Section: Research Paper

TINOSPORA CARDIFOLIA A WONDERFUL PLANT WITH THERAPEUTIC VALUES: A REVIEW

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Abstract:

Tinospora cardifolia which is commonly known as Giloy or Guduchi and grows in the form of a shrub has a wonderful role in ayurvedic drugs. In the modern medicine, number of chemicals have been isolated from different part of *Tinospora cardifolia* and were found very effective in the management of major ailments. On one hand *Tinospora cardifolia* has a very potential role as anti-diabetic drug and is also helpful in arthritis and malaria. A good number of researchers have found that *Tinospora cardifolia* is very effective as anti-cancer drug. *Tinospora cardifolia* is also used as immunomodulator and enhance the general health of individual. In the latest epidemic of COVID-19, researchs have proved that use of *Tinospora cardifolia* has helped a lot in early recovery. It is reported that with ayurveda intervention having *Tinospora cardifolia*, have accelerated the recovery in terms of symptoms and duration of hospital stay.

In the present review the major chemicals isolated from *Tinospora cardifolia* and their role in managing the blood parameters and other disease have been discussed. The review highlights the role of *Tinospora cardifolia* plant as anti-oxidant, anti- microbial, anti-diabetic, anti-stress, hypolipidemic and anti-HIV potential. Future scope of investigating the effect of *Tinospora cardifolia* on signaling and biochemical pathways is still open with enormous opportunities.

Introduction

Tinospora cordifolia commonly none as Guduchi and Giloy is a deciduous climbing shrub which comes under the family Menispermaceae. As far as availability is concerned, this plant is distributed throughout the tropical and subtropical Indian continent and China (Rana *et al*., 2012)

A large volume of Ayurvedic literature suggests the use of giloy as a constituent of several formulations used for the treatment of various diseases. *Tinospora cordifolia* plays a very importance in ayurvedic medicines used in the treatment of pain, asthama, fever, jaundice, cancer, diarrhea, bone fracture, poisonous snake and insect bite and eye disorders (Parthipan *et al*., 2011).

Biologically active compounds isolated from *Tinospora cordifolia:*

A good number of biologically active compounds like glycosides, steroids, phenolics, alkaloids, diterpenoids, lactones and polysaccharides, isolated from different parts of *Tinospora cordifolia* have been extensively used in medicines.

***Tinospora cordifolia*- Antioxidant properties and scavenging properties:**

Tinospora cordifolia had been helpful in protection against the aflatoxin induced nephrotoxicity due to the alkaloids present like tinosporin, palmatine, tetrahydropalmatine (Gupta and Sharma, 2011).

Tinospora cordifolia also inhibit fructose 1,6 bisphosphatase and glucose 6 phosphatase that results in restoration of glycogen content in liver. It has been shown to regulate the blood glucose level (Sangeetha *et al*., 2011).

Rawal *et al.,* (2004) has reported the strong free radical scavenging properties for hydroxyl radical (OH), NO radical, peroxy nitrite anion ($ONOO^-$) and superoxide anion (O_2^-). Mathey et al., (1999) and Khan *et al*., (2011) also reported the property of *Tinospora cordifolia* to reduce the toxic side effects of CP in mice by the formation of free radicals.

Methanol extract from the stem part of *Tinospora cordifolia* administered orally helps in increasing the catalase and erythrocyte membrane lipid peroxydase activity (Prince and Menon, 2003), (Sivakumar *et al.,* 2010) and (Prince and Menon, 2001). *Tinospora cordifolia* extracts also possess the possible inhibitor of antioxidant agents and aldolase reductase, hence reduces chemotoxicity which is induced by free radicals (Gacche *et al*.,2011).

***Tinospora cordifolia*- Reduces the Comorbidity factors:**

Most of the deaths during COVID-19 were reported due to the comorbidity factors like diabetes and heart ailments. As per the Centre for Disease Control & Prevention (CDC) 2019, older adults are more likely to get severely ill from COVID-19. More than 81% of covid deaths occurred in people over 65 age. The risk of severe COVID-19 increases as number of underlying medical conditions increases in person. Cancer, chronic kidney disease, chronic liver disease, chronic lung disease, Diabetes (Type 1 and Type 2), Heart condition, HIV infection, Overweight/ Obesity and pregnancy are the major comorbid conditions. A person with a condition listed above may greater symptoms & risk of severe illness from COVID-19 than people of similar age group who do not have those conditions.

Adekunle *et al*., (2020) has reported that patients with comorbidities usually have the worst prognosis and they should take all necessary precautions. It is believed that COVID-19 with other underlying health conditions or comorbidities like diabetes and hypertension has an increasingly rapid and severe progression of the disease leading to death (Singh *et al*., 2020).

***Tinospora cordifolia*- Antidiabetic property:**

Sangeetha et al., (2011) has reported that the stem part of *Tinospora cordifolia* is commonly used in diabetes therapy as it regulates the blood sugar level. *Tinospora cordifolia* is helpful in diabetes control by inhibiting glycogenolysis and gluconeogenesis. The major phytoconstituents isolated from *Tinospora*

cordifolia like tannins, cardiacglycosides, flavonoids, saponins and steroids are the mainly reported to play as antidiabetic role (Sudha *et.al*., 2011). The roots of *Tinospora cordifolia* are also helpful in diabetes control as it decreases the level of glycosylated haemoglobin, hydroperoxidase, seruplasmin and vitamin E in diabetic rat (Umamaheshwari and Mainzen Prince, 2007).

The crude chloroform and hexane, ethyl acetate and dichloromethane extracts from the stem of *Tinospora cordifolia* inhibit the activity of pancreatic and salivary amylase and glucosidase. It plays a potential role in treatment of diabetes melitus (chougale et.al., 2009). *Tinospora cordifolia* in combination with other ayurvedic drugs has also been helpful in treatment of diabetes by reducing GSH and Vitamin C (Umamaheshwari *et.al.*, 2007). The root extracts of *Tinospora cordifolia are* also having hypolipidimic effects besides hypoglycemic effect as it is reported that *Tinospora cordifolia extract causes increase in total haemoglobin, hepatic hexokinase* & body weight and lowers the serum ACP,LDH and ALP in diabetic rats (Stanely *et al.*, 2000).

***Tinospora cordifolia*- Anti arthritic, anti osteoporotic effect:**

Beta- Ecdysone (Ecd) extracted from *Tinospora cordifolia* is very effective in arthritis as it results in significant improve the joint cartilage and induces the osteogenic differentiation of mesenchymal stem cells of mouse (Gao *et al*., 2008). *Tinospora cordifolia* has also been reported for its anti-osteoporotic effect as the alcoholic extract of *Tinospora cordifolia* has shown the stimulation of growth of osteoblast, increase of differentiation of cell in osteoblastic lineage (Abiramasundari *et. al*., 2012). *Tinospora cordifolia* has also shown good results in synergic combination formulation with *Zingiber officinalis* in treatment of rheumatoid arthritis as evident from traditional medicines (Chopra *et.al.*, 2012).

***Tinospora cordifolia*- Antimicrobial activity:**

Besides the anti-diabetic, anti-oxidant and anti-arthritic properties, *Tinospora cordifolia* is also reported to have potential benefits against microbial infections (Narayanan *et.al*., 2011). It has the function in bacterial clearance and improved intacellular bactericidal capacities of neutrophills and phagocytic effects (Thatte *et.al*., 1992). It has also been found that *Tinospora cordifolia* extract has anti-stimulant property on macrophages (Sengupta *et.al.,* 2011). *Tinospora cordifolia* extracts have been reported having anti-microbial property against *Salmonella typhi, Salmonella paratyphi, Enterobactor aerogene, Escherchia coli, Staphylococcus aureus, Proteus vulgaris, Klebsella pneumonia and Serratia marcesenses* (gram positive bacteria). *Tinospora cordifolia* hydromethanolic extract when given as intra mammary infusion, showed activated Polymorphonuclear cells (Mukharjee *et.al.,* 2010) and (Purandare and Supe, 2007).

***Tinospora cordifolia*- Anti cancer effects:**

Tinospora cordifolia has been reported for its anti-cancer properties as the compounds isolated from *Tinospora cordifolia*. It has a potential role in decreasing anti-oxidant activity in hepatocellular carcinoma which was induced by diethylnitrosamine (DEN) *via* CAT, SOD and increasing the activity of hepatic marker SGOT and SGPT and on the other hand decreasing the serum transaminase level (Dhanasekaran *et.al*., 2009). *Tinospora cordifolia* extract inhibit the harmful effect of sub-lethal gamma radiations in male swiss albino mice. *Tinospora cordifolia* extract significantly affect the radiation induced rise in lipid peroxidation that results in decline concentration of GSH in testes (Sharma *et.al.,* 2011). *Tinospora cordifolia* extract is helpful in decreasing cell viability by increasing LDH and

decreasing GSH- S- transferase activity (Rao and Rao, 2010). The hydroalcoholic extract (80% ethanol: 20% distilled water) of aerial roots of *Tinospora cordifolia* on swiss albino mice showed the increase in enzyme activity of DTD, cytochrome P (450) reductase, SOD, cytochrome b5 reductase, catalyse in liver resulting the chemopreventive role of *Tinospora cordifolia* against carcinogenicity (Singh *et.al.*, 2006).

Polysaccharides extracted from *Tinospora cordifolia* were applied on B16- F10 melanoma cells and it was observed effective. It was noted that *Tinospora cordifolia* extract reduces the markers of neoplastic development significantly in animals which were treated as compared to the animals which were used as control (Leyon and Kuttan, 2004). Anti-angiogenic activity in B16-F10 melanoma cells was shown when *Tinospora cordifolia* extract was applied and a significant elevation in the level of IL-6, TNF-α, granulocyte monocyte colony stimulating factor (GM-CSF) & vascular endothelial cell growth factor was observed and the production of anti-angiogenic agent IL-2 & tissue inhibitor of metalloprotease-1 (TIMP-1) was increased (Leyon and Kuttan, 2004). On one hand when most of the synthetic chemotherapeutic agents are having toxic side effects (Diwanay *et.al.*, 2004), on the other hand extract of *Tinospora cordifolia* were found comparable or better than doxorubicin treatment in cancer.

***Tinospora cordifolia*- Anti HIV Effect:**

Anti HIV effect of *Tinospora cordifolia* was studied and it was found that there is a reduction in eosinophill count, stimulation of macrophages, β-lymphocyte & polymorphonuclear leucocytes. Haemoglobin percentage was also increased, thus proves the promising role of *Tinospora cordifolia* in HIV management (Akhtar, 2010). The recurrent resistance of HIV was decreaed by *Tinospora cordifolia* and better therapeutic outcome was observed (Kalikar *et.al.*, 2008).

***Tinospora cordifolia*- Antitoxic Effect:**

When *Tinospora cordifolia* extract is given orally, it prevents the liver damage occurrence induced by lead nitrate. In mice suffering from lead toxicity, decrease level of SOD, CAT and increased level of SGOT, SGPT and ACP was observed after *Tinospora cordifolia* treatment. *Tinospora cordifolia* has also shown the protective role when aqueous extract of stem and leaves overcomes the toxic effect of lead as evident from haematological values (Sharma and Pandey, 2010). *Tinospora cordifolia* has been reported in overcoming the cyclophosphamide (CP) induced toxicities in cancer treatment (Hamsa and Kuttan, 2012).

***Tinospora cordifolia*- Immunomodulatory Properties:**

Immunomodulatory properties of *Tinospora cordifolia* is well evident from number of documents (Tripathi *et.al.*, 1997; Bishayi *et.al.*, 2002 and Subramanian *et.al.*, 2002). Aqueous extract have been reported to enhance the cytokine production and immune effector cells stimulation (Upadhyaya *et.al.*, 2011). Enhanced immune response is reported in mice when stem cell crude extract was administered in mice and an elevated secretion on IL-1was observed besides macrophage activation. *Tinospora cordifolia* is very effective in prevention of oxidative damage (Raghu *et.al.*, 2009). Active compounds isolated from *Tinospora cordifolia* have been reported to have potential role as immunomodulatory and cytotoxic effect (Kapil and Sharma, 1997), (Tripathi *et.al.*, 1997) and (Bishayi *et.al.*, 2002). The active compounds have been reported to boost phagocytic activity of macrophages and production of reactive oxygen species (ROS) in human neutrophil cells (More and Pai, 2012).

Tinospora cordifolia have been shown to activate human lymphocytes with synthesis of anti-inflamatory cytokines (Koppada *et.al*., 2009). In mice model *Tinospora cordifolia* extracts have been reported in upregulation of IL-6 cytokine which results in acute reaction of inflammation, injury, differentiation of B-cells and activation of cytotoxic T-cells (Sudhakaran *et.al.*, 2006).

TINOSPORA CORDIFOLIA DRUG FORMULATIONS USED IN COVID-19:

Ayurveda, Indian ancient system has suggested a number of herbal formulations for respiratory tract infections (Sharma, P.V., 2012; Srikantha, M.K., 2014 and Bisht *et.al.*, 2009). Ayurvedic medicines having *Tinospora cordifolia* have been highly effective in respiratory disease and fever (Dhama *et.al.*, 2017 and Panchabhai *et.al.*, 2008). A large number of literature is available on antiviral property of *Tinospora cordifolia* (Krupanidhi *et.al.*, 2020; Gupta *et.al.*, 2010 & Saha and Ghosh, 2012). *Tinospora cordifolia* had also been very helpful in the treatment of COVID-19 patients (Kumar *et.al.*, 2020).

Kulkarni *et.al.*, (2021) conducted a study to evaluate the role of Ayurveda in Covid-19 Patients management. He conducted the molecular docking analysis of phytochemicals extracted from tulsi, ashwagandha & giloy and reported potential inhibition of SARS CoV-2 virus. It resulted in further translation of viral protein that plays assistance to further damage of vital organs of the host. In this study a significant improvement was observed in the patients who were on Ayurvedic treatment as compared to the usual care patients. The report concluded that, the combination of ayurveda (*Tinospora cordifolia*) was helpful to prevent severe respiratory tract infections when administered in patients suffering from viral infections. It was reported that, with ayurveda interventions an early onset and early recovery 4.85 (SD 1.8) days was observed. Although it also reported that in the COVID-19 cases, where no ayurveda treatment was given, the main disease duration was 11.5 ± 5.7 days (Lechien *et.al.*, 2020).

In other study conducted in China, same observation was made where it was observed an average time of recovery (10.63±1.93 days) for mild to moderate patient and 18.70±2.5 days for severe patients (Wu *et.al.*, 2020). In China also in a different single centre study, the mean recovery time was found 20-21 days (Yu *et.al*., 2020 and Bi *et.al.*, 2020).

In the study conducted by Wanjarkhedkar, P. (2020), to evaluate the additional benefits of ayurvedic treatment in COVID-19 patients. The ayurvedic formulations were given addition to the regular treatment. Patients who were given Dasamoolkaduthrayam Kashaya and Guluchyadi Kwathan in tablet form showed faster recovery and these patients were discharged earlier as compared to the control patients. These ayurvedic preparations appear to accelerate recovery of patient in terms of reduction of symptoms and duration of hospital stay.

The role of bioactive compounds from *Tinospora cordifolia* was found very effective against COVID-19 in a study conducted by Murugesan *et.al.*, (2021) using molecular docking technique. The study was aimed to examine the potential of bioactive compounds of Giloy (*Tinospora cordifolia*), Amla (*Emblica officinalis*) and Bhoomi amla (*Phyllanthus niruri*). In total 96 bioactive compounds were selected and were docked with C19 M^{pro} and further analyzed by molecular dynamic study. From this study it was observed that bioactive compounds of these three herbs have a significant role as a plausible inhibitor for COVID-19 M^{pro} and may further be very helpful in discovering and developing natural C19 therapeutic drug.

In a study conducted by Balkrishna *et.al.,* (2021) on formulation tablet of *Tinospora cordifolia* named Giloy Ghanwati. In the study, active compound identified by using HPLC technique were Palmatine, β Ecdysone, Cordiofolioside A and Magnoflorine. The author has reported the increased infiltration of granulocytes and macrophages in swim bladder of SARS CoV -2 spike protein induction group. A significant reduction in number of granulocytes in all groups was observed. The mortality seen with SARS Cov-2 spike protein was completely reversed with higher doses of Giloy Ghanwati but lower doses (6 and 28 µg/kg/day) could only reduce mortality to 89% over a period of 10 days on humanized zebra fish model. It was concluded from the study that treatment with Giloy Ghanwati reverse the pro-inflamatory cell infiltration in swim bladder and also rescued the necrosis seen in kidney. Behavioural fever indications of higher body temperature were also reversed upon treatment with Giloy Ghanwati. These results were in the line with previous work conducted by the same author using tri herbal population containing *Tinospora cordifolia* (Balkrishna *et.al.*,2020).

Conclusion:

In the present review, light was thrown on the economic importance and various phytochemicals isolated from the *Tinospora cardifolia*. Almost all the parts of the plant are used for therapeutic purpose. This plant has been successfully used in ayurvedic drugs from ancient times. Till now lots of research has been done and various therapeutic aspects of *Tinospora cardifolia*. have been found but still further studies are to be carried out to investigate the role of the wonderful plant at molecular and pathways level which will be further utilized in development of new drugs.

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