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# "From Ancient Roots to Modern Medicine: Unraveling Tinospora cordifolia's Antidiabetic Mystique"

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***Abstract:*** Tinospora cordifolia, a well-known herb in traditional Ayurvedic medicine, has gained attention for its potential anti-diabetic properties. This plant, commonly referred to as Guduchi, is rich in biologically active constituents, such as alkaloids, glycosides and flavonoids, which subsidize to its therapeutic effects. Various studies have proved its ability to lower blood glucose levels, improve insulin sensitivity, and encourage the regeneration of pancreatic beta cells. The active compounds, including berberine and Tinospora cordifolia side, are made-up to play key roles in these actions. Preclinical studies on animal models have shown promising outcomes, with Tinospora cordifolia significantly reducing blood glucose and improving insulin secretion. Additionally, human clinical trials have shown positive effects, particularly in type 2 diabetes, where the plant enhances the effectiveness of prevailing anti-diabetic drugs. Despite these hopeful findings, additional rigorous clinical research is required to confirm its efficacy, determine ideal dosages, and explore its long-term safety. This review aims to summarize the current understanding of Tinospora cordifolia as an anti-diabetic agent, highlighting its pharmacological mechanisms and therapeutic potential effect.

***Keywords:*** *Guduchi, Anti-diabetic herbal drug, berberine, Tinospora cordifoliaside, Ayurvedic medicine, glucose metabolism.*

## INTRODUCTION.

Diabetes Mellitus (DM) is a group of metabolic disorders considered by high blood glucose level (hyperglycemia) resulting from blemishes in insulin secretion, insulin action, or both. Insulin is a hormone secreted by the pancreas that allows the body to utilize glucose from food for energy. In diabetes, the body's ability to generate or respond to insulin is impaired, leading to excite the blood glucose levels.

There are types of Diabetes Mellitus-
a) Type 1 Diabetes (T1D): T1D is an autoimmune state where the immune system outbreaks and destroys the insulin-yeilding beta cells in the pancreas. Naturally, it is developed in childhood or youth but can occur at any age of life. Insulin therapy is necessary for life, people with type 1 diabetes must check their blood glucose level frequently and inject to regulate them.
b) Type 2 Diabetes (T2D): The main reason of T2D is insulin resistance, where the body's cells do not responds suitably to the insulin and over time, the pancreas are not able to secrete enough insulin to keep blood glucose level at its normal. Fundamentally, it affects adults, but gradually seen in children and adolescents due to increasing obesity rates. If a appropriate diet and exercise is included, the lifestyle can be altered. Also, medications and insulin are used to regulate the blood glucose level.
c) Gestational Diabetes: Gestational Diabetes progresses during the pregnancy, when the body is not able to produce adequate insulin to satisfy the necessary needs, and hence, leads to high blood sugar level. Its typically arises during the 24th week of pregnancy. This diabetes can be managed with a proper diet exercise, but insulin may be required in severe cases. Gestational Diabetes resolves after the parturition, but there's a advanced risk of developing type 2 diabetes in the women in future.

### 3.1 Background of T. cordifolia

Tinospora cordifolia, also referred to as Guduchi or Giloy, is a woody climber that is a perennial member of the Menispermaceae family. It is used broadly in Ayurveda, traditional Chinese medicine, and other traditional healing systems for its anti-inflammatory, anti-diabetic, and immune-boosting properties. Botanical Account, Scientific Name: Tinospora cordifolia, Common Names: Guduchi (Hindi), Giloy (Hindi), Amrita (Sanskrit), and Heart-leaved Moonseed (English), Plant Type: Climbing shrub with small, yellowish flowers and heart-shaped leaves.

Various names of Tinospora cordifolia in different regions:

| *Languages* | *Different Names* |
|---|---|
| *English* | *Tinospora cordifolia, Gulancha Tinospora cordifolia* |
| *Hindi* | *Gulanca, Giloy, Amrta* |
| *Kannada* | *Amrtaballi, Yuganiballi, Madhuparni* |
| *Malayalam* | *Chittamrtu, Amrtu* |
| *Sanskrit* | *Guduci, Amrta* |
| *Tamil* | *Amrutvalli, Cintilikkoti* |
| *Telugu* | *Tippantiga, Amrta* |
| *Unani* | *Gilo, Gulanchaa, Sat-e-Gilo(extract)* |

Table no.1

The biological purpose of Tinospora cordifolia are mostly due to its chemical components. Among them are polysaccharides, steroids, terpenoids, glycosides, and alkaloids. These compounds can be found in the plant's leaves, stems, or roots and are not restricted to any one area. Several studies have been conducted to isolate and purify these active constituents and clarify their distinct properties using spectroscopy and other high-throughput analytical techniques.

*Figure 1. The leaves of Tinospora cordifolia are heart-shaped, membranous, and alternative,with 4-6 pairs of veins and a pointed tip.*

*Figure 2. The stem of Tinospora cordifolia is a long ,slender, and cylindrical structure that is greenish-brown in color and woody at the base.*

*Figure 3.The Fruits of Tinospora Cordifolia are red, fleshy, drupe-like, with a single seed, turning red or purple when ripe.*

*Figure 4.The Flowers of Tinospora Cordifolia are small, yellowish-green, and unisexual, arranged in clusters on axillary racemes.*

**3.2 Morphological characteristics of Tinospora cordifolia**

Tinospora cordifolia is also known as "Queen of Herbs". It has coiling branches known as climbing shrub. The plant is basically divided into several different parts such as leaves, stem, fruits, flower aa well as parts like seeds, lamina, arial roots, too. The root cortex as an outer, thick wall with an inner parenchymatous area. The lamina is of oval shape which is 10-20 cm long and 15cm broad. The seeds are curved in shape and the embryo turns automatically curve. Hence, the endocarp as taxonomic characters and therefore well ornamented.

| | |
|---|---|
| Pharmacological Activities of T.cordifolia | Anti-cancer |
| | Anti-arthritic |
| | anti-Inflammatory |
| | Anti-osteoporasis |
| | Neuroprotective |
| | Anti-fungal |
| | Anti-toxic |
| | Anti-stress |
| | Anti-microbial |
| | Anti-oxidant |
| | Cardioprotective |
| | Anti-diabetic |
| | Immunomodulator |
| | Anti-malarial |
| | Anti-leprotic |
| | Anti-HIV |
| | Anti-bacterial |
| | Heptoprotective |
| | Anti-allergic |

**Table no.2**

### 3.3 T. cordifolia on Diabetes

Tinospora cordifolia, commonly known as Guduchi or Giloy, has shown promising potential in managing diabetes mellitus. This medicinal plant contains bioactive compounds such as alkaloids, glycosides, and terpenoids that contribute to its anti-diabetic properties. Studies have demonstrated that Tinospora cordifolia can help regulate blood glucose levels by enhancing insulin sensitivity and stimulating glucose uptake in peripheral tissues. The plant extract has been found to inhibit key enzymes involved in carbohydrate metabolism, such as α-amylase and α-glucosidase, thereby reducing postprandial glucose spikes. Additionally, Tinospora cordifolia exhibits antioxidant and anti-inflammatory effects, which may help mitigate diabetes-related complications. Animal studies have shown that the plant can regenerate pancreatic β-cells and increase insulin secretion, potentially improving glycemic control in both type 1 and type 2 diabetes. While clinical trials have yielded encouraging results, more extensive research is needed to fully elucidate the mechanisms of action and establish optimal dosing regimens for Tinospora cordifolia in diabetes management.

Guduchi, also known as Tinospora cordifolia, is a very powerful plant used in Ayurveda to treat diabetes and maintain the equilibriums of several organ functions. Its anti-diabetic uses have been stated in a number of Ayurvedic literature and Nighantu (lexicons/Ayurvedic materia medica) under the names Pramehaghna, Pramehahara, Mehaghna, and Mehahara. Its antidiabetic properties have also been said by the Indian Ayurvedic Pharmacopoeia. The herb has been used by the Korkus tribe (Melghat, Maharashtra, India) to treat fever, diabetes, and polyuria. In addition to being utilized in traditional medicine, Guduchi and a varied range of its derivative products—including active, natural principles and crude extracts—have been shown in multiple scientific journals to exhibit anti-diabetic effects in both clinical and experimental settings. These components have an impact on the glucose level and different metabolic cascades, either directly or indirectly. Even though there have been many studies conducted over the past few decades, there is little sporadic information available about its antidiabetic effectiveness. This review aims to identify the plant's likely mode of action and highlights its reported antidiabetic potential.

### 3.4 Research Methodology

Several articles were published, but only a small number of review articles and cross-references were gathered. The report also logically surveyed and examined recent advancements in antidiabetic research on Tinospora cordifolia, encompassing all records and articles available in Pubmed, Scopemed, Dhara online, and other related databases, including pharmacology, biomedicine, and health. By examining Ayurvedic claims in light of known experimental and clinical results, the search parameters were limited to the roles of plants in diabetes and associated problems.

### 3.4 Antidiabetic properties of phytoconstituents

Numerous physiologically active phytoconstituents that have been identified from various plant components, such as alkaloids, tannins, cardiac glycosides, flavanoids, saponins, and steroids, have been found to mediate its anti-diabetic potential. These substances may be used in clinical and experimental research since they have been shown to cover a variety of target activities in diabetes circumstances. Palmatine, jatrorrhizine, and magnoflorine are among the isoquinoline alkaloid-rich fraction from the stem that have been shown to exhibit insulin-releasing and insulin-mimicking effects both in vitro (using the rat pancreatic β-cell line, RINm5F) and in vivo. Berberine, another isoquinoline alkaloid, has been effectively studied and used in both human and experimental diabetes. It reduces high blood sugar levels just as well as metformin. Additionally, it suppresses FOXO1, which improves hepatic metabolism in insulin resistance and metabolic syndrome by integrating insulin signaling with mitochondrial activity. It lowers blood sugar and cholesterol levels and keeps blood pressure stable by activating adenosine monophosphate-activated protein kinase. Additionally, stem and root contain tinosporin, isocolumbin, palmatine, tinocordiside, cordioside, and ß-sitosterol substances that are said to have antioxidant, antihyperlipidemic, and antidiabetic effects. The following active components are present in the stem of T.cordifolia.

*Figure 5. Stem of T. cordifolia*

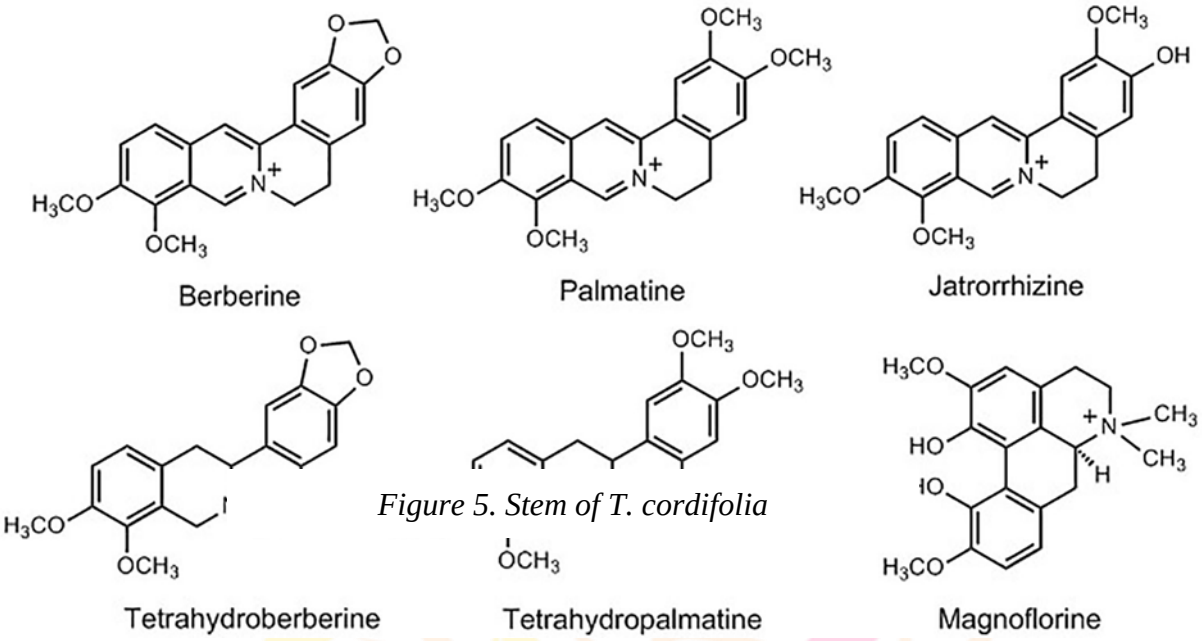


*Figure 6. Structure of active components of T. cordifolia*

It regulates blood pressure and lowers blood sugar and cholesterol levels by activating adenosine monophosphate-activated protein kinase. Furthermore, chemicals found in stem and root, such as tinosporin, isocolumbin, tinocordiside, cordioside, and β-sitosterol, have been shown to have antioxidant, antihyperlipidemic, and antidiabetic effects.

**3.5 Methods of Extraction**

a) Stems of T. cordifolia were chopped into little pieces and dried at 40 °C in an oven. After that, it was ground into a powder and kept for later use at 4 °C. The stem powder of T. cordifolia was extracted in a series using the following solvents: water, methanol, ethanol, acetone, ethyl acetate, and chloroform-ether (1:1).Each solvent (500 ml) was extracted twice, and the results were combined. The solvents of each extract were lyophilized, reconstituted with water, flash evaporated until dry, and yields were recorded. EAT cells were employed as a model system, and the effects of water, ethanol, and methanol extracts on glucose uptake were investigated.

b) Using a Soxhlet extractor, the powder was extracted with hexane after being defatted with petroleum ether at 60 to 80°C.The extracts were dried with a rotary vacuum evaporator at lower pressure.

**3.6 Miracle of Tinospora cordifolia in Diabetic Complications**

a) Nutritional supplements
This herb contains significant amounts of major and minor elements, including Zn, Mn, Cl, K, Ca, Ti, Cr, Fe, Co, Ni, Cu, Br, and Sr, in addition to its high protein and dietary fiber content. These elements function as micronutrients for restoring health and reducing degenerative processes in diabetes.
High fiber (15.19%), adequate protein (4.5%–11.2%), adequate carbohydrate (61.66%), and low fat (3.1%) are the crude figures for food composition in Tinospora cordifolia. There are 292.54 calories per 100 g of nutritional value. It contains enough iron (0.28%) to improve hematopoietic functions, particularly in diabetic nephropathy where erythropoietin release from the kidney is compromised, high potassium (0.845%) to regulate nerve impulses, high chromium (0.006%) to regulate carbohydrate utilization pathophysiological alterations in diabetes, and enough calcium (0.131%) to regulate nervous, cardiovascular, and musculoskeletal systems.

b) Protection of gastrointestinal tract in old age
Digestive disorders are prevalent in the elderly population. In addition to its potential effectiveness in treating nonspecific diarrhea, dysentery, peptic ulcers, and abdominal pain, pharmacological data supports Tinospora cordifolia's protective role in the gastrointestinal tract. The traditional claims of symptomatic alleviation in cases of dyspepsia, belching, bloating, gas, or stomach pain associated with the terms "Ajirna" or "Agnimandya" in Ayurvedic literature can be explained by these findings.

c) Protection of Heart

The qualities of Hridya (cardioprotective) and its application in Hridroga (cardiac diseases) are described by Ayurveda. In rats with ischemia-reperfusion-induced myocardial infarction, T. cordifolia administration resulted in a dose-dependent decrease in infarct size as well as in serum and heart lipid peroxide levels. In streptozotocin-induced diabetic mice, the stem extract has restored normal lipid metabolism changes brought on by diabetes mellitus, thereby helping the heart.

d) Diabetic Foot ulcer

The use of plant extract as an adjuvant in the surgical treatment of diabetic foot ulcers has been shown to be very helpful in immunomodulation for ulcer healing in a randomized control study. Therefore, it expedites the healing process.

e) Infertility and genital issues

Diabetes frequently causes impotence, erectile dysfunction, and loss of libido, which have an impact on a person's social and medical well-being. The number of mounts, penile erection index, ejaculatory behavior, and mating performance were increased in male Wistar albino rats treated with hydroalcoholic and aqueous extracts of the stem (400 mg/kg body weight). Stem extract reduces the weight of the ventral prostate, relieves urinary tract infections, dissolves urinary calculi, and lowers blood urea levels in uremia. Although there is no proof of direct antibacterial action, its anti-inflammatory and immune-modulating properties are probably related to its benefit in urinary tract infections.

**3.7 Herbal immune booster in Covid-19 pandemic**

Complementary and alternative medicine has become increasingly popular as a result of the COVID-19 pandemic. Tinospora cordifolia is a widely cultivated shrub that has been used extensively as a prophylactic against COVID-19 and for its immune-boosting qualities in India's traditional Ayurvedic system. During the four-month study period during the COVID-19 pandemic, six patients—two men and four women—with a median (IQR) age of 55 years and a history of consuming Tinospora cordifolia showed signs of severe hepatitis. Tinospora cordifolia consumption lasted 90 days on average (IQR). The median (IQR) peak levels of AST and bilirubin were 1350 IU/ml and 17.5 mg/dl, respectively. Following a biopsy, the patients showed an autoimmune pattern of drug-induced liver damage and either a definite (n = 4) or probable (n = 2) updated autoimmune hepatitis score. In addition to hypothyroidism and type 2 diabetes mellitus, four of these patients (all female) had underlying silent chronic liver disease of potential autoimmune etiology. During steroid tapering, one of the three patients who received steroid treatment decompensated. Following medication removal or continued steroid treatment, the liver profile, autoimmune serological markers, and symptoms of the other five patients all improved. After stopping the herb, the median (IQR) time to resolution was 86.5 days. The immune stimulant mechanism of Tinospora cordifolia may be supported by the fact that it appears to cause autoimmune-like hepatitis or reveal an underlying autoimmune chronic liver disease. We advise using this plant with caution, especially in people who are prone to autoimmune illnesses, as the same mechanism might result in serious liver poisoning. Furthermore, a thorough history of complementary and alternative medicine must be obtained from patients who present with acute hepatitis, even if they have autoimmune signs.

**3.8 Clinical Evidence**

Aqueous leaf digest (10 g/200 mL water) was tested for its impact on type-2 diabetics' postprandial blood glucose levels. It has been discovered that the herb significantly lowers blood sugar levels in people. A similar response was seen in another study, which supported its hypoglycemic potential. In that study, two Ayurvedic dosage forms, Guduchi Ghana (solidified aqueous extract) and Guduchi Satva (sedimented starchy aqueous extract), significantly reduced the signs and symptoms of type-2 diabetes and exhibited significant hypoglycemic and anti-hyperglycemic activity. According to statistics, Guduchi Ghana was found to be more successful than Guduchi Satva at regulating blood sugar levels. Guduchi's antidiabetic activity is further supported by two or more clinical investigations on its Kwatha (decoction) and Churna (fine powder) . Guduchi has been found to be safe for therapeutic use (dose: 500 mg/d, duration: 21 d, subjects: healthy individuals) and to play a significant role in normalizing altered liver functions (alanine transaminase, aspartate transaminase) by another clinical study. As a result, the herb regulates the metabolism of carbohydrates and fats by enhancing hepar function. All of these investigations support the findings of previous research on animals and demonstrate that it is a safe anti-diabetic drug in the Ayurvedic medical system.

**3.9 Interactions**

It's important to keep in mind the concepts of herb-drug interactions even if Tinospora cordifolia is less likely to have the same problems as the traditional medications used to treat diabetes. Although no adverse herb-drug interactions have been documented to date, further research in this area is still needed. Tinospora cordifolia and metformin administered concurrently demonstrated advantageous pharmacokinetic and pharmacodynamic interactions that improved antihyperglycemic and antihyperlipidemic effects. Berberine, a plant alkaloid, has been demonstrated to enhance the actions of 2,4-thiazolidinedione and metformin. It can partially replace the commercial medications, potentially reducing the toxicity and adverse effects of the latter. Tinospora cordifolia stem decoction is used in Ayurveda as a means of purifying Guggul (Commiphora wightii), an essential ingredient in many Ayurvedic antidiabetic formulations, through the "Shodhana" process, which involves mixing one substance with another to increase its activity and help counteract some of its undesirable effects. Tinospora cordifolia increased Guggul's activity. The effect of Guggul was much diminished when taken alone. Clinically desirable medication interactions may result from the use of Tinospora cordifolia combos.

**3.10 Toxicity**

Despite the fact that this herb has been the subject of numerous studies, there is currently no noteworthy evidence regarding its toxicity.The herb is thought to be safe at the dosage specified.

### 3.11 Discussion

Tinospora cordifolia's ancient and traditional use in diabetes is supported by recent antidiabetic studies; the current review outlined various pharmacological and clinical evidence to indicate that it had a mild to moderate but significant blood glucose lowering effect; long-term use of its various extracts and dosage forms may be beneficial over chemical drugs in alleviating some of the chronic manifestations and complications caused by diabetes; and its use in conjunction with conventional drug treatments, such as insulin or a chemical agent, permits the use of lower doses of drug and/or decreased frequency of administration, which reduces the most common side effects.

Previous research shows that its extracts can help avoid treatment side effects or problems from diabetes. Therefore, it addresses all areas of management—preventive, curative, and restorative—which are unavoidably necessary to combat diabetes. Conventional synthetic medications are unable to offer all of the aforementioned advantageous qualities. In order to identify hypoglycemic principles and clarify the biological roles of other herbs in this context, the current review calls for further research into the composition, isolation, purification, and characterization of bioactive products (active, natural principles, and crude extracts).

because the plant's interactions with manmade antidiabetic medications were both pharmacokinetic and pharmacodynamic. When taken with diabetic drugs, the dosage and frequency may need to be adjusted or reduced since they may cause blood sugar levels to drop too low. Blood sugar levels need to be regularly checked. Tinospora cordifolia has the "Shodhana" process (discussed previously) and is supported by a contemporary pharmacological investigation when combined with other drugs in Ayurvedic formulations. The reason behind Tinospora cordifolia combination formulations will be established by investigating the potential for certain additive or synergistic effects of Tinospora cordifolia with other substances, as well as the pharmacokinetic and pharmacodynamics of such combinations.

The anti-diabetic claims of Tinospora cordifolia in Ayurvedic literature are consistently supported by evidence from both humans and animals; however, multicentric large-scale clinical trials would be more confirmatory, particularly for in-depth cause-effect evaluations, tracing the mechanism of action, and assessing the safety and interaction with conventional drugs when prescribed concurrently. There haven't been any negative reactions to the plant yet. It has thus been demonstrated to be a safe method of managing diabetes.

### 3.12 Conclusion

In conclusion, Tinospora cordifolia (Guduchi) demonstrates significant potential as an antidiabetic agent, supported by its ability to regulate blood glucose levels, enhance insulin sensitivity, and provide antioxidant benefits. While promising preclinical and traditional evidence highlights its efficacy in managing diabetes, further clinical studies are essential to validate its therapeutic potential, establish safe dosages, and determine long-term effects. As a natural remedy, Tinospora cordifolia could serve as a complementary treatment in diabetes management pending more rigorous scientific evaluation.

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