics, including COVID-19 . Supportive molecular and pharmacokinetic investigations confirm its relevance in both acute and chronic disease management.

Although Giloy generally demonstrates a favorable safety profile, concerns have been raised regarding dosage and product quality, as sporadic reports of hepatotoxicity have been linked to adulterated or improperly prepared formulations. Therefore, future research priorities must focus on standardization, bioavailability enhancement, and long-term safety assessments to facilitate its global therapeutic integration.[6]

Looking ahead, interdisciplinary approaches that combine traditional medical knowledge with advances in molecular biology, pharmacokinetics, and computational modeling will be crucial in expanding Giloy's therapeutic applications. Large-scale randomized clinical trials, development of novel delivery systems, and omics-based molecular research represent important steps to fully establish its role in precision and integrative medicine.[1]

In summary, Giloy emerges as a culturally significant, scientifically validated, and therapeutically promising medicinal plant. With ongoing research, strict regulatory oversight, and robust clinical validation, it holds the potential to make a substantial contribution to global healthcare

17. Source of Funding

None.

18. Conflict of Interest

None.

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