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Review Article

Immunomodulatory activity of *Tinospora cordifolia*

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ABSTRACT

Guduchi also known as *Tinospora cordifolia* , having heart shaped leaves, belongs to family Menispermaceae native to Indian subcontinent. The aqueous and methanol stem extract of *Tinospora cordifolia* is being used for their Immunomodulatory activity as they revive immune imbalance which helps in preventing and healing many diseases. *Tinospora cordifolia* is intensively being studied for its immunomodulating effects because of its wide-ranging uses in treating diseases related to immune system in indigenous medicine. Various clinical trials for the treatment of *Salmonella typhimurium*, HIV infection and other viral infections with TC is scientifically evaluated. In such conditions effective immune system is needed for curing the disease. *T. Cordifolia* has been proved for its ability to activate and modulate the immune system. Present paper is an attempt to assemble the information based on several experimental and clinical reports on immunomodulating role of *Tinospora cordifolia.*

1. Introduction

The human immune system is well organized comprising of many different immune cells like macrophages, neutrophils, T-lymphocytes, natural killer cells and various other specialized immune molecules like cytokines and antibodies that have evolved to mediate resistance against infections. Extensive use of antibiotics in infectious diseases, causes an emergence of multidrug-resistant strains of many pathogens that are posing serious challenges. There is a need to find suitable replacements for some of the currently used antibiotics.[1] Medicines from ayurvedic plants are believed to promote good health and preserve organic resistance against infection by restoring body balance and conditioning the body tissues. Bioactive phytochemicals which include lignans, flavonoids, terpenoids, alkaloids, polyphenols, coumarins, saponins, tannins present in herbs can enhance immune system. *Tinospora cordifolia* (TC) is a valuable plant found to be a perfect immune-stimulatory herb.[2] Apart from the normal anti-bacterial, anti-viral, anti-cancer, properties, and various health benefits, *T. cordifolia* exhibits immune-stimulatory efficiency by augmenting macrophage chemotaxis, phagocytosis and promotes interaction with other immune-regulatory lymphoid cells.

Taxonomical classification	
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Ranunculales
Family	Menispermaceae
Genus	*Tinospora*
Species	*Cordifolia*[2]

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Table 1: Vernacular names of TC [2]

Languages	Vernacular name
English	Tinospora
Kannada	Amrutha balli
Punjabi	Gilo
Oriya	Guluchi
Marathi	Gulvel
Malayalam	Chittamrutu
Kashmiri	Amritha, Gilo
Bengali	Gulancha
Sanskrit	Chakralakshanika
Hindi	Gurcha
Gujarati	Garo, Galac

Table 2: Morphological description [2]

Plant parts	Morphological description
Stem	Large climbing, deciduous ascending shrub with greyish brown-black colour, soft wooded, dry, cylindrical and circumference range from 5 mm to 25 mm.
Root	Long filament like fleshy aerial roots arise from branches.
Leaves	Simple, 5-10 cm long, exstipulated, alternating, long petiolate (2.5 - 7 cm), rounded chordate with reticulated midrib.
Flower	Yellow or yellow-greenish, and small. The male flowers are clustered in adjunct and racemose panicles, while the female flowers are usually solitary.
Fruit	The fruits are in aggregates of 1 to 3 and present as orange and ovoid smooth drupelets on a thick stalk with border sub-terminal form and had coloured scarlet.
Seed	Curved seed, recognized as the moonseed family, known as "heart leave moonseed". As the seeds are curved in shape, the embryo also turned into curving form.

1.1. Chemical composition of T. cordifolia

T. cordifolia contain many constituents which have been isolated and elucidated. They are diterpenoid lactones, phenolics, alkaloids, steroids, polysaccharides, glycosides, aliphatic compounds, and sesquiterpenoids. Diterpenoid lactones have anti-inflammatory, antioxidant and neuroprotective activity. Steroids used to treat rheumatoid arthritis, inflammatory bowel disease and asthma. Alkaloids used as anaesthetics and cardioprotective agent. Sesquiterpenoids and glycosides are used in cardiovascular disease and in antimalarials. [2]

2. Immunomodulatory Activity

Tinospora cordifolia due to its potential in improving the immune system and the body resistance against infections it has been extensively used in Ayurveda. Arabinogalactan polysaccharide (G1-4A) which is a compound found in *T. cordifolia's* stem. It has protective action against lipopolysaccharide-induced endotoxic shock by modulating cytokines and nitric oxide excretion by murine macrophages. Immunomodulatory active components present in *T.cordifolia* are N-methyl-2-pyrrolidone, N-formylannonain, 11-hydroxymustakone, cordifolioside A, tinocordiside, syringin, and magnoflorine have been reported for their ability to regulate the immune system. [2]

In mice, it has been studied and reported that the extract of T. cordifolia can upregulate the cytokine IL-6, with subsequent events that include activation of the inflammatory response and cytotoxic T cells as well as differentiation of B cells. Further it has been investigated on rats suggested that there is a cytotoxic effect of the active compounds, including compounds in aqueous extracts, such as alkaloids, glycosides di-terpenoid lactones, phenolics, steroids, aliphatic compounds, sesquiterpenoids, and polysaccharides. And studied that, the alpha-d-glucan derived from *T. cordifolia* was able to activate human lymphocytes and down regulate the production of inflammatory mediators. [3]

3. Pharmacological Activities of Tinospora Cordifolia

3.1. In-vitro studies

Extracts of TC has been found to enhance lysosomal secretion in several cell lines. TC powder (80 μg/ml) showed enhanced secretion of lysosome by macrophage cell line J774A according to different time intervals (24 & 48 h) this was due to activation of macrophage by immunomodulator. Production of nitric oxide and lysosome shows one of the main microcidal mechanisms of macrophage.

Apart from being immunomodulator, TC extracts (dry stem, 500 μg/ml) also enhanced antioxidant defences

Table 3: Chemical compositions of the *Tinospora cordifolia* herb [2]

Type of Chemical	Plant Parts and Active Compounds				
	Stem	**Leaves**	**Roots**	**Whole Plant**	**Other Aerial Parts**
Alkaloids	Mangoflorine, Berberine, Palmitine, Tembatartine, Choline Tinosporin	Tinosporin, Tinosporic Acid.	Tembatartinemang oflorineCholine Tinosporin Isocolumbin Tetrahydro Palmatine	Tinosporic Acid	-
Glycosides	18 Nonderodane Glycoside, Furanoid diterpene Glycoside, Tinocordiside Tinocordifoliside, Cordioside, Cordifolioside A, B, C, D, Syringin, Syringinapiosyl Glycoside, Palmatosides C & P, Cordifoliside A, B, C, D, E.	-	-	-	-
Diterpenoid	Diterpenoid Tinosporon Columbin	-	-	-	-
Diterpenoid Lactones	Diterpenoid, Tinosporon Columbin	-	Jatrorrhizine	Clerodane Derivatives, P, Tinosporisides, Jateorine, Columbin, Tinosporal, Tinosporide	-
Steroids	Sitosterol, Octacosanol, Heptacosanol, Nonacosan-15-One, Tetrahydrofuran, Hydroxyecdysone, Makisterone A, Giloinsterol, Ecdysterone.	-	-	-	Sitosterol Hydroxyecdysone
Sesqui-Terpenoi	Einocordifolin	-	-	-	-
Miscellaneous Compounds	Arabinogalactan	-	Jatrorrhizine	Tinosporidin , Cordifol, Cordifelone, Giloin, Giloinin	-

Table 4: Immunomodulatory activity of *Tinospora cordifolia* in vitro.

Sl. No.	Model	Treatment	Result	Ref
01	Macrophage J774 cell line (Balb/C mice) Ecoli	80 ug/ml of TC	↑Zone of inhibition ↑Lyzozome ↑NO	[5]
02	Liver & Spleen homogenates C3H mice (8 -12 wk) 100μg peroxynitrite	500 μg/ml Methanol extract of TC	↓TBARS, ↑SOD, ↑Catalase ↑LOOOH	[4]

(increased SOD and Catalase) and decreased oxidative damage (reduced TBARS) in liver and spleen homogenates isolated from 8-12 week old CH3 mice,[4]

3.2. Animal studies

Upadhyaya and co-workers studied the effect of aqueous (Aq.) extract of *T. cordifolia* on B16F10 mice (at a dose of 1 mg/kg) helped in boosting of phagocytic activity of macrophages by increasing the production of NO from peritoneal murine macrophages. NO is the key molecule in the regulation of immune response and this further strengthens the role of macrophage in producing NO by direct lysis of B16F10 melanoma cells in vitro.[6]

Alsuhaibani and co-workers studied AECT and MECT of *T. cordifolia* on BALB/C mice (murine macrophage cell line J774) infected with Salmonella typhimurium (at a dose of 100 mg/kg orally for 7days). Result was measured by zone of inhibition, which showed anti-salmonella activity of methanol extract was higher as inhibition zone was 12 mm, where as in aqueous extract treated mice it was just 5 mm. However, macrophages treated with aqueous and methanol extract secreted greater levels of IFN-y, TNF-α, and IL-6 and thereby reduced the bacterial load.[7]

Bishayi and co-workers studied the effect of Aq. extraction *T. cordifolia* on adult male albino rats (at a dose of 100 mg/kg body weight for 15 days) had deleted the immunosuppressive effect (decreased phagocytic capacity, chemotactic migration and cell adhesiveness) of CCl4 intoxication because of significant increment in the functional capacities of rat peritoneal macrophages. SGOT, SGPT, SALP and bilirubin level will be decreased nearer to normal level as they were increased in CCl4 intoxication.[8]

Aranha and co-workers studied the effect of Aq. extract of *T. cordifolia* which was subjected to protein precipitation on BALB/c mice (at a dose of at 30 μg on days 1, 14, 21, 28, 35 and 42 through nostril) showed increase in body weight ($p<0.005$) on day 50 compared to day 1 in test group, thus showed humoral immune response (serum IgG and IgA increased) and indicated its intrinsic immunogenicity.[9]

Sachan and co-workers studied the Immunomodulatory potential of Aq. extract of *T. cordifolia* on (SPF) chicks infected with very virulent IBDV (vvIBDV) (at a dose of 50 μg/bird/day via intramuscular injection and 10 ml/bird/day orally for 4 weeks). It showed significant increase ($p < 0.05$) in immune response genes in PBMCs like IL-2 (5.657 _ 0.1663), IFN- (15.15 _ 0.2288), IL-4 (8.458 _ 0.277), and IL-1_ (13.09 _ 0.2681) expressions in chicken PBMCs compared to the control group as these were decreased in infection by virus.[10]

Ranjith and co-workers studied the effect of Aq. extract of *T. cordifolia* on Wistar rats (150-200g of body weight) (at a dose of 10 mg/kg body weight for 14 days) significantly increased the antibody production against SRBC. Even at a concentration of 5 microgram/ml showed.

3.3. Human studies

Sharma and co-workers studied how *Tinospora cordifolia* enhances immunity in children. Shade dried *T. cordifolia* plant powder was administered orally to 200 children of age 1-15 years (at dose of 100 mg/kg bw twice daily after food with honey for 60 days). There was a significant increase in TLC, ALC and lymphocyte percentage on 30^{th} day ($p<0.05$) as well as 60^{th} day ($p<0.001$) as compared to 0^{th} day and test group. They concluded that T. cordifolia can be used as adjuvant to vaccination in order to boost the immune system.[12]

Castillo and co-workers studied the effect of *T. cordifolia* lotion on Paediatric patients diagnosed with scabies caused by *Sarcoptes scabiei*, by applying on skin. Then the analysed peripheral blood samples collected from anticubital vein from 0^{th} day, 14^{th} day and 28^{th} day showed the decrease level of interleukins at 14^{th} and 28^{th} day compared to control (IL-1, IL-6 & IL-8)y) and nearer to normal level. These interleukins serve as inflammatory agent inducing the production of acute phase and complement protein by hepatocytes.[13]

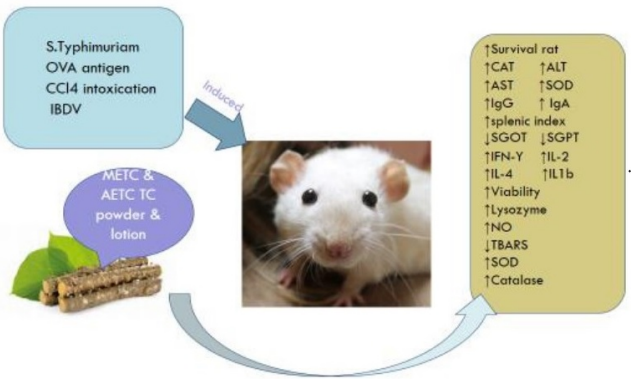

Fig. 1: Mechanism of Immunomodulatory activity of *Tinospora cordifolia.*

4. Conclusion

A number of studies substantiate immunomodulatory activity of *Tinospora cordifolia.* Above discussed studies showed that how the aqueous and methanol extracts of *T. cordifolia* which contained active compounds in the form of alkaloids, glycosides, lactones and steroids have increased immune response and phagocytic activity. And also, these extracts fight against infections like in salmonellosis[7] and IBDV[10] by increasing interleukins level. Above studies also suggested to use *T. cordifolia* as vaccines in children[12] Glycoproteins present in aqueous extract of T. cordifolia stem acts on macrophages and stimulates the production of effector molecules like nitric oxide and cytokine mediators and in augment the antigen specific

Table 5: Immunomodulatory activity of *Tinospora cordifolia in animals.*

	Model	Treatment	Result	Ref
01	Balb/C mice	AETC: 1 mg/kg i.p	↑NO	6
02	Balb/C Mice (2 wk) 5×10^5 viable S. typhimuriam bacteria intravenously.	METC :100 mg/dayOral 7 days	↑Survival rate ↑ CFU, ↑ALT, ↑ AST ↑ SOD, ↑CAT	7
03	Albino rats (♂) CCl_4 (0.7 ml/kg bw) 7 days	AETC : 100 mg//kg bw Oral 15 days	↓SGOT, ↓SGPT ↑SALP ↑Phagocytic capacity	8
04	Balb/c Mice (n=6)	Ova 30 ug + Guduchi (60 ug) days 1, 14, 21, 28, 35, & 42 intranasal	↑Serum IgG ↑Splendic Index Ig A V	9
05	Spf Wl Birds (3 Wks) (n=20) virulent strain of IBDV was introduced to 10 day old SPF embryonated chicken eggs intra membrane	AETC: 10 ml/day Oral 28 days	↑IFN-Y ↑IL-2, ↑IL-4 ↑IL-1b	9
06	Wistar rats (150-200 g) (n=6) 0.5×10^9 cell/ml of SRBC injected after 14 days of treatment	AETC :- 10 mg/kg bw 14 days	↑Antibody production	11

Table 6: Immunomodulatory activity of *Tinospora cordifolia* in humans.

Sl. No.	Model	Treatment	Result	Ref
01	Children (1-5 yr) , (♂ ♀) (n=200)	TC powder 100 mg/kg bw twice a day 60 days	↑TLC ↑ALC	12
02	Pediatric patients with sacoptes scabies mite (2-22yr) (♂ ♀) (n=30)	TC lotion (1 kg TC powder + 3L 80% ethanol) was applied neck to feet after bath for 14 days	↑IL-1 ↑IL-6 ↑IL-8	12

recall response, thereby enhances immune response.[6] *T. cordifolia* on (SPF) chicks infected with very virulent IBDV has decreased the infection[10] T. cordifolia lotion on Pediatric patients diagnosed with scabies caused by *Sarcoptes scabiei,* has reduced the infection by its anti-inflammatory activity when applied on skin.[13] *T. cordifolia* showed enhanced secretion of lysosome by macrophage cell line J774A according to different time intervals.[5]

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Srivastava AK, Singh VK. (GILOY): A Magical Shrub. *Asian J Adv Med Sci*. 2021;3(3):22–30.
2. Saeed M, Naveed M, Leskovec J, Kamboh A, Kakar A, Ullah I, et al. Tinospora cordifolia) as an eco-friendly feed supplement in human and poultry nutrition. *Poultry Sci*. 2020;99(2):801–11.
3. Sharma U, Bala M, Kumar N, Singh B, Munshi RK, Bhalerao S. Immunomodulatory active compounds from Tinospora cordifolia. *J Ethnopharmacol*. 2012;141(3):918–44.
4. Desai VR, Kamat JP, Sainis KB. An immunomodulator from Tinospora cordifolia with antioxidant activity in cell-free systems. *J Chem Sci*. 2002;114:713–9.
5. More P, Pai K. Immunomodulatory effects of Tinospora cordifolia (Guduchi) on macrophage activation. *Biol Med*. 2011;3(2):134–40.
6. Upadhyaya R, Paandey RP, Sharma V, Ankitha V. Assesment of the Multifaceted Immunomodulatory Potential of the Aqueous Extract of Tinospora cardifolia. *Res J Chem Sci*. 2019;1(6):71–9.
7. Alsuhaibani S, Khan MA. Immune-Stimulatory and Therapeutic Activity of Tinospora cardifolia: Double-Edge Sword against Salmonellosis". *J Immunol Res*. 2017;2017(9):1787803.
8. Bishayi B, Roychowdhury S, Ghosh S, Sengupta M. Hepatoprotective and immunomodulatory properties of Tinospora cordifolia in CCl4 intoxicated mature albino rats. *J Toxicol Sci*. 2002;27(3):139–46.
9. Aranha I, Venkatesh YP. Humoral immune and adjuvant responses of mucosally-administered Tinospora cordifolia immunomodulatory protein in BALB/c mice. *J Ayurveda Integrat Med*. 2020;11(2):140–6.
10. Sachan S, Dhama K, Latheef SK, Samad HA, Mariappan AK, Munuswamy P, et al. Immunomodulatory Potential of Tinospora cordifolia and CpG ODN (TLR21 Agonist) against the Very Virulent, Infectious Bursal Disease Virus in SPF Chicks. *Vaccines (Basel)*. 2019;7:6789546.
11. Ranjith MS, Singh AJR, Shankar SG, Vijayalakshmi GS, Deepa K, Sindhu H, et al. Enhanced Phagocytosisand Antibody Production by Tinospora cardifolia - A new dimension in Immunomodulation. *Afr J Bioitechnol*. 2008;7(2):81–5.
12. Sharma DN, Sharma A. Tinospora cordifolia Enhances Vyadhikshamatwa (immunity) in Children. *J Pharmacol Jphyto*. 2015;4(4):227–30.
13. Castillo AL, Ramos JDA, Francia JLD. Interleukin-1, Interleukin-6, Interleukin-8 Levels in Scabies-infected Pediatric patients: A Single Blind, Randomized Trial. *Int J Pharma Sci Drug Res*. 2014;6(3):178–9.

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