



The Review: *Tinospora Cordifolia* an Effective Treatment as Anti- Leprotic Agent

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Abstract : *Tinospora cordifolia*, also known as "Guduchi," is used in the traditional ayurveda system to treat a number of diseases. The objective of this review is to provide an extensive literature analysis and overview of traditional and contemporary information about *Tinospora cordifolia* for human health. It is a native of India and is a glabrous, succulent, woody climbing plant. It does well in the tropical climate, regularly attains its optimum height, and scales the branches of big trees. Alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolic, aliphatic compounds, and polysaccharides are just a few of the many kinds of substances that are isolated from *Tinospora cordifolia*. *Tinospora cordifolia* has been utilized in traditional medicine for centuries, and research shows that it offers pharmacological benefits including hypoglycemic, anti-inflammatory, hepatoprotective, and immune modulator activity, and antioxidant, antitumor, antineoplastic, and antifertility activity. The World Health Organization, or WHO, around 80% of the 5.86 billion people living in the world rely on traditional medicine for their main healthcare, the majority of which use herbs or their active ingredients. Being mindful of the importance of crop rotation between other crops and medicinal plants or herbs is important. In the eight-year period from 2001 to 2008, their production represented more than 100% of all publications published worldwide; in the following eight years from 2009 to 2020, this share fell to 98.53%. About 70 genus and more than 350 species of the plant family Menispermaceae can be found in tropical regions. Many body organs and tissues can be impacted by leprosy (Hansen's disease). Skin signs are effectively monitor in the early stages of a medical condition, giving them the first recognized symptoms to cause clinical suspicions. Peripheral nerves and the skin are the main sites of leprosy damage. The disease has been known about for many centuries well before time of the Bible. The classification of Hansen's illness has altered over many years as contemporary medical research advanced. Leprosy patients frequently experience prejudice, exclusion from society, social stigma, poor quality of life (QoL), low self-esteem, and irreversible disfigurements. Research has demonstrated that leprosy significantly lowers patients' quality of life. As leprosy is no longer emphasized in medical courses, practicing doctors frequently do not detect

Index Terms - *Tinospora cordifolia*, WHO, Menispermaceae, Menispermaceae, AETC, MET, leprosy; Hansen's disease

INTRODUCTION AND HISTORY

Mycobacterium leprae, a biological agent that causes the infectious disease leprosy or Hansen's disease, that most affects the human skin and peripheral nerves, first discovered by the Norwegian scientist Gerhard Hansen. Leprosy is mentioned by the Bible, however it's unsure whether it is Hansen's illness or another. This term was used to denote different skin conditions with varied cause and symptoms. Leprosy was an especially cruel illness for a long time, causing sufferers to be separated in leprosaria, mostly in Europe. They had to wear bells to indicate their presence.[1] In order to, eliminate Leprosy from all countries, the World Health Organization formulated "the final push", a strategy based on the early case detection and treatment with multi-drug therapy. [2] Plants are the important source of drugs, due to the extensive diversity of molecules with medicinal potential, and can make an effective contribution to the search of new bioactive products, semi-synthetic medicines or lead compounds for the development of medicines. [3] In ancient medical history of ayurveda *Tinospora cordifolia* family Menispermaceae is one of the most widely used shrub as medicine. Commonly it is known as guduchi, amritha valli. *Tinospora cordifolia* occupied with wide variety of bioactive principles and it is medically proven important plant (Pathan et al., 2017). *Tinospora cordifolia*, the versatile herbal drug is the distinctive source of constituents which is having antidiabetic, immunomodulatory, antioxidant, antimicrobial, antitoxic and anticancer activity. [4]

TYPES OF LEPROCY

There are different types of leprosy

A. Lepromatous leprosy (LL)

B. Tuberculoid leprosy (TL)

- C. Borderline lepromatous leprosy (BL)
- D. Borderline tuberculoid leprosy (BT)
- E. Indeterminate

CLASSIFICATION OF LEPROCY

WHO classified for therapeutic purpose.

- A. Paucibacillary leprosy (non infectious) - TL, BT- with 2-5 skin lesions.
- B. Multibacillary leprosy (Infectious) – LL, BL.- more than 6 skin lesions

Signs and Symptoms

- Discoloured patches of skin, usually flat, that may be numb and look faded (lighter than the skin around)
- Growths (nodules) on the skin.
- Thick, stiff or dry skin.
- Painless ulcers on the soles of feet.
- Painless swelling or lumps on the face or earlobes.
- Loss of eyebrows or eyelashes.

MYCOBACTERIUM LEPRAE

Mycobacterium leprae also known as Hansen's bacillus spirally these are largely found in warm climate and warm tropical countries. [5] *Mycobacterium leprae* an intracellular, pleomorphic, acid-fast and pathogenic bacterium. *M. leprae* is an aerobic bacillus (like rod-shaped) surrounded by the characteristic of waxy coating and unique to mycobacteria. In size and shape, it closely resembles to *Mycobacterium tuberculosis*. Due to its thick waxy coating, *M. leprae* stains with a carbolfuchsin (dye) rather than with the traditional Gram stain. The culture takes numerous weeks to mature. Optical microscopy of *M. leprae* shows in clumps rounded masses, or in groups of bacilli side by side and ranging from 1–8 μm in length and 0.2–0.5 μm in diameter.[6]

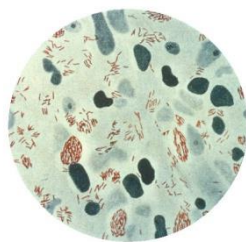


Figure. 1: *Mycobacterium leproae*

Leprosy Pathophysiology

1. *Mycobacterium leprae*

M. leprae, an acid-fast bacillus is a major human pathogen. In addition to humans, leprosy has been observed in nine-banded armadillo and three species of primates [7]. The bacterium can also be grown in the laboratory by injection into the footpads of mice [8]. Mycobacteria are known for their notoriously slow growth. With the doubling time of 14 days, *M. leprae* has not yet been successfully cultured in vitro [9, 10]. The genome of *M. leprae* has been sequenced in totality [11]. It presents with less than 50% coding capacity with a large number of pseudogenes. The remaining *M. leprae* genes help to define the minimal gene set necessary for in vivo survival of this mycobacterial pathogen as well as genes potentially required for infection and pathogenesis seen in leprosy. *M. lepromatosis* is a newly identified mycobacterium which is described to cause disseminated leprosy whose significance is still not clearly understood [10, 11].

2. Genetic Determinants of Host Response

Human genetic factors influence the acquisition of leprosy and the clinical course of disease [12]. Single-nucleotide polymorphism (SNP) association studies showed a low lymphotoxin- α (LTA)-producing allele as a major genetic risk factor for early onset leprosy [13]. Other SNPs to be associated with disease and/or the development of reactions in several genes, such as vitamin D receptor (VDR), TNF- α , IL10, IFN- γ , HLA genes, and TLR1 are also suggested [14–15]. Linkage studies have identified polymorphic risk factors in the promoter region shared by two genes: PARK2, coding for an E3-ubiquitin ligase designated Parkin, and PACRG [16]. A study also suggests that NOD2 genetic variants are associated with susceptibility to leprosy and the development of reactions (type I and type II) [17].

3. Transmission

Two exit routes of *M. leprae* from the human body often described are the skin and the nasal mucosa.[18] Lepromatous cases show large numbers of organisms deep in the dermis, but whether they reach the skin surface in sufficient numbers is doubtful [19]. Although there are reports of acid-fast bacilli being found in the desquamating epithelium of the skin, there are reports that no acid-fast bacilli were found in the epidermis, even after examining a very large number of specimens from patients and contacts [20]. However, fairly large numbers of *M. leprae* were found in the superficial keratin layer of the skin of lepromatous leprosy patients, suggesting that the organism could exit along with the sebaceous secretions [21]. The quantity of bacilli from nasal mucosal lesions in lepromatous leprosy ranges from 10,000 to 10,000,000 [22]. Majority of lepromatous patients show leprosy bacilli in their nasal secretions as collected through blowing the nose [23]. Nasal secretions from lepromatous patients could yield as much as 10 million viable organisms per day [24]. The entry route of *M. leprae* into the human body is also not definitively known. The skin and the upper respiratory tract are most likely; however, recent research increasingly favours the respiratory route [25, 26].

4. Incubation Period

Leprosy's stagnant onset and the lack of appropriate immunological methods make estimating the incubation period difficult. Based on the very rare cases of leprosy among newborn babies, the minimum incubation period recorded is as short as a few

weeks [27]. As per studies done on war veterans who were known to have been exposed to endemic areas for brief periods but generally lived in nonendemic locations, the greatest incubation period documented is as long as 30 years or above. The average incubation period is thought to be between three and 10 years [28].

Tinospora cordifolia

Herbal preparations are medicines made from one or more herbs present in significant measure to provide specific cosmetic advantages identifying and treating human or animal diseases [29]. It is often referred to as phytomedicine or herbal medicine. Herbal medicine was the main method of treatment in the early decades of the twentieth century because there were no antibiotics or analgesics. Due to the rising use of the allopathic medical system and its quick healing effects, herbal therapy has steadily lost favour with the populace. For example Curcuma, as a sample, has been applied in Traditional Chinese Medicine for more than two anti-inflammatory and powerful antioxidant for treatment for thousands of years [30, 31]. Because herbal medicines have fewer negative effects and are better suited to the human body, over 70–80% of people continue to utilise them for their main health [32]. The use of herbal medicine has increased, and it is more effective than synthetic medicines.

T. cordifolia is also known as Guduchi/Amrita and by the Latin names *Tinospora cordifolia* (Wild) Hook. f. & Thomson, *Tinospora Gulancha*/Indian *Tinospora*, and *Giloya*. Its scientific name is *Tinospora sinensis* (Lour.) Merr. It can be found in Myanmar, Sri Lanka, and China [33] and is a member of the Menispermaceae family.

In addition to enhancing the immune system and the body's resistance to infections, *giloya* is effective in the treatment of helminthiasis, heart problems, leprosy, rheumatoid arthritis, and other situations [34]. It also maintains normal white blood cell structure, function, and levels. Also, it helps in the treatment of digestive disorders such hepatitis and liver problems like hyperacidity, colitis, worm infestations, lack of appetite, abdominal pain, excessive thirst, and vomiting. The chemical components of the plant, which also include diterpenoid lactones, glycosides, steroids, sesquiterpenoids, phenolic compounds, essential oils, a mixture of fatty acids, and polysaccharides, are what give rise to the plant's pharmacological effects [35]. These chemical constituents are also found in the root, stem, and parts of the body of the plant.

Anti-Microbiological Action

When tested on different microorganisms with different solvents, *T. cordifolia* demonstrated excellent antifungal and antibacterial activity [36]. According to Jeyachandran et al., an in-vitro analysis of stem extracts against both gram-positive and gram-negative bacteria indicated good therapeutic activity against the infectious disease. *T. cordifolia* methanolic extract was utilized to combat both bacterium groups. [37]. According to Narayanan et al., plant extracts have antibacterial activity against Gram-positive bacteria such as *Proteus vulgaris*, *Escherichia coli*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella typhimurium*, *Klebsiella pneumoniae*, *Enterobacter aerogene*, *Shigella flexneri*, *Staphylococcus aureus*, and *Serratia marcescens* [38]. *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* clinical isolates were inhibited by the aqueous, ethanol, and acetone extract of *T. cordifolia*. [39]

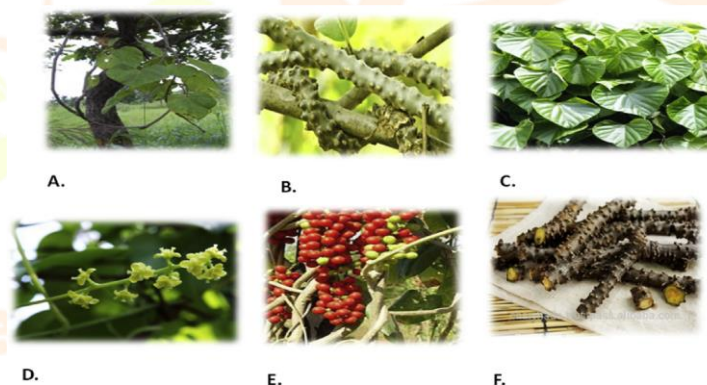


Fig. 2. Morphology of *Tinospora cordifolia* A) stem B) root C) leaves D) flower E) fruit F) seed.

Morphology of *Tinospora cordifolia*-

Plant Morphology A dry, thirsty, woody climbing plant not far from India is called *Tinospora cordifolia*. [40] It does well in the tropical climate, sometimes grows to huge heights, and scales the stems of big trees. The stem is highly spiralled and longitudinally cleft, grey and creamy white, and covered in large, lenticular spots which resembles rosette leaves. [41] White, flexible, and porous, plant wood takes on a yellow tint when exposed to air after becoming freshly cut. Simple, alternate, exstipulate, long petiolate, chordate-shaped leaves that also have multicoated reticulate venation. From the branches, a long thread that simulates aerial roots rises. [42] Flowers are unisexual and short. Female flowers grow singly, whereas male blooms form clusters. With six sepals in two whorls,

Taxonomical classification Kingdom:

Plantae Division: Magnoliophyta

Class: Magnoliopsida,

Order: Ranunculaceae

Family: Menispermaceae.

Genus: *Tinospora*

Chemical Constituents

Alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds, and polysaccharides are just a selection of materials that could be isolated from *Tinospora cordifolia*. Other materials isolated from *Tinospora cordifolia* include tinosporone, tinosporic acid, cordifolisides A to E, syringen, berberine, giloin, gilenin, crude giloininand, picrotene, bergenin, gilosterol, tinosporol, tinosporidine, sitosterol, cordifol, hept [43] Moreover, it also contains a small amount of phyosterols, glycosides, saponins, and flavonoids. The antioxidant activity which is discovered may be caused by these active ingredients acting alone or in combination. [44] This family is a good source of terpenes and alkaloids. This plant has abundant leaves.

A. Terpenoids -

Tinosporide²⁴, Furanolactone diterpene Furanolactone clerodane diterpene, furanoid diterpene, Tinospora-side, ecdysterone makisterone and several glucosides isolated as poly acetate, phenylpropene disaccharides cordifolioside A, B and C, cordifolioside D and E, Tinocordioside palmatosides C and F, glucoside cordioside. Sesquiterpene tinocordifolioside, Sesquiterpene tinocordifolin"

B. Alkaloids

Tinosporine, Magnoflorine, Tembetarine, Berberine, Choline, Palmatine, Jatrorrhizine, 1,2-Substituted pyrrolidine, Alkaloids, viz. jatrorrhizine, palmatine, beberine, tembetarine", choline.

C. Lignans

3(a, 4-dihydroxy-3-methoxybenzyl)-4-(4-hydroxy-3-methoxybenzyl), .

D. Steroids

44 Giloinsterol, B-sitosterol, 20 α -Hydroxy ecdysone,

F. Others

Giloin, Giloinin, Tinosporan acetate, Tinosporic acid, Tinosporal acetate, Tinosporidine, Heptacosanol, Cordifolone, Octacosanol, Tinosponone Tinosporic acid, tinosporal, tinosporon, 20-hydroxyecdysone, two phytoecdysan immunologically active arabinosides nogalactan

PHYTOCHEMISTRY -T. cordifolia (Guduchi) mainly consists of alkaloids, glycosides, steroids, aliphatic compounds, essential oils, mixture of fatty acid, calcium, phosphorous, protein and polysaccharides (Figure2)[45]

ASPECTS OF TINOSPORA CORDIFOLIA THAT ARE ACTIVE AND ITS THERAPEUTIC ACTIVITIES

The active components of T. cordifolia's stem and root are alkaloids. They contain tinosporin, magnoflorine, choline, berberine, and tembetarine. Tetrahydropalmatine, isocolumbin, palmetine, jatrorrhizine, aporphine alkaloids, and jatrophin showed immunomodulatory, anti-cancer, anti-diabetic, antiviral, anti-inflammatory, and antipsychiatric effects.[46-47] Furanolactone, diterpenoid Lactones, Cleodrane derivatives [(5R, 10R)-4R-8R-dihydroxy-cleroda-13(16), 14-dieno-17, 12S:18, 1S-dilactone], columbin tinosporides, tinosporin, and jateorine are also found in the whole T. cordifolia plant. The physiological activities they showed were vasorelaxant, anti-inflammatory, anti-microbial, anti-hypertensive, and anti-viral. 27-31 Steroids (B-sitosterol, -sitosterol, 20-hydroxyecdysone, giloinsterol, Makisterone A, and Ecdysterone) are present in the shoot section of T. cordifolia. They are successful in treating early inflammatory arthritis's glucocorticoid-induced osteoporosis. By the reduction of c-Myc, they cause cell cycle arrest in the G2/M phase and inhibit TNF-, IL-1, IL-6, COX-2, and apoptosis. [48-49]

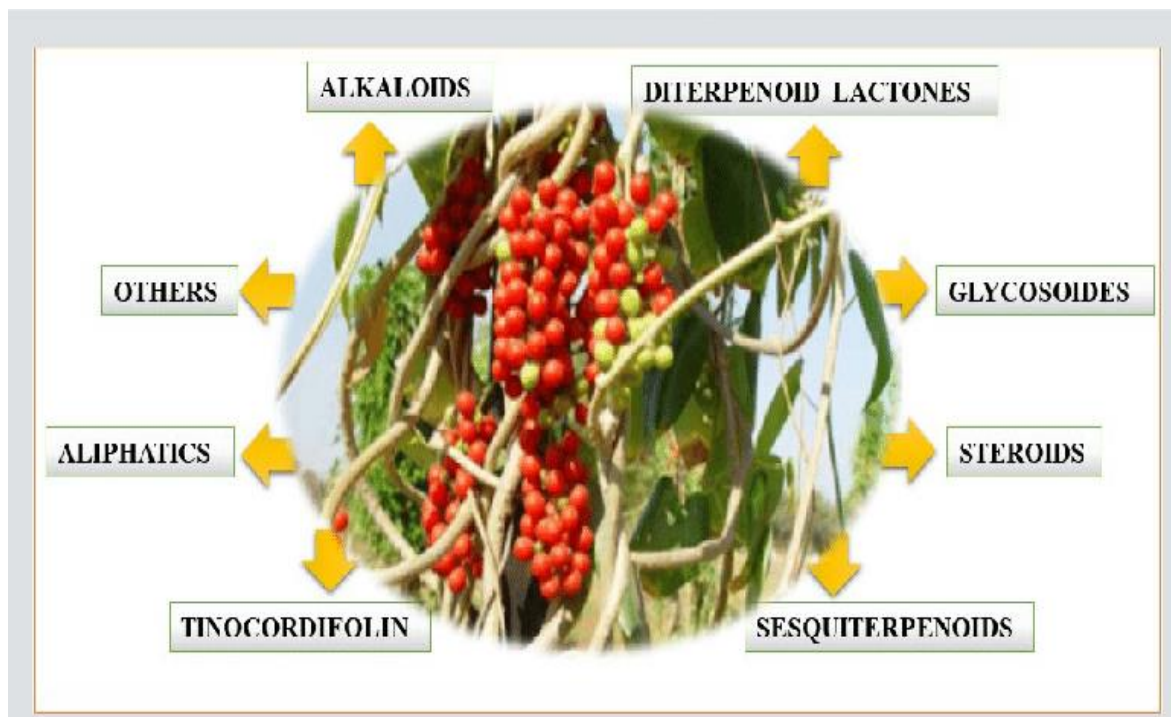
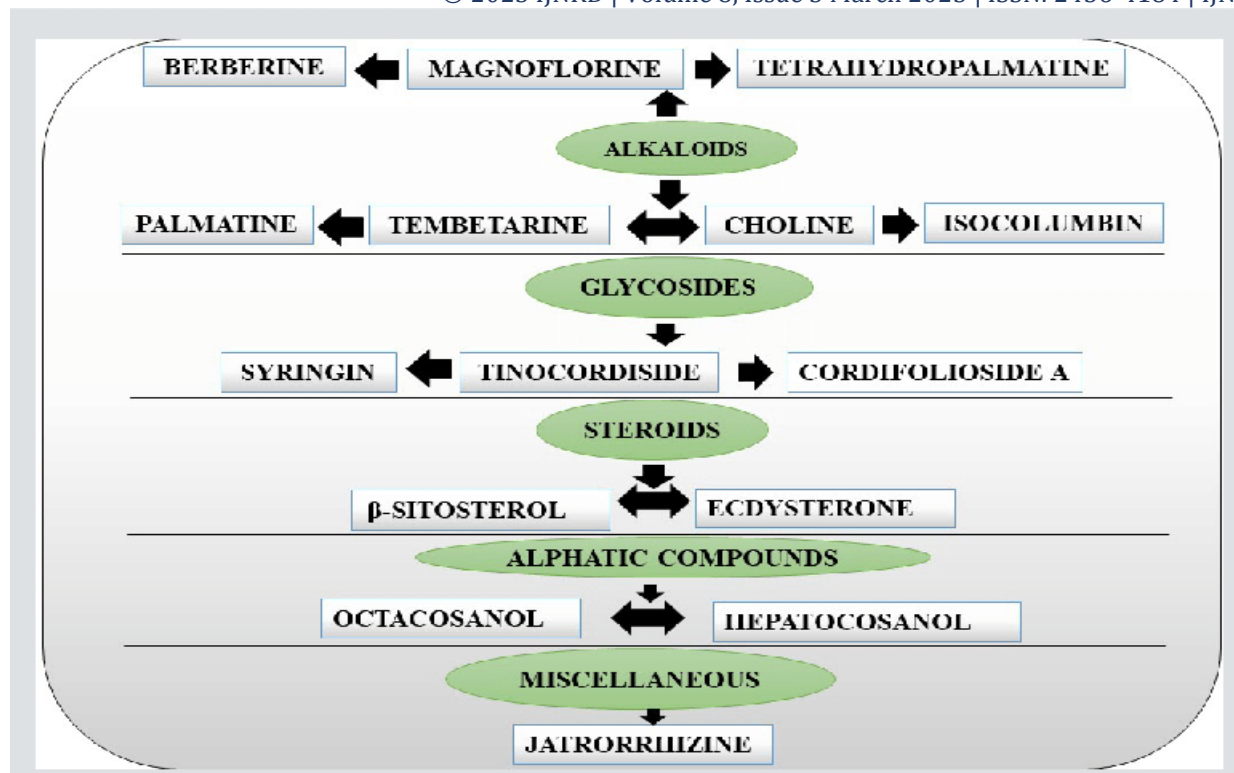


Figure 3: Active Compounds of T. Cordifolia



Glycosides are detected in the stem of *T. cordifolia*. These contain the following active components: 18-norcleodrane glucoside, Tinocordifolioside, Cordioside, Cordifolioside A, B, C, D, and E, Furanoid Diterpine Glucoside, Syringin, and Pregnane Glycoside. Apiosylglycoside and palmatoside syringin. In neurological disorders such as ALS, Parkinson's disease, dementia, and motor and cognitive disorders, immunomodulation was established. To show anti-cancer properties, they inhibit NF- κ Band. [50-52] The whole *T. cordifolia* plant is made up of aliphatic compounds. Octacosanol, Nanocosan15-1 dichloromethane, and heptacosanol are the active components. They had anti-inflammatory and antinociceptive activity. They also inhibit TNF- from binding to DNA and protect rats against Parkinsonism brought on by 6-hydroxydopamine. [53] Sesquiterpenoids and Tinocordifolin, that have antibacterial effects, are found in the stem of *T. cordifolia*. 45 Some *T. cordifolia* sections also contain active compounds including Jatrorrhizine, Tinosporic Acid, 3, (a, 4-di hydroxy-3-methoxy-benzyl)-4-(4- hydroxy-3-methoxy-benzyl) tetrahydrofuran, N-trans-feruloyltyramine as diacetate, Giloin. They showed a protective effect against HIV (human immunodeficiency virus).[54,55] The chief Phytoconstituents of *T. cordifolia* are diterpenoid furano lactone, cordifolide, cordifol, heptacosanol, tinosporide, β -sitosterol, tinosporine, clerodane furano diterpine, tinosporaside, and columbin respectively (Figure 3). Alkaloids such as magniflorine, Berberine, palmatine, non-glycoside giloin, gilosterol, tembertarine, choline and tinosporin has been reported from the stem part of the *T. cordifolia*. [56]

CONCLUSION-

T. cordifolia is a resourceful plant that provides countless biological effects. chemicals that are active and that have been indicated to have therapeutic potential. There are reports in pharmacological and clinical trials which show the healing and regenerative properties of this plant in treating a number of illnesses. The various bioactive substances, including as sesquiterpenoids, alkaloids, steroids, glycosides, and others, have been found to have potential applications, particularly as immunotherapy and antioxidants. *T. cordifolia* is an outstanding medication that hasn't yet been found to have any negative or toxic side effects, based on the many studies that have been done on it.

In conclusion, this review provides detailed information on the natural anti-toxin, antidiabetic, anticancer, immunomodulatory, antioxidant, and antibacterial activity of *T. cordifolia* and can be applied to future research investigations in the creation

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