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Review Article

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Tinospora cordifolia with Reference to Biological and Microbial Properties

S.K. Dwivedi and Enespa*

Department of Environmental Science, Babasaheb Bhimrao Ambedkar (A Central) University, Lucknow-226025, U. P. India
**Corresponding author*

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A B S T R A C T

Tinospora cordifolia is a deciduous climbing shrub described as '*the one who protects the body against diseases*' belonging to family Menispermaceae known as Amrita (Guduchi). It is widely used by tribal's for the treatment of many diseases including gastrointestinal disorder. The biological and chemical significance of this plant is mainly because of the leaves, barks androots contain various bioactive compounds such as alkaloids, glycosides, lactones,steroids, polysaccharides and aliphatic compounds having various medicinalimportance *viz.*, immunomodulatory or immunostimulatory, antitumor, cognition, anti-inflammatory, anti-neoplastic, antihyperglycemia, antihyperlipidemia, antioxidant, antituberculosis, gastrointestinal and hepatoprotection, anti-osteoporotic, anti-angiogenic, anti-malarial, anti-allergic and side effects prevention of the cancer chemotherapy. The present review is birds eyeview on traditional use, biologicaland chemical activity of *Tinospora cordifolia.*

Introduction

India is well known historically as a land of herbs, shrub, spices and aromatic plants and continues to be one of the leading producers of medicinal plants in the world (Prajapati *et al.*, 2005).Medicinal plants since times immemorial have been used as a source of medicine (Shukla and Gardner, 2006). The widespread use of herbal remedies and healthcare preparations as those described in ancient texts such as the Vedas and the Bible and obtained from commonly used traditional shrub and medicinal plants have been traced to the occurrence of natural products with medicinal properties (Talbot *et al*., 2006).

Tinospora cordifolia (Willd.) Miers exHook. F. and Thoms (Menispermaceae) (Upadhyay *et al.*, 2010**)** is an important shrub in folk and Ayurvedic system of medicine found throughout India, especially tropical part of India and Karnataka (Shivakumar and Krishnamurthy, 2002) followed by China. It is described as '*the one who protects the body against disease*'. It is also called as marginal shrub due to its property of curing a lot of diseases in modern system of medicine (Srivastava, 2011). It contains therapeutic strength, detoxifying and cleansing the whole system, specifically via liver. It is widely used as anti-bacterial

(Dorman and Deans, 2000)), antifungal (Dwivedi and Enespa, 2012) analgesic (Bousquet *et al.*, 1994), antipyretic (Ikram *et al*., 1987) and also for the treatment of jaundice, skin diseases, anemia etc. The stem is used in dyspepsia, debility and urinary diseases (Ahmad *et al*., 2009). Fever and urinary diseases (Bishayi *et al*., 2002). The biter principle present shows several medicinal applications viz., antiperiodic, antispasmodic, antiinflammatory, immunomodulatory or immunostimulatory, antitumor, cognition, antineoplastic, antihyperglycemia, antihyperlipidemia, antioxidant, antituberculosis, gastrointestinal and hepatoprotection, anti-osteoporotic, antiangiogenic, anti-malarial, anti-allergic and antipyretic properties (Stanely *et al*., 2000; Rathi *et al*., 2002; Bishayi *et al.*, 2002; Stanely and Menon, 2003; Rawal *et al.*, 2004; Singh *et al*., 2004, 2005; Purandare, 2007; Wang *et al*., 2010). The root is a powerful emetic and used for visceral obstructions, stem extract as antioxidant while its water extract is used in leprosy and antidiabetic cases. It's raising the efficiency of protective white blood cells and builds up our immune system so thatsome of the health experts prescribe *T. cordifolia* for some sexually transmitted diseases such asgonorrhea (Raghu *et al*., 2009). The water, ethanol/methanol, methylene chloride extracts of *T. cordifolia* have been evaluated for antineoplastic effects. Tumor mass reduction and increased survival time have been observed with administration of the extract in mice with induced carcinomas (Leyon and Kuttan, 2004; Jagetia and Rao, 2006). At low doses, an ethanol extract of *T. cordifolia* increased bone marrow cell counts, while higher doses resulted in decreased counts in mice with induced lymphoma (Singh*et al*., 2006).*T. cordifolia* induces proliferation and myeloid differentiation of bone marrow precursor cells in a tumor-bearing host (Singh *et al.*, 2005), activates tumor-associated macrophages-derived dendritic cells (Singh *et al*., 2005) was effective against various cancers (Mittal and Singh, 2009), killing the cancer cells very effectively in vitro (Jagetia and Rao, 2006), inhibits skin carcinogenesis in mice(Chaudhary *et al.*, 2008) and inhibits experimental metastasis (Leyon and Kuttan, 2004). *T. cordifolia* may offer an alternative treatmentstrategy for cancer in combination with gamma radiation (Rao *et al*., 2005;Goel *et al*., 2004).

The pharmaceutical significance of this shrub is mainly because of various bioactive compounds found in this plant such as glucoside, alkaloidal constituents including berberine, three fatty alcohol, a bitter glucoside giloin, a non-glucosidic bitter substance gilonin (Singh *et al.*, 2003).

Occurrence and Botanical Description of *Tinospora cordifolia*

Tinospora cordifolia indigenous to India, China, Myanmar, Sri Lanka, Thailand, Philippines, Indonesia, Malaysia, Borneo, Vietnam, Bangladesh, North Africa, West Africa, and South Africa (Pendse *et al*., 1981;Singh *et al.*, 2003; Mia *et al*., 2009; Jain *et al.*, 2010)and also contains about 70 genera and 450 species. It typically grows in deciduous and dry forests at elevations up to 1000ft.

T. cordifolia is a climbing shrub native to lower elevation in tropical areas of the Indian subcontinent and climbs numerous types of trees (Premila, 2006). It prefers wide range of soil, acid to alkaline and needs moderate level of soil moisture**(**Sharma *et al*., 2010c**)**.

It is also known as Gilo (Arabic); *Amarlata* (Assamese); *Gadancha, Guluncha, Giloe (*Bengali*); K'uan chu Hsing* (Chinese);

Culancha (French); *Tinospora* (English); *Gado, Galo, Gulo* (Gujerati); *Giloe, Gulbel, Gurcha* (Hindi); *Amrytu, Sittamrytu* (Malayalam); *Ambarvel, Giroli, Gulvel* (Marathi), *Garjo* (Nepali); *Gulancha* (Oriya); *Gulbel* (Persian); *Gilo (*Punjabi, Kashmiri), *Amrita, Guduchi*, (Sanskrit); *Gurjo* (Sikkikim); *Amridavalli*, *Niraidarudian* (Tamil); Guduchi, Iruluchi (Telugu) and *Guruch* (Urdu) (Kirtikar and Basu, 1918; Anon, 1956; The Ayurvedic Pharmacopoeia of India, 2001).

Tinospora cordifolia is a deciduous plant that grows to 1.0 meters (3.3feet) high by 0.5 meters (1.65 feet). Stem of *T. cordifolia* are succulent and having long filliform fleshy aerial roots which arise from the branches. Bark is thin, greyish or creamy white in colour, when peeled fleshy stem is exposed. It often attains a great height and mostly climbs up the trunks of large neem trees. Leaves of *T. cordifolia* are heart shaped, membranous, juicy and cordate. *T. cordifolia* has greenish flowers, which are unisexual (Hooker, 1875; Kirtikar and Basu, 1918) and bloom in summer. Male flower are small, yellow or green coloured occur in clusters whereas Female flower occur singly. Fruits are Pea shaped, fleshy, shiny turn red when boiled and occur in winter. Seeds of *T. cordifolia* are curved and pea size.

Constituents of *Tinospora cordifolia*

T. cordifolia contains high fibre (15.9%), sufficient protein (4.5%-11.2%), carbohydrate (61.66%), and low fat (3.1%). Its nutritive value is 292.54 calories per 100 g. It has high potassium (0.845%), high chromium (0.006%), sufficient iron (0.28%) and calcium (0.131%), important in various regulatory functions (Nile and Khobragade, 2009).

The chemical constituents present in *T. cordifolia* belonging to different classes such as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides. Three major groups of compounds; protoberberine alkaloids, terpenoids and polysaccharides are considered as putative active constituents of *T. cordifolia* (Chintalwar*et al*., 1999; Bisset and Nwaiwu, 1983). These chemical constituents in different parts of plant and their role in various therapeutic actions have been presented in Table 1 and 2.

Therapeutic and Biological Activities

Tinospora cordifolia,known as guduchi, is a plant prescribed in Ayurveda, the Indian traditional system of Medicine as a Rasayana (Thatte and Dhanukar, 1986). Guduchi is a promising drug entity which should enter the world market by evidence-based research for therapeutics (Jagetia and Rao 2006).It is successfully used to cure many diseases. Some medicinal properties of *T. cordifolia* in disease control are as followes:

Anti-cancer/ Antitumor Activity

Extracts of *Tinospora cordifolia* (TCE) have been shown to possess anti-tumor properties. According to Jagetia and Rao (2006) the decline in the clonogenicity, glutathione-S-transferase (GST) activity, increase in lipid peroxidation with a peak at 4 h and lactate dehydrogenase (LDH) release with a peak at 2 hHeLa cells, were exposed to various concentrations of TCE. Alcoholic extract of *T. cordifolia* has been reported to be cytotoxic in a transplantable mouse tumor. Increased lipid peroxidation, LDH(decline in surviving fraction) release accompanied by a decline in GST concentration by guduchi is some of the important events

leading to cell death. Lipidperoxidation is an important event related to cell death and has been reported to cause severe impairment of membrane function through increased membrane permeability and membrane protein oxidation and eventually cell death by damaging the cellular DNA. Administration of the polysaccharide fraction from *Tinospora cordifolia* was found to be very effective in reducing the metastatic potential of melanoma cells, inhibition in the metastases formation in the lungs of syngeneic mice, when the drug was administered simultaneously with tumour challenge. Biochemical parameters such as lung collagen hydroxyproline, hexosamines and uronic acids that are markers of neoplastic development were reduced significantly in the treated animals (Jagetia and Rao, 2006).

Anti-diabetic and Hyperglycaemic activity

Tinospora cordifolia is widely used for treating the diabetes mellitus. According to Stanely *et al.*(2000) the aqueous *T. cordifolia* root extract (TCREt) to alloxan diabetic rats caused a significant reduction in blood glucose and brain lipids. The extract caused an increase in body weight, total haemoglobin and hepatic hexokinase. The root extract also lowers hepatic glucose -6-phosphatase and serum acid phosphatase, alkaline phosphatase and lactate dehydrogenase in diabetic rats thus TCREt has hypoglycaemic and hypolipidaemic effect (Stanely *et al.,* 2000). The extract also prevented a decrease in body weight (Stanely and Menon, 2001).

The aqueous, alcoholic and chloroform extracts of the leaves of *T. cordifolia* in doses of 50, 100 and 200 mg/kg body weight to normal and alloxan-diabetic induced rabbits exerted significant hypohlycaemic effect (Wadood *et al.,* 1992). An Ayurvedic compound formulation Transina (TR) containing *T. cordifolia* and other drugs was studied for hyperglycaemia and superoxide dismutase (SOD) activity of pancreatic islet cells. The result indicates that the earlier reported antihyperglycaemia activity of streptozotocin (STZ) being the consequence of decrease in islet SOD activity leading to the accumulation of degenerative oxidative free radicals in islet beta cells (Bhattacharya *et al.,* 1997).

Anti-inflammatory Activity

Anti-inflammatory potency of water extract of *T. cordifolia* has been proved by the study on induced oedema arthritis and on human arthritis. The dried of *T. cordifolia* produced significant anti-inflammatory effect in both acute and sub-acute models of inflammation. *T. cordifolia* was found to be more effective than acetylsalicylic acid in acute inflammation (Jana *et al.,* 1999). The aqueous stem extract of *T. cordifolia* has been antagonize the various autocoids in the pathophysiology of clinical joint inflammation.

Antioxidant Activity

The alcoholic root extract of *T. cordifolia* has antioxidant defence mechanism in alloxan induced diabetic rats and also significant increase in the concentration of thiobarbituric acid reactive substances in liver and kidney. The decreased concentration of glutathione (GSH), activity of superoxide dismutase (SOD) and catalase in liver and kidney of diabetic rats (Prince *et al*., 2004). Methew and Kuttan (1997) reported the antioxidant activity and amelioration of cyclophosphamide-induced toxicity. The direct and indirect antioxidant actions of *T. cordifolia* probably act in corroboration to manifest the overall radio-protective effect (Goel *et al*., 2002).

Anti-stress Activity

Ethanol extract of *T. cordifolia* at the dose of 100 mg/kg exhibited significant anti-stress activity compared with diazepam at the dose of 2.5 mg/kg (Sarma *et al*., 1996).

Anti-ulcer Activity

The ethanol root extract of *T. cordifolia* was observed to induce a marked protective action against restrain stress induced ulcerization comparable to that of diazepam (Sarma *et al.,* 1995).

Digestive Activity

The antiamoebic effect of a crude drug formulation containing *T. cordifolia* against *Entamoeba histolytica* was studied. According to Sohni *et al*. (1995) reported varying degrees in inhibition of the enzymes, *viz.,* DNase, RNase, acid phosphatase, alkaline phosphatase and protease activities of crude extracts of axenically cultured amoebae.

Hypolipidaemic Activity

The aqueous extract of *Tinospora cordifolia* roots has hypolipidaemic properties. The extract of *T. cordifolia* roots (2.5 and 5.0 g : kg body weight) for 6 weeks resulted in a significant reduction in serum, tissue cholesterol, phospholipids and free fatty acids in alloxan diabetic rats. The effect of *T. cordifolia* roots at 2.5 and 5.0 g/kg body weight was better than glibenclamide. Insulin restored all the parameters to near normal values and it was observed that a level of serum lipids in alloxan diabetic rats was higher. The level of serum lipids was usually raised in diabetes and such an elevation represents a risk factor for coronary heart disease (Shamaony *et al.,* 1994). Lowering of serum lipids levels through dietary or drugs therapy seems to be associated with a decrease in the risk of vascular disease (Rhoads *et al.,* 1976). The abnormal high concentration of serum lipids in diabetes is mainly due to the increase in the mobilization of free fatty acids from the peripheral depots, since insulin inhibits the hormone sensitive lipase. On the other hand, glucagon, catecholamines and other hormones enhance lipolysis.

The marked hyperlipemia that characterizes the diabetic state may therefore be regarded as a consequence of the uninhibited actions of lipolytic hormones on the fat depots (Shamaony *et al.,* 1994). According to Kumar and Menon (1992) the levels of cholesterol, phospholipids and free fatty acids in liver, kidney and heart in alloxan diabetic rats was higher.

Immuno-modulatory Activity

*T. cordifolia*is used to improve the immune system and the body resistance against infections. The alcoholic and aqueous extracts of *T. cordifolia* have been tested successfully for immuno-modulatory activity. Pretreatment with *T. cordifolia* reduced mortality in mice injected with *E. coli* intraperitoneally. This was associated with significantly improved bacterial clearance as well as improved phagocytic and intracellular bactericidal capacities of neutrophils in the *T. cordifolia* treated group. According to Desai *et al.* (2002) the dry stem crude extract (DSCE) of *T. cordifolia* contained a polyclonal B cell mitogen, G1-4Awhich enhance the immune response in mice.

Treatment of *T. cordifolia* extract also deleted the immunosuppressive effect of CCl_4.There was significant increment in the functional capacities of rat peritoneal macrophages. Treatment by *T. cordifolia*

extract may be the critical remedy for the adverse effect of CCl_4 in liver function as well as immune functions (Bishayi *et al*., 2002). In clinical study, it has afforded protection in cholestatic patients against *E. coli* infection (Dhuby, 1997). The water extract of *T. cordifolia* was found to be more potent than other extract (Manjreker *et al*., 2000). According to Atal *et al.* (1986) *T. cordifolia* improves the phagocytic function without effecting the humoral or cell mediated immune system.

Hepatoprotective Activity

Effect of *T. cordifolia* extract on modulation of hepatic functions is also reported. Treatment with *T. cordifolia* extracts (100 mg/kg body weight for 15 days) in CCl_4 intoxicated rat it was found that liver was protected (Bishayi *et al.,* 2002). According to Reddy *et al.* (1993) the chloroform extract of *T. cordifolia* failed to reduce the liver toxicity in tested dose (200 mg/kg). The extract of *T. cordifolia* had also exhibited *in vitro* inactivating property against Hepatitis B and E surface antigen in 48-72 hrs (Mehrotra *et al.,* 2000).

Cognition (Learning and Memory) Activity/ Mental disorders

Dementia is a syndrome of failing memoryand other intellectual functions with little or no disturbance in consciousness (Ropper *et al.,* 2009).Degeneration of the cerebral neurons is oneof the commonest and vital causes fordementia with increasing age, thereby leading to deterioration in quality of life in elderly. *T. cordifolia* (TC) extract effects on learning and memory in normal and cyclosporine induced memory deficit rats and also used as mental disorders (Kulkami and Verma, 1993).

Antimicrobial Properties

Herbal medicine represents one of the most important fields of traditional medicine all over the world. To promote the proper use of herbal medicine and to determine their potential as sources for new drugs, it is essential to study medicinal plants. Contrary to the synthetic drugs, antimicrobials of plant origin are not associated with side effects and have an enormous therapeutic potential to heal many infectious diseases. Plant-based antimicrobials have enormous therapeutic potential as they can serve the purpose with lesser side effects that are often associated with synthetic antimicrobials (Iwu *et al*., 1999). Thousands of secondary plant products have been identified and it is estimated that thousands of these compounds still exist. Since secondary metabolites from natural resources have been elaborated within living systems, they are often perceived as showing more "drug – likeness and biological friendliness than totally synthetic molecules" making them good candidates for further drug development (Koehn and Carter, 2005; Balunas and Kinghorn, 2005; Drahl *et al*., 2005) .

In recent years the use of eco-friendly technologies especially use of plant extracts are gaining tremendous importance for the control of plant disease in agriculture because they are less harmful to the human health and environment (Duru *et al.,* 2003), and also these are considered as potential alternatives to chemical agents which are hazardous to human and animal health (Mukhopadhyay, 1996).

The activity of plant extracts on bacteria and fungi has been studied by a very large number of researchers in different parts of the world (Vuuren and Naidoo, 2010; Bhengraj *et al.,* 2008).Human infections, particularly skin and mucosal surfaces, constitute a serious problem, especially in tropical and subtropical developing countries (Portillo *et al.,* 2001). In humans,

fungal infections range from superficial to deeply invasive or disseminated, and have increased dramatically in recent years. The treatment of mycoses has lagged behind bacterial chemotherapy and fewer antifungal than antibacterial substances are available. Therefore, a search for new antifungal drugs is extremely necessary (Fortes *et al.*, 2008).

Infectious diseases, particularly skin and mucosal infections, are common in most of the tribal inhabitants due to lack of sanitation, potable water and awareness of hygienic food habits. An important group of these skin pathogens are the fungi, among which dermatophytes and Candida spp. are prominent (Fan *et al*., 2008; Toledo *et al.*, 2011). Antimicrobial properties of certain Indian medicinal plants were reported based on folklore information (Gupta and Banerjee, 2008; Tharkar *et al.*, 2010; Duraipandiyan *et al.*, 2010), and a few attempts were made on inhibitory activity against certain pathogenic bacteria and fungi.

T. cordifolia has been shown to possess anti-allergic (Badar *et al.*, 2005), anti-diabetic (Prince *et al*., 1998), anti-hepatotoxic (Bishayi *et al.*, 2002), anti-pyretic (Bafna *et al.*, 2005) and anti-inflammatory properties (Purandare *et al*., 2007). This activity can be attributed to tinocordifolin (Maurya and Handa, 1998); sesquiterpene glucoside, tinocordifolioside (Maurya *et al*., 1997); cordifoliside D and cordifoliside (Gangan *et al*., 1995); tinosponone and tinocordioside, clerodane (Maurya *et al.*, 1995); cordioside (1995).

The *Tinospora cordifolia* extract have been used to possess desirable bioactivities including fungicidal activities (Soliman and Badeaa, 2000), bactericidal (Dorman and Deans, 2000; Aher and Wahi, 2010), insecticidal (Isman, 2000) and nematocidal (Pandey *et al*., 2000) activities. The antifungal activity of *Tinospora cordifolia* leaf extract against *Fusarium oxysporum* f.sp. *lycopersici* and *Fusarium solani* causing tomato and brinjal wilt have been studied at three concentrations *viz.*, 25, 50, 75% (v/v) *in vitro* by poisoned food technique and recorded 100% resultagainst both the pathogenic *Fusarium* at 75% concentration (Dwivedi and Enespa, 2012). Singh *et al.* (2010) reported the antifungal activity of methanolic crude extract of *Acorus calamus*, *Tinospora cordifolia* and *Celestrus paniculatus* against *Alternaria solani, Curvularia lunata, Fusarium sp., Bipolaris* sp. and *Helminthosporium* sp. at different concentrations (1000, 2000, 3000, 4000 and 5000 µg/ml). At 5000 µg/ml crude extract of *Tinospora cordifolia* was found to be highly effective against *Helminthosporium* sp. followed by *Acorus calamus* against *Alternaria solani*. On the other hand at 5000 ug/ml, *Celestrus paniculatus* showed better activity against *Alternaria solani* and *Helminthosporium* followed by *Acorus calamus* against *Alternaria solani* at 4000ug/ml. At 5000 ug/ml, all the three crude extracts showed least activity against the fungus *Curvularia lunata* and *Fusarium* sp. except *Acorus calamus* that showed better activity against *Curvularia lunata*.

Duraipandiyan and Ignacimuthu (2011) reported that the antifungal activity of hexane, ethyl acetate and methanol extracts of *Albizzia procera, Asclepias curassavica, Atalantia monophylla, Azima tetracantha, Cassia fistula, Cinnomomum verum, Costus specious, Nymphaea stellata, Osbeckia chinensis, Piper argyrophyllum, Punica granatum, Tinospora cordifolia* and *Toddalia asiatica* against human pathogenic fungi *viz. Trichophyton rubrum* MTCC 296,*T. rubrum*57/01, *Trichophyton mentagrophytes*66/01, *Trichophyton simii* 110/02, *Epidermophyton floccosum* 73/01,

Scopulariopsis sp. 101/01 *Aspergillus niger* MTCC 1344, *Botrytis cinerea, Curvularia lunata* 46/01, *Magnaporthegrisea* and *Candida albicans* MTCC227. The ethyl acetate extracts inhibited large number of fungal growth and hexane also nearly showed the same level of inhibition against fungal growth while the methanol extracts showed the minimum antifungal activity. The promising antifungal activity observed in *A. procera, C. Speciosus, C. Fistula and T. asiatica.*

Bansal *et al.* (2012) reported that the antimicrobial effect of different extracts of *Tinospora cordifolia* against four pathogenic bacteria (*Escherichia coli*, *Staphylococcus aureus*, *Streptococcus mutans* and *Pseudomonas aeruginosa*) and one fungus (*Candida albicans*). The efficacy of extracts was measured in terms of zone of inhibition (mm). Butanol extract was the most effective against all the tested microbes as compared to the other tested extracts. The decoction and toluene was ineffective against all the microbes except *E. coli* where benzene was ineffective. The phytochemical screening of various extracts revealed the presence of tannins, steroids, flavonoids, cardiac glycosides and saponnins. These results suggested that butanol extract is not only the important source of antimicrobial component but can also be used for developing novel antimicrobial biorationals of plant origin.

Mahesh and Satish (2008) reported that antimicrobial activity of methanol leaf and bark extracts of *Tinospora cordifolia* against bacterial strains *viz. Bacillus subtilis, Escherichia coli, Pseudomonas fluorescens, Staphylococcus aureus* and *Xanthomonas axonopodis* pv. *Malvacearum* and fungal strains *viz. Aspergillus flavus, Dreschlera turcica* and *Fusarium verticillioides. T. cordifolia* leaf extracts showed almost similar zone of inhibition against all the tested bacteria except *Xanthomonas axonopodis* pv. *Malvacearum,* which showed highest antibacterial activity (17 mm). The bark extract of *T. cordifolia* showed varied in the zone of inhibition from 10-14 mm against all the tested bacteria. The *T. cordifolia*leaf extract recorded better (14 mm) zone of inhibition (antifungal activity) against*D. turcica* followed by bark extract (13mm).

The antifungal activity and minimum inhibitory concentration (MIC) of *Valeriana jatamansi* (Sugandhbala), *Coleus barbatus* (Pathar choor), *Berberis aristata* (Kingore), *Asparagus racemosus* (Satrawal), *Andrographis paniculata* (Kalmegha), *Achyranthes aspera* (Latjiri), *Tinospora cordifolia* (Giloei), *Plantago depressa* (Isabgol) plant extracts against *Aspergillus niger* and *Candida albicans* at different solvents such as hydro-alcohol (50 % v/v) and hexane as medicines. Hydro-alcoholic extracts of all the plants showed maximum antifungal activity in comparison to hexane extracts. Hydroalcoholic extracts of *Andrographis paniculata* and *Achyranthes aspera* showed maximum potency against *Aspergillus niger* and *Candida albicans* at highest MIC value of 0.5 and 0.3 mg/ml respectively. Hexane extracts of *Andrographis paniculata* showed highest MIC value of 0.7 mg/ml against *Aspergillus niger* (Mathur *et al.*, 2011). However the antibacterial activity of aqueous and methanolic (fruit and stem) extracts of *Tinospora cordifolia* was tested against four human pathogenic bacteria namely *Bacillus cereus, Bacillus fusiformis, Escherichia coli and Klebsiella pneumonia* by using paper disc agar diffusion method. All extracts of stem and fruit exhibited significant antibacterial activity against the tested bacteria. However, the strongest antibacterial activity was observed in

methanol fruit extract of *Tinospora cordifolia* against *Klebsiella pneumoniae* with maximum inhibition zone (22 mm). The aqueous fruit extract showed minimum antibacterial activity against *Bacillus cereus* with (10 mm) zone of inhibition. The stem extract in the methanol solvent exhibits highest zone of inhibitory growth against *K.pneumoniae* with (18 mm) zone of inhibition while least antibacterial activity was recorded against *B.fusiformis* with 9.5 mm zone of inhibition (Agnihotri *et al*., 2012).

According to Verma and Kakkar (2010) reported the antibacterial effect of stem methanol extract of *Tinospora cordifolia* against pathogenic microorganisms (*Escherichia coli, Staphylococcus aureus* and *Staphylococcus albus)*. Results showed that widest zone of inhibition (14.4 mm) were demonstrated by the methanolic extract of *Tinospora cordifolia* stem against *E. coli* via agar well diffusion methodas compared to paper disc method (10 mm). Jeyachandran *et al*. (2003)reported that antibacterial activity of the aqueous, ethanol and chloroform extracts from the stems of *Tinospora cordifolia* using disc diffusion method, measured in terms of inhibition (cm) against *Escherichia coil, Proteus vulgaris, Enterobacter faecalis, Salmonella typhi* (Gram-negative), *Staphylococcus aureus* and *Serratia marcesenses* (Gram-positive). It revealed that the ethanolic extracts exhibited significant antibacterial activity against *Proteus vulgaris, Escherichia coli* and moderate activity was observed against *Enterobacter faecalis.* In the same extract less inhibition was observed against *Salmonella typhi, Staphylococus aureus* and *Serratia marcescens.*

Singh and Singh (2012) reported the antibacterial activities of *Tinospora cordifolia* (Willd) stem extract prepared with methanol (hot and cold) against bacterial strains *Salmonella typhi***,** *Staphylococcus aureus, Shigella dysenteriae, Escherichia coli* and *Pseudomonas aeruginosa*. *In vitro* antibacterial activity of hot and cold methanol stem extracts was performed by cup plate agar diffusion method using ciprofloxacin in Dimethyl sulphoxide as a standard drug for the comparing antibacterial activity. Both Hot and cold methanol extracts of *Tinosporacordifolia* stem contain significant antibacterial activityagainst all test bacterial strains but hot methanol extractof *T.cordifolia* stem showed more significant activityagainst all tested bacterial organisms.

Mahesh and Satish (2008) reported thatthe leaf extract of *Tinospora cordifolia* showed maximum antibacterialactivity compared to other parts; methanolicextract of plant sample showed maximumactivity (Kakkar and Verma, 2011), and soluble fraction of themethanolic extract of plant showedantibacterial activity (Kawsar*et al.*, 2011).

Forty nine different plantsused in traditional Indian medicine were examinedagainst *Aspergillus niger* using agar well diffusionmethod(Bobbarala *et al*., 2009). The methanolic extracts of 43 plants exhibitedvarying degrees of inhibition activity against the fungi.Among the forty nine plants studied, 86% of the plants hadantifungal activity, while the remaining 14% had noantifungal activity. The extract from *Grewia arborea*showed maximum activity. *Emblica officinales, Heldigordia populipolia, Hyptis sueolences, Moringa heterophylla, Strychnos nuxvomica* and *Vitex negundo*did not exhibit antifungal activity against *A. niger.*

Sharma and Trivedi (2002)studied fresh leaf extracts of *Datura stramonium, Calotropis procera, Verbesenaenceloides, Parthenium hysterophorus, Morus alba, Phyllanthus amarus,Eichhornea crassipes, Ricinus communis, Jatropha curcas, Azadirachta indica, Tinospora cordifolia, Clerodendron multiflorum, Catharanthus roseus* and *Adhatoda vesica* against root-knot nematode, *Meloidogyne incognita* and wilt fungus, *Fusarium oxysporum* f. sp. *cumini* infesting cumin. In the preliminary studies, almost all the plant species exhibited nematicidal and antifungal property. *Calotropis procera* and *Ricinus communis* gave best results against the nematodeand *Datura stramonium* and *Calotropis procera* showed maximum antifungalactivity against *Fusarium oxysporum* f.sp. *cumini*.

Issakul (2013) reported that application of botanical herbicides as one of alternative ways to reduce the use of harmful herbicides in agricultural pest management. Eighteen species of Thai local plant extracts i.e. *Murraya paniculata* (L.) Jack. leaf, *Hydrocotyle umbellata* L. leaf, *Mammea siamensis* T. Anders. seed, *Duranta erecta* L. leaf, *Pluchea indica* Less. leaf, *Aglaia Odorata* Lour. leaf, *Leucaena leucocephala* de wit. leaf, *Ipomoea aguatica* Forsk, *Eucalyptus camaldulensis* Dehnh leaf, *Leea macrophylla* Roxb.ex Hornem. leaf, *Metha cordifolia* Opiz. leaf, *Casuarina junghohniana* Mfg. leaf, *Stemona curtisii*. Hook.F. root, *Cassis fistula* Linn.pod, *Tinospora crispa* (L.) Miers ex Hook.f.& Thoms.stem, *Brachiaria mutica* (Forsk.) Stapf leaf, *Raphanus sativus* var. longipinnatus L. root and *Zollingeria dongnaiensis* Pierre leaf were screened for the highest herbicidal activity in laboratory by the filter paper method. *Aglaia odorata* leaf extract demonstrated the highest germination inhibitory activity. It also had a highest significant efficiency to inhibit both root and shoot of Mimosa seedling. *Aglaia odorata* was selected for determination of its herbicidal efficiency under pot experiment. *Aglaia odorata* leaf extract at the concentration of 4 % w/v exhibited stronger toxicity on germination and growth of Mimosa seedling than control (solvent) treatment in pot experiment.

Khan and Srivastava (2012) reported the water (at room temperature and at elevated temperature), 70% ethanol, 80 % methanol, acetone, ethyl acetate and chloroform extracts of *Tinospora cordifolia* (Giloy) against bacterial pathogens such as *Escherichia coli, Staphylococcus aureus* and *Pseudomonas aeruginosa* using agar well diffusion method at 100 mg/ml concentration was evaluated for their antibacterial properties. Water (at room temperature and at elevated temperature), ethanolic and ethyl acetate extracts of *Tinospora* leaves showed an average inhibitory zone of 14mm, 14.5mm, 17mm and 12.5mm respectively which indicates that ethanolic extract shows best result having zone of inhibition more than that of tetracycline (12mm against all pathogens) while extracts of methanol, acetone and chloroform didn't show any result. In case of *Tinospora* stem and root best result was shown by hot aqueous extract with a zone of inhibition of 16mm and 17mm respectively. The ethanolic extract of root also gave a zone of 17mm.

Sankhala *et al.* (2012) revealed that *Tinospora cordifolia* is an excellent drug, which could be a good remedy for various ailments of animals as well as human beings yet the safety and potential indications in human beings and animals have to be established using modern techniques. Uddin *et al.* (2011) used *Tinospora* for isolation of its secondary metabolites andevaluation of biological activities with special emphasis to

the antimicrobial screening and cytotoxic study**.** The chemical constituents have been reported from this shrub belong to different classes, such as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides (Upadhyay*et al.,* 2010).

Table.1 Chemistry of Tinospora cordifolia

Part	Chemical type	Active principle	Reference
Stem	Alkaloids	Berberine, palmatine D, choline D, tinosporine, Magnoflorine, tetrahydropalmatine, isocolumbin	Padhya, 1986; Sarma*et al*., 1998; Kumar*et al*., 2000
		18-norclerodane glycoside	Khan*et al*., 1989
		Furanoid diterpene glycoside	Bhatt and Sabata, 1989; Swaminathan*et al*., 1989
	Glycosides	Tinocordiside	Maurya*et al*., 1995; Ghosal and Vishwakarma, 1997
		Syringin	Sipahimalani*et al*., 1994; Kapil and Sharma,1997
		Syringin-apiosylglycoside	Khan*et al*., 1989; Bhatt and Sabata, 1989
		Tinocordifolioside, cordioside, cordifolioside A, cordifolioside B, palmatoside C31, palmatoside F31, cordiofoliside B2, cordifoliside D2, cordifoliside	Swaminathan*et al*., 1989; Ghosal and Vishwakarma, 1997; Maurya*et al*., 1997
	Sesquiterpenoid	Tinocordifolin	Maurya and Hardass, 1998
Root	Alkaloid	Palmatine	Pathak*et al*., 1995
Aerial parts	Steroids	b-sitosterol, d-sitosterol, g-sitosterol b-hydroxyecdysone, ecdysterone, makisterone, giloinsterol jateorine, columbin	Pathak*et al*., 1995; Ganga*et al*., 1997
	Diterpenoid lactones	Furanolactone, tinosporon , columbin	Hanuman*et al*.,1680; Qudrat*et al*., 1966; Ahmad*et al*., 1978
Whole plant	Aliphatic compound	Octacosanol, heptacosanol	Dixit and Khosa, 1971
	Miscellaneous compound	Nonacosan-15-one 3, (a,4-dihydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxy-benzyl)-tetrahydrofuran, Tinosponidine, 6 cordifol, 6 Cordifelone, 6 Jatrorrhizine	Khaleque*et al*., 1971

Table.2 Action of some important phytochemicals of Tinospora cordifolia

Phytochemicals	Activity	Mechanism of action	Reference
Quinones	Antimicrobial	Binds to adhesions, complex with cell wall, inactivate enzymes	Cowan, 1999
Flavanoids	Antimicrobial	Complex with cell wall, binds to adhesins Inhibits release of autacoids and prostaglandins,	Cowan, 1999
	Antidiarrhoeal	Inhibits contractions caused by spasmogens, Stimulates normalization of the deranged water transport across the mucosal cells, Inhibits GI release of acetylcholine	Kumar *et al.*, 2010
Polyphenols and Tannins	Antimicrobial	Binds to adhesions, enzyme inhibition, substrate deprivation, complex with cell wall, membrane disruption, metal ion complexation	Cowan, 1999
	Antidiarrhoeal	Makes intestinal mucosa more resistant and reduces secretion, stimulates normalization of deranged water transport across the mucosal cells and reduction of the intestinal transit, blocks the binding of B subunit of heat-labile enterotoxin to GM1, resulting in the suppression of heat-labile enterotoxin-induced diarrhea, astringent action	Maniyar*et al.*, 2010; Kumar *et al.*, 2010
	Antihelmintic	Increases supply of digestible proteins by animals by forming protein complexes in rumen, interferes with energy generation by uncoupling oxidative phosphorylation, causes a decrease in G.I. metabolism	Sutar *et al.*, 2010; Patel*et al.*, 2010
Coumarins	Antiviral	Interaction with eukaryotic DNA	Vidyadhar *et al.*, 2010
Terpenoids and essential oils	Antimicrobial	Membrane disruption Inhibits release of autocoids and	Cowan, 1999
	Antidiarrhoeal	prostaglandins	Maniyar*et al.*, 2010
Alkaloids	Antimicrobial	Intercalates into cell wall and DNA of parasites	Cowan, 1999
	Antidiarrhoeal	Inhibits release of autocoids and prostaglandins	Maniyar*et al.*, 2010
	Antihelmintic	Possess anti-oxidating effects, thus reduces nitrate generation which is useful for protein synthesis, suppresses transfer of sucrose from stomach to small intestine, diminishing the support of glucose to the helminthes, acts on CNS causing paralysis	Mute *et al.*, 2009; Mali *et al.*, 2007
Lectins and Polypeptides	Antiviral	Blocks viral fusion or adsorption, forms disulfide bridges	Vidyadhar *et al.*, 2010
Glycosides	Antidiarrhoeal	Inhibits release of autocoids and prostaglandins	Maniyar*et al.*, 2010
Saponins	Antidiarrhoeal	Inhibits histamine release *in vitro*	Maniyar*et al.*, 2010
	Anticancer	Possesses membrane permeabilizing properties	Shaibani *et al.*, 2009
	Antihelmintic	Leads to vacuolization and disintegration of teguments	Sharma *et al.*, 2010a
Steroids	Antidiarrhoeal	Enhance intestinal absorption of Na+ and water	Maniyar*et al.*, 2010

Growth Regulatory Activities of Different Extracts of *Tinospora cordifolia* on Some Food Crops

There are different types of plant such as herbal or medicinal, fruit trees, woody, necrotic, herbaceous, shrubs, weeds etc. in plant kingdom. Most of them have effective medicinal values, growth regulatory, herbicidal and pesticidal effects and also toxic values. According to WHO, around 80% of the world's 5.86 billion inhabitants depend on traditional medicine for their primary health care, majority of which use plant or their active principles (Gias Uddin, 1998).The attention is being needed to the importance of rotation in medicinal plant or between medicinal herbs and other crops (Basotra *et al.,* 2005; Guo *et al.,* 2006; Nazir *et al*., 2007). Various types of extracts of *T. cordifolia* and *Shial mutra* having bioactive compound increase or decrease germination and growth rate of crops (Roy *et al.,* 2004; Roy, 2006).

Aktar *et al.* (2012) investigated the growth regulatory activities of different extracts of *Tinospora cordifolia* on radish (*Raphanus sativus*), swamp cabbage (*Impoea aquatica*) and lady's finger (*Hibiscus esculentus*) with the attempt for chemical investigation of effective plant extract. The chloroform extract of *Tinospora cordifolia* significantly increased and enhanced germination, growth of shoot length and root length of radish and lady's finger whereas and delayed germination, growth of shoot length and root length of swamp cabbage seeds compared with control. In the same way, ethanol extract of *Tinospora cordifolia* significantly increased germination, growth of shoot length and root length of swamp cabbage followed by control and chloroform extract. The different extracts of *Tinospora cordifolia* contain growth regulatory active principle. Among the extracts, chloroform extract showed better performance in terms of percent germination, growth of shoot and root length of radish and lady's finger whereas according to Singh *et al.* (2009) conducted to estimate the allelopathic effects of *Tinospora cordifolia* on food crops and obtained result that higher concentration of leaf and old shoot extracts inhibited the germination of *Sesamum orientala* and *Eleusine coacana* while higher concentration stimulate the germination of *Cajanus cajan*. The lower concentration of new shoots stimulates germination as compared to higher concentration. The higher concentration of leaf, new shoot and old shoot had suppressed radicle and plumule growth of all tested food crops as compared to lower concentration.

On the other hand, according to Raoof and Siddiqui (2011) studied the allelopathic effects ofLeaf and stem aqueous extracts of*Tinospora cordifolia* weed on seed germination and seedling growth of weed plants (*Chenopodium album* L. *Chenopodium murale* L., *Cassia tora* L. and *Cassia sophera* L.) at 0.5 to 4.0% concentrations. Aqueous extracts from leaf and stem inhibited germination, root length, shoot length and dry weight of weed species decreased progressively when plants were exposed to increasing concentration (0.5, 1, 2 and 4%). Aqueous extract of leaves shows the maximum inhibition while stem shows the least affect on weeds.

In conclusion, the scientific research on *T. cordifolia* suggests a huge biological potential of this plant. It is widely used in ayurvedic medicine for the treatment of various ailments. It is strongly believed that detailed information as presented in this review on biological and microbial properties of the extracts might provide detailed evidence for the use of this plant in different medicines. Antimicrobial potential

shown by these plants further warrant their exploration for the development of novel effective chemotherapeutic agents. *T. cordifolia* is an excellent drug, which could be a good remedy for various ailments of animals as well as plants, yet the safety and the potential indications in human beings and animals have to establish using modern techniques.

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