A Clinical Approach of the Aerial Parts of Tinospora Cordifolia as an Anti-Inflammatory and Other Medicinal Properties

Harshit Goel[1], Dr. Neeti Srivastav[2], Dr. Shalini Sharma[3]
[1]*Research Scholar, Sunder Deep Pharmacy College, Dasna, Ghaziabad 201015, U.P, India*
[2]*Associate Professor, Sunder Deep Pharmacy College, Dasna, Ghaziabad 201015, U.P, India*
[3]*Director, Sunder Deep Pharmacy College, Dasna, Ghaziabad 201015, U.P, India*

Abstract **- This review article focuses on the anti-inflammatory and other properties of the *Tinospora cordifolia* with special emphasis in colitis and inflammatory bowel disease. *Tinospora cordifolia* belongs to the family Menispermaceae, generally known as Giloy. The treatment of the colitis is based on the pathogenesis of the disease. Now days, herbal based treatments are popular because of its improved drug delivery and potential efficacy. *Tinospora cordifolia* possess various properties such as anti-inflammatory, anti-spasmodic and anti-viral because of the certain phytochemicals i.e. alkaloids, terpenoids, lignans to be precisely. This study will encompass the clinical advantages of the *Tinospora cordifolia* as anti-inflammatory drug in mainly colitis. The future scope in the continuation of the research on this topic may cover the signaling involves in the colitis and IBD.**

Index Terms **- Colitis, *Tinospora cordifolia,* inflammatory bowel diseases.**

INTRODUCTION

Tinospora cordifolia popularly known as Giloy belongs to the family Menispermaceae is a plant or shrub used to climb on the other shaded trees [1]. *Tinospora cordifolia* is broad leaved plant with the diverse potential characteristics, blossom yellow flowers, and usually grow at the typical higher altitude. The flowers used to be cultivated in both the seasons - winter and summer. The variety of the active phytochemical used to find in the various parts (roots, stem, leaves, and shoot) of the plants such as steroids, alkaloids, terpenoids, and aliphatic compounds [2].

Natural resources such as plant are considered as the medicinal treasure for the Ayurveda. These plants are gaining attention towards the importance of their own medicinal properties [3]. These herbal plants are the most desirable topic for the researcher as they have insignificant side effects along with remarkable clinical bioavailability. As per literature, *Tinospora cordifolia* possess the various features for example anti-inflammatory, anti-spasmodic, antioxidants [4].

The plant is widely available in India and is cultivated as temple garden plant. The fruit of the tree has certain medicinal uses and also been used for eating. The leaves are believed to have anti-inflammatory, anti-spasmodic, anti-allergic, antioxidant and anti-pyretic activity.

Botanical Name: *Tinospora cordifolia*
English Name: Guduchi/Giloy
Family: Menispermaceae
Parts of Plant used: Leaf, Fruit, Root, Bark
Cultivation: All over India [5]

Tinospora species are known for its tender woody texture generally used to climb over the shaded tree with the help of the tendrils. Leaves are oval in shape, broad leaved, dentate margin, basal and lateral veins and usually elongated in size of 3-6 and 1-3 respectively. Male flower and female flower consist of six sepals, in two series, outer series smallest. Flowers blossom in the winter and summer [6].

Phytochemical Profile

A wide variety of the phytochemicals are available in this plant and parts of the plant. The plant extract is studied by different methods to identify the phytochemicals. The phyto-chemical constituents belong to different categories of the chemicals classes such as alkaloids, glycosides, steroids, phenolic, aliphatic compounds, polysaccharides. It has been reported that the leaves are rich in protein (11.2%), calcium and phosphorus. The basic structures and

fundamental procedure of finding the chemical structures are mentioned in the literature [7]. These phytochemicals have series of positive effects in certain kind of diseases. However, clinical studies have been identified the course of action and pathways to treat the disease by these phytochemicals [8].

Tests for Carbohydrates using Benedict's test

The extract of the seeds were dried and stored at room temperature. The extract was poured in the sample collector and added 2ml of Benedict's reagent. The test tube was then boiled on the flame for few minutes. Upon boiling the solution turned in to reddish brown color sediment. This is the indication of carbohydrate [9].

Test for reducing sugar

The extract was shifted in the closed tube and mixed with the water. After filtration with the whatman paper, the filtrate was again shifted in the test tube. On the filtrate Fehling's solution A and B was added drop by drop. When the reaction stops an orange to yellow color appear which identify the presence of reducing sugar [9].

Tests for Amino Acids using Ninhydrin test

Formulated extract was added in the closed test tube and then 3 mL water added. 5% Ninhydrin solution was prepared in the separate tube. In the solution, reactor solution was added drop by drop. After few minutes the reaction stops and produces the blue color, which confirm the presence of amino acid [10].

Tests for Proteins using Biuret test

In the test tube, the crude drug was added along with the 3 mL of 4% NaOH and 1% CuSO4. When color changes to pink, it indicates the presence of the protein[11].

Tests for Vitamin C

To perform the presence of Vitamin C, the crude drug was mixed with the 5 mL of water in the test tube. Sodium nitroprusside was added to the tube drop by drop and along with it sodium hydroxide solution was added. After this 600 microliters of HCl was added to the solution in the test tube. The solution color turns yellow once reaction is completed, indicating the presence of Vitamin C [12].

Tests for Chloride

The crude drug extract was prepared using nitric acid (3mL). To the solution silver nitrate added drop by drop. After reaction stops it give colorless precipitate which identifies the silver chloride [12].

Tests for Tannins

Crude drug solution was taken in the test tube. Onto the solution 5% $FeCl_3$ was added slowly. The color changes to black indicating the presence of tannins[12].

Tests for Alkaloids using Wagner's test

The crude drug filtrate was taken in to the test tube. On to the solution, Wagner's reagent was added drop by drop. The solution color changes to reddish brown that shows the presence of the alkaloids [13].

Tests for Steroids

Crude drug sample was taken in the test tube, to the sample 2 ml chloroform and 2 ml concentrated H_2SO_4 was mixed drop by drop. After the reaction is completed the ring is observed that confirms the presence of Steroid [13].

Table- 1: Phytochemicals Present in *Tinospora Cordifolia* [14]

S.No.	Phytochemical Constituents
1	Carbohydrates
2	Proteins
3	Amino acids
4	Steroids
5	Glycosides
6	Saponins
7	Flavonoids
8	Alkaloids
9	Tannin
10	Phenolic

Table- 2: Chemical Constituents of *Tinospora* Cordifolia [15]

Sn	Chemical Name	Active Principles	Part in which present
1	Alkaloids	Berberine, Palmatine,	Stem
		Tembetarine, Magnoflorine, Choline, Tinosporin, Isocolumbin, Palmatine, Tetrahydropalmatine, Magnoflorine	Root

2	Glycosides	18-norclerodane glucoside, Furanoidditerpeneglucoside, Tinocordiside, Tinocordifolioside, Cordioside, Cordifolioside A, Cordifolioside B, Syringin, Syringin-apiosylglycoside, Palmatosides C, Palmatosides F, Cordifoliside A, Cordiofoliside B, Cordifoliside C, Cordifoliside D, Cordifoliside E	Stem
3	Diterpenoid lactones	Furanolactone, Clerodane derivatives and [(5R,10R)-4R-8R-dihydroxy-2S-3R:15,16- diepoxy-cleroda-13 (16), 14-dieno-17,12S: 18,1S-dilactone] and Tinosporon, Tinosporides, and, Jateorine, Columbin	Whole plant
4	Steroids	β -sitosterol, δ-sitosterol, 20 β-Hydroxyecdysone. Ecdysterone, Makisterone A, Giloinsterol.	Aerial part & Stem
5	Sesquiterpenoid	Tinocordifolin.	Stem
6	Aliphatic compound	Octacosanol, Heptacosanol,	Whole Plant

Pharmacological Profile

Anti-inflammatory

Vineetha, V. P., et al, 2021, identified that the extract of the T. *cordifolia* and introduced in the animals which were having the paw edema. This study was performed in the rats and edema was induced with the help of the carrageenan. The carrageenan experiment was done along with the important parameters i.e. rota rod and Cold hyperalgesia. This model is based on the fluid accumulation, when cells are injured, the area of the injury gets accumulated by the blood and other vital fluids. The inflammation and redness can be seen at site of the injury because of the fluids only. The methanolic extracts were prepared and administered in the animals at three different doses (low, mid and high) along with the reference control and negative control [16].

The recovery period was identified as the increase in the locomotors activity and reduces the inflammation. The paw edema score was significantly reduced in the T. cordifolia group, although, other groups of the plant was less significant than the high dose but comparable to the controls animals [17].

Anti-Inflammatory activity by paw size observation

Test was carried out in five groups, from which group 1 was considered as control and group 5 was considered as standard and rest other were named as TC-100, TC-200, and TC-300. The fifth group contains aspirin 150mg/kg. After 30min, in the right paw carragean was administered, and then paw size was evaluated by using Vernier Caliper at intervals of 1, 2, 3 and 4 hours [18]. The evaluated results revealed approximate value of paw size from different group. TC-100 showed 0.695 mm, 0.5825 mm, 0.585 mm and 0.56 mm at 1-, 2-, 3- and 4-h intervals respectively. TC-200 showed 0.69, 0.56, 0.51 and 0.457 mm at 1-, 2-, 3- and 4-h intervals respectively. TC-300 group observed 0.73, 0.5025, 0.4050 and 0.3175 mm at 1-, 2-, 3- and 4-h intervals respectively [19].

Acetic acid-induced writhing test for analgesic activity

Analgesic activity was evaluated by analyzing the writhing response of mice through the intraperitoneal insertion of acetic acid. In this study, total 40 healthy animals were selected for the different groups such as negative control, positive control and test groups. After 5 min of administration of acetic acid, animals were isolated in separate cages and writhing response was evaluated in cumulative way for 10min [20]. It was observed that from all extracts, the hexane extract was the most promising. At a dose of 400mg/kg, it showed 56.28% inhibition [21].

Extract of T. cordifolia in Anti-inflammatory models (Alcoholic and Aqueous)

In models of acute and sub-acute inflammation, the alcoholic extract *of Tinospora cordifolia* has been reported to have anti-inflammatory properties. In a dose of 50 mg/100 g given orally and intraperitoneally, the aqueous extract of the stem effectively reduced the acute inflammatory reaction elicited by carrageenan [22]. It also reduced the development of antibodies against the typhoid "H" antigen. Another study found that an aqueous extract of *T. cordifolia* had a significant anti-inflammatory effect in the cotton pellet granuloma and formalin induced arthritis models; the effect was comparable to indomethacin,

and its mode of action appeared to be similar to that of a nonsteroidal anti-inflammatory agent [23].
In both acute and sub-acute inflammation models, the dried stem of *T. cordifolia* had a strong anti-inflammatory effect. The plant was found to be more efficacious than acetylsalicylic acid in acute inflammation, but inferior to phenylbutazone in subacute inflammation [24].

Aqueous extract of T. cordifolia

T. cordifolia has anti-gingival properties due to its anti-inflammatory properties. Further it has been shown has been shown that during animal studies it possessed anti-inflammatory properties. According to one study, aqueous extract of *T. cordifolia* proved efficient in preventing oedema formation [25]. During the early stages of inflammation, the mechanism of action was to block the actions of histamine and 5 HT. *T. cordifolia* stems contain a variety of compounds that have anti-inflammatory properties. Alkaloids, glycosides, diterpenoid lactones, steroids, and aliphatic chemicals are all important anti-inflammatory substances in humans. Interleukin 1, β.Interleukin 6, and COX-2 inhibitors are all inhibited by steroids [26].

Anti-inflammatory Mechanism of action

Stabilization of lisosomes

Anti-inflammatory drugs work by stabilising the lysosome membranes, which regulates the metabolic activities that occur during the inflammatory response. These chemicals are renowned for their ability to block the release of phospholipases, hence preventing tissue injury. In the experiment used in this study, the RBC membrane is comparable to the lysosomal membrane [27]. RBCs lysis occurs when they are exposed to a hypotonic solution. The addition of *Tinospora crispa* extracts, on the other hand, considerably reduced hemolysis. This finding supports membrane stability as a plausible mechanism for the extract's anti-inflammatory properties [28].

LPS-activated THP-1 cells

LPS-activated THP-1 cells were used to test the anti-inflammatory impact of *T. cordifolia* (Willd.) Miers dry leaf extracts. Lipopolysaccharide is a gram-negative bacterium endotoxin that causes inflammation by attaching to the toll-like receptor-4 (TLR-4) and then upregulating the NF-κB signalling pathway by proteosomal degradation of the inhibitory subunit of the heterodimeric NF-κB protein in the cytosol [29]. This increases nuclear translocation, where it binds to the promoter region of proinflammatory mediators like TNF-α. The presence of these and other mediators in the blood vessel wall leads to the onset of a variety of chronic inflammatory disorders. The inhibitory activity of *T. cordifolia* was investigated in this study [30].

COX-2 Inhibition

This research has extracted that *T. cordifolia* possess anti-inflammatory activity as it can block the COX-2 inhibitors. This claims that the plant possess selective inhibitory characteristic. *T. cordifolia* improved the potential of being selective inhibitors which is a potent analgesic and anti-inflammatory herbal drug [31]. Macrophages stimulated with bacterial lipopolysaccharide (LPS) are a good in vitro model for testing herbal items' anti-inflammatory properties. Formulations that modify the production of LPS-inducible cytokines could be exploited to produce new medications to treat diseases characterised by uncontrolled macrophage activation [32].

Antioxidant activity

Arunachalam, K., et al., 2021, has developed a formulation of *T. cordifolia* to reduce the superoxide ions from the cells and to probe the activity of this formulation, free scavenging method was followed. They identified that DPPH (1-diphenyl-2-picrylhydrazyl) activity was higher and also observed that the inhibitory effect was maximum at a concentration of 5µg/ml, which was comparable to control values [33].
The identification of the total flavonol and phenolic content concentration was identified as maximum which possess antioxidant property. Also reported that hydro-alcoholic extract of the *T. cordifolia* possess the antioxidant activity which can reduce the superoxide dismutase to minimum concentration [34].

Antimicrobial activity

Prajwala, B., et al., 2021 have identified that *T. cordifolia* showed antimicrobial activity in its methanolic extract. They performed the experiment in *in -vitro* to see gram positive bacteria activity in the presence of the proper nutrition. The gram-positive bacteria was grown in the nutrient broth and plated on

to the agar plate [35]. After the exposure of the test item, the result has been analyzed. In this experiment the plant extract showed excellent results which support the antimicrobial activity [36]. In the continuation to this Mittal, J., Pal, et al., 2021, has identified the antimicrobial potential on the different anaerobic bacteria [37].

These bacteria were grown in the sterile environment and exposed to the plant extract, which followed by the different concentrations of the plant extract. The results were enough convincing to identify this plant as the antimicrobial. Duhan, P., et al.,2021 have reported the enormous potential to kill the bacteria in the agar plate [38].

This experiment was conduct with *S. typhi* strains. The strains of the *S.typhi* were grown to the late exponential stage and plated on the agar plates. The colonies were counted against the background lawns. The colonies were counted and compared with the negative controls and reference controls for the analysis purpose. The result showed that the *T. cordifolia* inhibit the growth of the bacteria [39].

Anti-diabetic activity

Kumar, V., et al, 2021 explained that the anti-diabetic activity of the plants due to the phytochemicals such as alkaloids, tannins, cardiac glycosides, flavonoids and, saponins, etc. They identified that the plant possessed the anti-diabetic activities because of its ability to bind and reduce the activity of the alpha-glucosidase enzyme in the pancreas [40].

Tinospora cordifolia extract was prepared in water and the study was performed in the Wistar rat. The water extract was able to bind and reduce the activity of the glucose, insulin, and triglycerides.

The same experiment was performed without water by B., Rasane, P., &Bajpai, V. K. (2020) prepared the extract in the alocohol and found that the level of glucose was coming down. They have identified the pre and post glucose levels were low to normal [41].

Another study was performed by the Mandar, B. K., et al, 2021, in the diabetic rats. They have identified the *Tinospora cordifolia* extract could easily bind the insulin and reduce the glucose level in just 30 days. The obtained results identified the efficacy was almost 50-60%. No mortality and morbidity was recorded during the experimental period [42].

Anticancer activity

Patil, S., et al., 2021 have performed the experiments with the *Tinospora cordifolia* extract in methanol. The model was performed with the help of the 7, 12-dimethyl-benz (a)anthracene DMBA. Th extract was given them by oral route at the different concentrations. Low, mild and high dose was performed well in the experimental period. The skin cancer was reduced to 40% when compared to the other control groups of the animals. At the high dose 600mg/kg have worked well in comparison to the other concentrations of the drug [43].

Another study was performed by the Pant, C., et al., 2021 in the athymic mice. The animals were introduced the cancer by MG 87 cells in the mid brain. The cells were grown in the DMEM medium and at the density of the 10^6 were introduced in the brain. The ethanolic extract of the *Tinospora cordifolia* was able to control and decrease the size of the brain tumor and increase the quantity of the glial cells in the brain [44].

Anti-HIV activity

Kumar, P., et al, 2020 confirmed in his research that clinical evidence proved that the *T. cordifolia* root extract has potential to retain the level of the lymphocytes and macrophages in the blood. It has the potential to increase the level of the hemoglobin, and polymorphonuclear leucocytes [45].

Wound healing

Singh, A. K., et al, 2017 proved in his research that the potential of the wound healing is enormous in the extract of the *T. cordifolia*. The result were convincing when compared to the other groups. It increased the healing process and collagen strength. The collagen fibers started to regenerate and also increased the tensile strength of the tendon and other joints. From this study, it was claimed that it may alter the decorin and fibrin protein bonding [46].

Anti-osteoporotic effects

Munshi, R., et al, 2019 demonstrated that the *T. cordifolia* extract enhanced the role of the minerals and other proliferative bone matrix like structures. It regenerated the matrix by helping to stimulate the growth of the osteoblasts. Additionally, the cartilage strength of the joints was increased [47].

CONCLUSION

T. cordifolia is a herbal plant which possesses all the required characteristics to fall in the medicinal plant family. With the help of the phytochemical properties it is been identified and proved that this plant can treat various diseases. As per literature review it has been identified that *T. cordifolia* can act as anti-inflammatory, antioxidant, antimicrobial, antibacterial, anticancer, hypolipidemic, in the treatment of hepatic disorder.

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