Journal of Medicinal Plants Studies
Year: **2014**, Volume: **2**, Issue: **2**
First page: **(32)** Last page: **(47)**
ISSN: **2320-3862**
Online Available at **www.plantsjournal.com**

Received: 10-01-2014
Accepted: 09-02-2014

Journal of Medicinal Plants Studies

Tinospora cordifolia: a multipurpose medicinal plant- A review

Jitendra Mittal [1], Madan Mohan Sharma [2*], Amla Batra [3]

1. Department of Biosciences, Manipal University Jaipur, PIN- 303007, Rajasthan, India
   [Email: jitendra.mittal@muj.manipal.edu]
2. Department of Biosciences, Manipal University Jaipur, PIN- 303007, Rajasthan, India
   [Email: madanmohan.sharma@jaipur.manipal.edu]
3. Lab. No. 5, Department of Botany, University of Rajasthan, Jaipur, PIN- 302055 Rajasthan, India
   [Email: amlabatra@gmail.com]

Traditional systems of medicine such as Ayurvedic, Uninai, Siddha and Homeopathy (AYUSH) have been in practice in a great account. Owing to population rise, inadequate supply of drugs, prohibitive cost of treatments, side effects of several allopathic drugs and development of resistance to currently used drugs for diseases have led to increased emphasis on the use of plant materials as a source of medicines for a wide variety of human ailments as witnessed by the use of folk medicines in the present scenario.
This review article describes the prominence of a medicinal plant *Tinospora cordifolia* in therapeutics such as use of crude extract of plant for the amelioration of various diseases, morphology, growth constraints, biochemical composition, biological activities, research work done, projects sanctioned to this plant species and the future prospects of this important neglected plant species for research in the field of plant tissue culture, natural products and nano-biotechnology.

Keyword: Medicinal Plants, Plant Extract, Tissue Culture, Natural Products, Biodiversity.

1. Introduction:

India is bestowed with enormous biodiversity of medicinal plants. Among them *Tinospora cordifolia* has a wide array of bioactive principles as well as it has been proven medicinally important plant, have not received considerable scientific attention.

Medicinal plants have been used as natural medicines. This practice has been in existence since prehistoric times. There are different ways in which plants have been found useful in medicines such as crude extract of plants has been used directly because of the presence of natural chemical constituents such as berberine, morphine, psilocin, vincristine etc. [1] and natural compounds for the synthesis of drugs such as tubocurarine, colchicine, nicotine, quinine etc. for therapeutic purpose by folk people. Many modern medicines such as digitalis, vinblastine, aspirin, quinine and paracetamol had their origin from the natural compounds of medicinal plants viz., foxglove (*Digitalis purpurea*), madagascar periwinkle (*Vinca rosea*), willow bark (*Salix spp.*), quinine bark (*Cinchona officinalis),* respectively [2].

A large number of plants are being used in medicine for therapeutic or prophylactic purposes. The therapeutic properties of medicinal plants are attributed owing to the presence of active substances such as alkaloids, flavonoids, glycosides, vitamins, tannins, and coumarins [3]. These natural compounds physiologically affect the body of human beings, interact with the pathogens and interrupt their growth at different stages of development and make the body disease free.

Tinospora cordifolia (Willd.) Miers ex Hook. F. and Thoms belonging to the family Menispermaceae, is a large, deciduous, climbing shrub found throughout India, especially in the tropical parts ascending to an altitude of 300 m. and also in certain parts of China [4]. It is known as heart leaved Moonseed plant in English, Guduchi in Sanskrit and Giloy in Hindi.

2. Growth Requirement

The plant is very rigid and it can be grown in almost all climates but prefers warm climate. Planting is usually done during rainy season (July to August). As it is climber so it requires support for its growth. Fast growing species such as Neem (*Azadirachta indica*), Jatropha (*Jatropha curcas*) and Moringa (*Moringa oleifera*) have been planted to provide support for its growth. *Tinospora cordifolia* growing with Neem (*Azadirachta indica*) is called as NEEM GILOY has chemical composition as similar as neem as well as giloy and show better therapeutic properties [5].

T. cordifolia prefers medium black or red soil for its cultivation. Giloy can also be successfully grown in large variety of soils, ranging from sandy to clay loam. However, the soil should be well drained with sufficient moisture and rich with organic matter for its growth.

3. Growth Constraints

T. cordifolia can be propagated by seeds and vegetative cuttings. However, both the ways are not suitable for large scale production and having problems in traditional methods of propagation. Viability of seeds is very less, poor seed set and germination of seeds are the main problems associated with its clonal propagation. Vegetative cuttings are also not suitable due to less productivity and also dependent upon weather conditions for its further growth. Keeping in view the Growth constraints, plant tissue culture techniques may be suitable methods for its large scale production in a lesser time and space.

4. Threats to This Plant

Due to the presence of immense medicinal properties, this plant has been overexploited by pharmaceutical companies and folk people for traditional remedies have led to the acute scarcity of this plant to meet the present-day demand. Due to its high demand, *T. cordifolia* has been listed amongst 29 highly prioritized medicinal plants of agro climatic zone 8 (Rajasthan, U.P. and M.P.) of India as identified by National Medicinal Plant Board, New Delhi, Government of India. This plant has also been listed in 178 medicinal plant species in high Volume Trade by NMPB, New Delhi, India [6]. Hence, this plant has been selected for the review article to make public or scientific community very well aware and update them about morphology, growth constraints, an array of its chemical compounds, medicinal properties, pharmaceutical products, research work done till date in different aspects, various research projects sanctioned by different funding agencies etc.

5. Morphological Description

Tinospora cordifolia is a large deciduous, extensively spreading climbing shrub with a number of coiling branches. Different parts of Tinospora have following type of morphology.

6. Stem

Stem of this plant is rather succulent with long, filiform, fleshy and climbing in nature. Aerial roots arise from the branches. The bark is creamy white to grey in colour and deeply left spirally [7] (Figure 1A).

7. Arial Root:

Arial roots are present, these aerial roots are characterized by tetra to penta-arch primary structure. However, cortex of root is divided in to outer thick walled and inner parenchymatous zone [8] (Figure 1F).

8. Leaves

Leaves of this plant are simple, alternate, ex-stipulate, long petioled approximately 15 cm,

round, pulvinate, heart shaped, twisted partially and half way round. Lamina is ovate, 10-20 cm long, 7 nerved and deeply cordate at the base and membranous [9] (Figure 1B).

Fig 1: Morphology of different parts of *T. cordifolia* A. Stem, B. Leaf, C. Fruit, D. Inflorescence, E. Flower, F. Aerial Roots

9. Flowers

Flowers are unisexual, recemes, greenish yellow in colour, appears when plant is leaf less. Male flowers are clustered and female flowers exist in solitary inflorescence. Sepals are 6 in 2 series of 3 each. Outer ones are smaller than the inner sepals. Petals are also 6, smaller than sepals, free and membranous. Flowering occurs during March to June [10] (Figure 1D AND 1E).

10. Fruit

They are orange-red in colour, fleshy, aggregate of 1-3 and ovoid, smooth, drupelets on thick stalk with a sub terminal style scars. Fruits develop during winter [11] (Figure 1C).

11. Seed

Curved seed have been reported in this species. Hence this family is named as moonseed family also. As seeds are curved in shape, embryo also turned in to curve shape automatically. Moreover, the endocarp is variously ornamented and provides important taxonomic characters.

12. Natural Products

A variety of chemical constituents such as alkaloids, diterpenoid lactones, steroids, glycosides aliphatic compounds, polysaccharides have been reported from different parts of Tinospora cordifolia. Various natural products (active compounds) isolated from different plant parts along with their biological activities have been given here for readers reference (Table-1).

13. Biological Activities

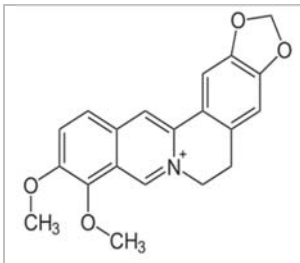
The major biological activities of Tinospora cordifolia summarized in the following manner

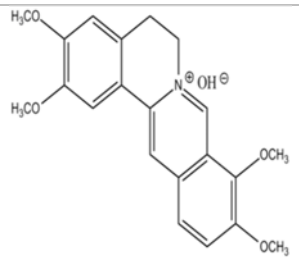
Table 1: Major and sub groups of natural products present in different parts of Tinospora cordifolia and their biological activities

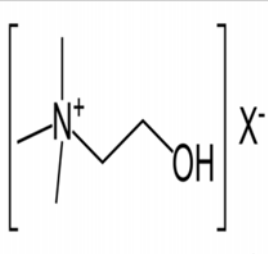
Active Component	Compound	Plant Part	Biological Activity (In Human being)	References
Alkaloids	Berberine, Choline, Tembetarine, Magnoflorine, Tinosporin, Palmetine, Isocolumbin, Aporphine alkaloids, Jatrorrhizine, Tetrahydropalmatine,	Stem, Root	Anti-viral infections, Anti-cancer, anti-diabetes, inflammation, Neurological, immunomodulatory, psychiatric conditions	(12-17)
Diterpenoid Lactones	Furanolactone, Clerodane derivatives [(5R,10R)-4R-8R-dihydroxy-2S-3R:15,16-diepoxy-cleroda-13 (16), 14-dieno-17,12S:18,1S-dilactone], Tinosporon, Tinosporides, Jateorine, Columbin	Whole Plant	Vasorelaxant: relaxes norepinephrine induced contractions, inhibits Ca++ influx, anti-inflammatory, anti-microbial, anti-hypertensive, anti-viral. Induce apoptosis in leukemia by activating caspase-3and bax, inhibits bcl-2.	(18-22)
Glycosides	18-norclerodane glucoside, Furanoid diterpene glucoside, Tinocordiside, Tinocordifolioside, Cordioside, Cordifolioside Syringin, Syringin-apiosylglycoside, Pregnane glycoside, Palmatosides, Cordifolioside A, B, C, D and E	Stem	Treats neurological disorders like ALS, Parkinsons, Dementia, motor and cognitive deficits and neuron loss in spine and hypothalamus, Immunomodulation, Inhibits NF-kBand act as nitric oxide scavenger to show anticancer activities.	(23-29)
Steroids	β–sitosterol, δ-sitosterol, 20 β-hydroxyecdysone, Ecdysterone, Makisterone A, Giloinsterol	Shoot	IgA neuropathy, glucocorticoid induced osteoporosis in early inflammatory arthritis, induce cell cycle arrest in G2/M phase and apoptosis through c-Myc suppression. Inhibits TNF-α, IL-1 β, IL-6 and COX-2.	(30-32)
Sesquiterpenoid	Tinocordifolin	Stem	Antiseptic	(33)
Aliphatic	Octacosanol,	Whole	Anti-nociceptive and anti-	(34-36)

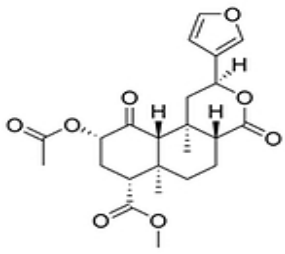
compound	Heptacosanol Nonacosan-15-one dichloromethane	plant	inflammatory. Protection against 6-hydroxydopamine induced parkinsonisms in rats. Down regulate VEGF and inhibits TFN-α from binding to the DNA.	
Others	3,(a,4-di hydroxy-3-methoxy-benzyl)-4-(4-compounds hydroxy-3-methoxy-benzyl)-tetrahydrofuran, Jatrorrhizine, Tinosporidine, Cordifol, Cordifelone, Giloinin, Giloin, N-trans-feruloyltyramine as diacetate, Tinosporic acid.	Root, Whole Plant	Protease inhibitors for HIV and drug resistant HIV.	(37-38)

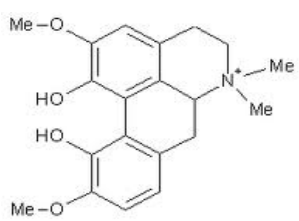
The chemical structures of medicinally potent chemical compounds reported in this plant are being depicted here, which would help researchers to identify these chemicals from the same or different plant resources. The structures of important natural products are as follows:

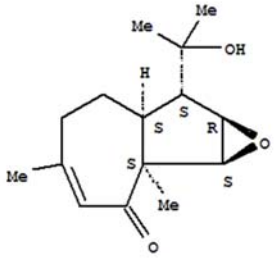

Berberine

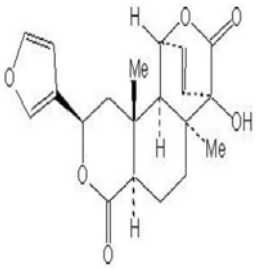

Plamatine

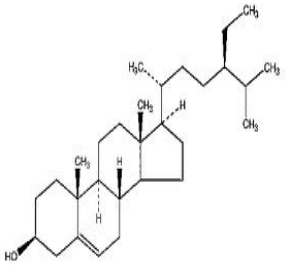

Choline

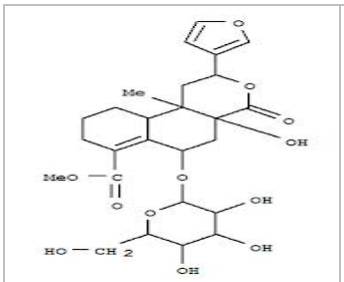

Furanolactone

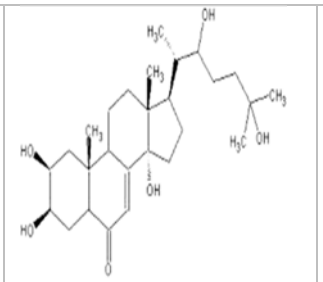

Magnoflorine

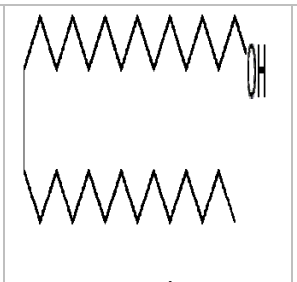

Tinocordifolin

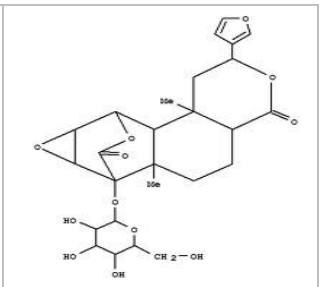

Isocolumbin

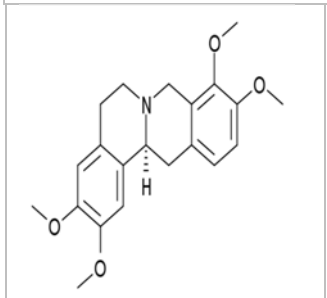

β–sitosterol

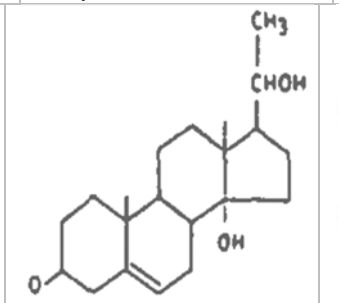

Cordioside

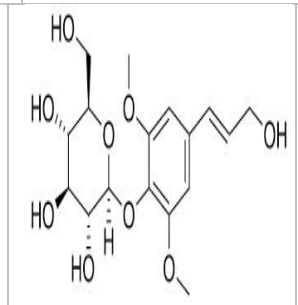

Ecdysterone

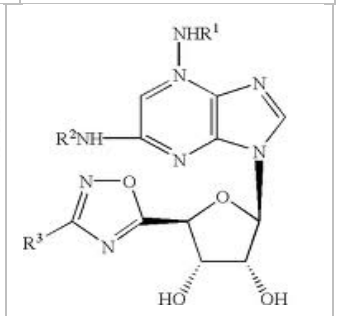

Octacosanol


Palmatosides


Tetrahydropalmetine


Pregnane glycoside


Syringin


Tetrahydrofuran

Using the above mentioned potent chemical compounds from this plant species, various pharmaceutical market products have been produced by the different companies (Table 2)

Table 2: Pharmaceutical products of T. cordifolia and their biological roles

Name of Market Product	Biological Roles
Tinospora Cordifolia Pellets	A number of diseases
Guduchi	The immune system and the body's resistance to infections
Abhaibhubejhr	Anti-stress
Safe herb	Cure by Anemia and sexual disabilities.
Brave Heart Capsule	It lowers the lipid levels especially cholesterol and LDL-cholesterol in body, diuretic
Cirrholiv capsules	Hepatoprotective
Cirrholiv-ds syrup	Hepatoprotective
Mussaffen	Blood purifier and anti-allergic
MadhuMehari	Cure by urinary problems, maintain blood sugar, fatigue
Tonplex	Increase immunity
Rebuild	Anti- stress and anti- oxidant

14. Anti-Diabetic Activities

The stem of this plant is generally used to cure diabetes by regulating level of blood glucose [39]. It has been reported to act as anti-diabetic drug through explanatory oxidative stress, promoting insulin secretion by inhibiting gluconeogenesis and glycogenolysis. The anti-diabetic properties exhibited by this plant species are attributed due to the presence of alkaloids (Magnoflorine, Palmetine, Jatrorrhizine) [17], tannins, cardiac glycosides, flavonoids, saponins, steroids etc. [40]. The crude extract of stem in ethyl acetate, dichloromethane, chloroform and hexane inhibits the enzymes like salivary, amylase and glucosidase resulting increase in post-prandial

glucose level and shows potential activities against Diabetes mellitus disease [41].
The root extract of this plant has also been reported to have anti-diabetic properties which decrease the level of glycosylated haemoglobin, hydroperoxidase and vitamin E [42].

15. Immunomodulatory Activities:
T. cordifolia is well known for its immunomodulatory response. This property has been well documented by scientists [43-45]. A large variety of compounds which are responsible for immunomodulatory and cytotoxic effects are 11-hydroxymuskatone, N-methyle-2-pyrrolidone, N-formylannonain, cordifolioside A, magnoflorine, tinocordioside and syringin [46].
These natural compounds have been reported to improve the phagocytic activity of macrophages, enhancement in nitric acid production by stimulation of splenocyte, [47] and production of reactive oxygen species (ROS) in human neutrophil cells [48].

16. Anti-toxic Activities
Aqueous extract of this plant has already been reported to show scavenge activity due to the presence of antioxidant against free radicals generated during aflatoxicosis [15]. Further alkaloids such as choline, tinosporine, isocolumbin, palmetine, tetrahydropalmatine and magnoflorine from *T. cordifolia* showed protection against aflatoxin induced nephrotoxicity [15]. Furthermore *T. cordifolia* shows protective effect by lowering the concentration of thiobarbituric acid reactive substance (TBARS) and enhancing the glutathione (GSH), ascorbic acid, protein and the activities of antioxidant enzymes viz., superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase, glutathione S-transferase (GST) and glutathione reductase (GR) in kidney [15]. However, leaf and stem extract *of T. cordifolia* has been reported to show hepatoprotective effect in male albino mice against lead nitrate induced toxicity. Similarly, oral dose of plant extract prohibited the lead nitrate induced liver damage [49-50].

17. Anti-HIV Activities
Root extract of this plant has been shown a decrease in the regular resistance against HIV [51]. This anti HIV effect was exposed by reduction in eosinophil count, stimulation of B lymphocytes, macrophages, level of hemoglobin and polymorphonuclear leucocytes [51-52].

18. Anti-Cancer Activities:
T. cordifolia shows anti-cancer activity, this activity is mostly shown in animal models. Root extract of *T. cordifolia* has been shown radio protective role due to extensively increase in body weight, tissue weight, tubular diameter. Dichloromethane extracts of TC shows cytotoxic effects owing to lipid peroxidation and release of LDH and decline in GST [16]. In pre-irradiating mice, root extract has widely affected radiation, induced rise in lipid peroxidation and resulted in the decline of GSH in testes [47]. Most of the synthetic chemotherapeutic agents laid toxic side effects on the living organisms [53]. The effect of Giloy has been reported better than doxorubicin treatment [54].

19. Anti-Microbial Activities
Methanolic extract of *T. cordifolia* has been reported against microbial infection [55]. Anti-bacterial activity of *T. cordifolia* extract has been bio assayed against *Escherichia coli, Staphylococcus aureus, Klebsiella pneumonia, Proteus vulgaris, Salmonella typhi, Shigella flexneri, Salmonella paratyphi, Salmonella typhimurium, Pseudomonas aeruginosa, Enterobacter aeruginosa, Enterobacter aerogene* [55-57]. Further, *T. cordifolia* extract has been reported against bacterial growth and improved phagocytic and intracellular bacterial capacities of neutrophils in mice [58].

20. Anti-Oxidant Activities
Methanolic extract of stem of *T. cordifolia* has been reported to anti-oxidant activity, by increasing the erythrocytes membrane lipid peroxide and catalase activity. It also decreases the activity of SOD, GPx in alloxan induced diabetic rats [59-60]. Extract of *T. cordifolia* has

been reported its free radical scavenging properties [61].

Leaf extract of *T. cordifolia* reported to have an alpha-glucosidase inhibitor, characterized as saponarin was found to be also significant anti-oxidant and hydroxyl radical scavenging activity [53]. Due to the presence of alkaloids it shows protection against aflatoxin-induced nephrotoxicity [15]. *T. cordifolia* aqueous extract has a radio protective activity, enhancing the survival of mice against a sub-lethal dose of gamma radiation [50, 62].

Keeping in view the above mentioned medicinal properties, this plant has been listed an important plant amongst the 32 prioritized plants by NMPB, New Delhi, Government of India. Various funding agencies have been sanctioned the large amount to research on this important ignored plant species in the form of major research projects to different organizations/ institutions, are also being represented here for the help of scientists (Table 3). At the same time, type of research work done on this potent medicinal plant species are also being given here (Table 4).

Table 3: Various research projects sanctioned on *Tinospora cordifolia* by different funding agencies

S.N.	Title	Area	Funding Agencies	Year	Amount
1	Studies on Reproductive biology and genetic diversity of *Rauwolfia serpentina, Tinospora cordifolia* and *Asparagus racemosus*	Reproductive Biology	Department of Science and Technology, Govt. of India, New Delhi	2006-2009	9,30,000.00
2.	Prevention of Radiation induced reproductive dysfunctions by *Tinospora cordifolia* (an Indian medicinal plant) extract.	Biochemistry and Pharmacology	Indian Council of Medical Research, Govt. of India, New Delhi	2007-2010	NA
3.	Studies on Modulation of Redox Status and Anti-Inflammatory Effects of *Fagonia cretica Linn, Tinospora cordifolia* and *Rubia cordifolia*	Pharmacology	Department of Science and Technology, Govt. of India, New Delhi	2009-2012	NA
4.	In vitro studies on inhibition of eicosanoid metabolism for control of arthritis by extracts of stem of *Tinospora cordifolia*	Biochemistry and Pharmacology	Department of Science and Technology, Govt. of India, New Delhi	2011-2012	21,17,008.00
5.	Yield Enhancement Strategies for Production of Therapeutic Compounds by Cell and Tissue Cultures of *Tinospora cordifolia*	Plant Tissue Culture and Pharmacology	Department of Biotechnology, Govt. of India, New Delhi	2011-2014	21,15,000.00

** NA- Not Available

Table 4: Recent Update of Research work done on *Tinospora cordifolia by various researchers*

Types of research work done on *Tinospora cordifolia*	Explant	References
Biochemical Research		
Alkaloids From *Tinospora cordifolia* Miers	Root	[63]
Antifungal and HPLC analysis of the crude extracts of *Acorus calamus*, *Tinospora cordifolia* and *Celastrus paniculatus*	Whole plant	[73]
Tinospora cordifolia induces enzymes of carcinogen/drug metabolism and antioxidant system, and inhibits lipid peroxidation in mice	Whole plant	[76]
Purification and characterization of a thiol amylase over produced by a non-cereal non-leguminous plant, *Tinospora cordifolia*	Whole plant	[77]
Amritosides A, B, C and D: clerodane furano diterpene glucosides from *Tinospora cordifolia*	Whole plant	[78]
Adenosyl-l-methionine:(s)-coclaurine-n-methyl transferase From *Tinospora cordifolia*	Whole plant	[82]
Magnoflorine from *Tinospora cordifolia* stem inhibits a-glucosidase and is antiglycemic in rats	Root	[85]
Plant Tissue Culture Research		
Effect of growth regulators, carbon source and cell aggregate size on berberine production from cell cultures of *Tinospora cordifolia Miers*	Leaf	[64]
Micropropagation of *Tinospora cordifolia* (Willd.) Miers ex Hook. F and Thoms– a multipurpose medicinal plant	Shoot	[65]
In vitro propagation of *Tinospora cordifolia (wild.) Miers ex hook. F. Thoms*	Stem and leaf	[66]
In vitro clonal propagation through mature nodes of *Tinospora cordifolia* (willd.)Hook. F. and Thoms.: an important ayurvedic medicinal plant	Nodal segment	[67]
In vitro regeneration of *Tinospora cordifolia* (willd.) Hook. f. and thoms: an important diabetic plant	Petiole, leaf and nodal segment	[75]
Conservation of biodiversity of highly important medicinal plants of India through tissue culture technology- a review	Shoot tip and Nodal Segment	[79]
Identification of *Tinospora cordifolia* (Willd.) Miers ex Hook F. and Thomas Using RAPD Markers	Stem Nodal cutting	[80]
Activity Against Various Diseases (Biological Activity)		
Hepatoprotective and Immunomodulatory Properties of T. cordifolia In CCl_4 Intoxicated mature albino rates	Whole plant	[44]
Evaluation of the antineoplastic activity of guduchi (*Tinospora cordifolia*) in cultured HeLa cells	Stem	[56]
An immunomodulator from *Tinospora cordifolia* with antioxidant activity in cell-free systems	Dry Stem extract	[72]
Evaluation of antileishmanial potential of *Tinospora sinensis* against experimental visceral leishmaniasis	Whole Plant	[74]

In vitro antibacterial activity of methanolic root extract of *Tinospora cordifolia* (wild)	Root	[81]
Anti-diabetic property of Tinospora cordifolia and its active compound is mediated through the expression of Glut-4 in L6 Myotubes	Stem	[86]
Androgenic action of Tinospora cordifolia ethanolic extract in prostate cancer cell line LNCaP	Stem	[87]
Effects of supplementation of Tinospora cordifolia to crossbred cows peripartum	Stem	[88]
Effects of Tinospora cordifolia supplementation on semen quality and hormonal profile in rams	Whole Plant	[89]
Comparative Hepatoprotective Potential of *Tinospora cordifolia, Tinospora sinensis* and *Neem-guduchi*	Stem	[90]
The anti-mycobacterial activity of Tinospora Cordifolia medicinal plant used for the treatment of leprosy and Tuberculosis	Stem	[91]
Glucose uptake-stimulatory activity of *Tinospora cordifolia* stem extracts in Ehrlich ascites tumor cell model system	Stem	[101]
Molecular Analysis		
Genetic diversity analysis of *Tinospora cordifolia* germplasm collected	Petiole, Lenticel, Stomatal Trichome, Stem	[68]
Assessment of Genetic Diversity in Medicinal climber of *Tinospora cordifolia* (willd.) Miers (Menispermaceae) from Gujrat, India	Stem	[69]
Molecular phylogeny in Indian Tinospora species by DNA based molecular markers	Leaf	[70]
Green Synthesis/ Nano Biotechnology Research		
Green synthesis, characterization and in vitro antibacterial activity of silver nanoparticles by using *Tinospora cordifolia* leaf extract	Leaf	[71]
Synthesis of pediculocidal and larvicidal silver nanoparticles by leaf extract from heartleaf moonseed plant, *Tinospora cordifolia* Miers.	Leaf	[92]
Endophytic Research		
Taxol producing endophytic fungus Fusarium culmorum SVJM072 from medicinal plant of *Tinospora cordifolia*- a first Report	Whole Plant	[84]

21. Future Prospects

Traditions of plant-collection and plant based medications have been handed over from generation to generation. Plants collected from different sources show wide disparity in therapeutic values. In the recent years there has been greater expansion of indigenous drug industry in India. Consequently the demand for the medicinal plants has enormously increased. According to latest estimate, there are about eight thousand licensed pharmacies of Indian Systems of Medicine in the country, engaged in the

manufacture of drugs to meet the requirement of people [83]. The total annual requirement of the raw materials of these pharmacies was estimated in tones. Presently, the increasing demand is fulfilled by cutting trees from their natural habitat and/or uprooting there trees/shoots/leaves on nominal charges or by illegal cuttings. This plant species has huge therapeutic potential, it has been over exploited by human activities. So there is an urgent need to conserve it. Plant tissue culture techniques are the alternative method to rapid propagation of this plant for its conservation and for the enhancement of secondary products.

Fungal endophytes are extremely common and highly diverse microorganisms that live within plant tissues, but usually remain asymptomatic. These organisms reside in the living tissues of host plant and do so in a variety of relationships, ranging from symbiotic to slightly pathogenic [93-94]. They occupy a wide range of different habitats due to their vast nutritional diversity as heterotrophs and symbionts. Exploitation of endophytes in production of several metabolites (primary and secondary) is now at the front of Biotechnology along with other groups of organism. Endophytic fungi were found associated with T. cordifolia [84]. The major factors associated with the biological success of these organisms in nature are their metabolic and biochemical diversity. This has allowed adaptation and exploitation of unique environments with other organisms. The endophytic fungi may produce a plethora of substances of potential use to modern medicine, agriculture and industry [95].

Recently, the phytodiversity is also being used by the scientists to produce nanoparticles. Green synthesis technology has been introduced for the synthesis of noble metallic nanoparticles using plant extract. This method for the synthesis of nanoparticles is environmental friendly, cheap and easy [96-100]. These nanoparticles play an indispensable role in drug delivery, diagnostic, imaging, sensing, gene delivery, artificial implant, tissue engineering and now days in medicinal textiles for their antimicrobial activities. In such a way, we will have opportunity to get benefited by the plants. Hence, further studies are required in the field of tissue culture to raise the success rate, molecular analysis of any genetic changes if comes through indirect regeneration process, exploration of a variety of fungal endophytes to reveal the exact pathway of natural product synthesis in the plant cells, and in the field of nano biotechnology to solve the emerging problems of various incurable diseases through drug delivery system by nanoparticles.

22. References

1. Balandrin MF, Klocke JA, Wurtele ES, Bollinger WH. Natural Plant Chemicals: Sources of Industrial and Medicinal Materials. Science 1985; 228:1154-1160.
2. Briskin DP. Medicinal Plants and Phytomedicines, Linking Plant Biochemistry and Physiology to Human Health. American Society of Plant Physiology 2000; 124:507-514.
3. Daniel M. Medicinal Plants: Chemistry and Properties. vol.2, Science Publication, 2006, 24-36.
4. Anonymous. Wealth of India: Raw materials. CSIR, New Delhi, 1976, 10.
5. Chaudhari S, Shaikh N. Gaduchi-the best ayurvedic herb. The Pharma Innovation Journal 2013; 2(4):97-102.
6. National Medicine Plant Board. www.nmpb.nic.in. 04 April, 2014.
7. Khosa RL, Prasad S. Pharmacognostical studies on Guduchi (*Tinospora cordifolia* Miers). J Res Ind Med 1971; 6:261-269.
8. Aiyer KN, Kolammal M. Pharmacognosy of Ayurvedic Drugs. Edn 1, The Central Research Institute 1963, series 1.
9. Raghunathan K, Sharma PV. The aqueous extract of *T. cordifolia* used reduction of blood sugar in alloxan induced hyperglycemic rats and rabbits. J Res Ind Med 1969; 3:203-209.
10. Kirtikar KR, Basu BD. Indian Medicinal Plants. Edn 2, Vol. 1, M/S Bishen Singh, Mahendra Pal Singh; 1975.

11. Nadkarni KM, Nadkarni AK. Indian Materia Medica. Edn 3, Vol. 1, M/S Popular Prakasan Pvt. Ltd 1976.
12. Upadhaya AK, Kumar K, Kumar A, Mishra HS. *Tinospora cordifolia* (Willd.) Hook. F. and Thoms. (Guduchi)-alidation of the Ayurvedic pharmacology through experimental and clinical studies. Int J Ayurveda Res 2010; 1:112-121.
13. Rout GR. Identification of *Tinospora cordifolia* (Willd.) Miers ex Hook F & Thoms using RAPD markers. Z Naturforsch C 2006; 61:118-22.
14. Patel SS, Shah RS, Goyal RK. Anti-hyperglycemic, anti-hyperlipidemic and antioxidant effects of Dihar, a poly herbal ayurvedic formulation in streptozotocin induced diabetic rats. Indian J Exp Biology 2009; 47:564-570.
15. Gupta R, Sharma V. Ameliorative effects of *Tinospora cordifolia* root extract on histopathological and biochemical changes induced by aflatoxin-b (1) in mice kidney. Toxicol Int 2011; 18:94-98.
16. Jagetia GC, Rao SK. Evaluation of the antineoplastic activity of guduchi (*Tinospora cordifolia*) in ehrlich ascites carcinoma bearing mice. Biol Pharm Bull 2006; 29:460-466.
17. Patel MB, Mishra S. Hypoglycemic activity of alkaloidal fraction of *Tinospora cordifolia*. Phytomedicine 2011; 18:1045-1052.
18. Sriramaneni RN, Omar AZ, Ibrahim SM, Amirin S, Mohd ZA. Vasorelaxant effect of diterpenoid lactones from and rographis paniculata chloroform exract on rat aortic rings. Pharmacognosy Res 2010; 2:242-246.
19. Yang S, Evens AM, Prachands, Singh AT, Bhalla S, Devid K *et al*. Diterpenoid lactone and rographolide, the active component of and rographis paniculata. Clin Cancer Res 2010; 16:4755-4768.
20. Zhao F, He EQ, Wang L, Liu K. Anti-tumor activities of and rographolide, a diterpene from And rographis paniculata, by inducing apoptosis and inhibiting VEGF level. J Asian Nat Prod Res 2008; 10:467-473.
21. Kohno H, Maeda M, Tanino M, Tsukio Y, Ueda N, Wada K *et al*. A bitter diterpenoid furano lactone columbine from calumbae Radix inhibits azoxy methane-induced rat colon carcinogenesis. Cancer let 2002; 183:131-139.
22. Dhanasekaran M, Baskar AA, Ignacimuthu S, Agastian P, Duraipandiyan V. Chemopreventive potential of Epoxy clerodane diterpene from *Tinospora cordifolia* against diethyl nitrosamine-induced hepyocellular carcinoma. Invest New Drugs 2009; 27:347-355.
23. Ly PT, Singh S, Shaw CA. Novel environmental toxins: Steryl glycosides as a potential etiological factor for age- related neurodegenerative diseases. J Nrurosci Res 2007; 85:231-237.
24. Karpova EA, Voznyi YV, Dudukina TV, Tsvetkva IV. 4-Trifluoromethylumbelliferyl glycosides as new substrates form revealing diseases connected with hereditary deficiency of lysosome glycosidases. Biochem Int. 1991; 24:1135-1144.
25. Kapil A and Sharma S. Immunopotentiating compounds from *Tinospora cordifolia*. J Ethopharmacol 1997; 58:89-95.
26. Chen S, Wu K, Knox R. Structure-function studies of DT-diaphorase (NQO1) and NRH: Quinone oxidoreductase (NQO2). Free Radic Biol Med. 2001; 29: 276-284.
27. Badwin AS. Control of oncogenesis and cancer therapy resistance by the transcription factor NF-kappa B. J of Clin Invest 2001; 107:241-246.
28. Yang JH, Kondratyuk TP, Marler LE, Qiu X, Choi Y, Caoh *et al*. Isolation and evaluation of kaempferol glycosides from the fern neocheiropterispalmatopedata. Phytochemistry 2010; 71:641-647.
29. Kim SK, Kim HJ, Choi SE, Park KH, Choi HK, Lee MW. Antioxidative and inhibitory activities on nitric oxide (NO) and prostaglandin E2 (COX-2) production of

flavonoids from seeds of prunustomentosa Thunberg. Arch Pharm Res 2008; 31:424-428.
30. Lv J, Xu D, Perkovic V, Ma X, Johnson DW, Woodward M *et al*. Corticosteroid therapy in IgA nephropathy. J Am Soc Nephrol 2012; 23:1108-16.
31. McKeown E, Bykerk VP, Deleon F, Bnner A, Thorne C, Hitchon CA *et al*. Quality assurance study of the use of preventative therapies in glucocorticoid-induced osteoporosis in early inflammatory arthritis: Result from the CATCH cohort. Rheumatology (Oxford) 2012; 51:1662-1669.
32. Sundarraj S, Thangam R, Sreevani V, Kaveri K, Gunasekaran P, Achiraman S *et al*. ϒ-Sitosterol from *acacia nilotica* L. induces G2/M cell cycle arrest and apopyosis through c-Myc suppression in MCF-7 and A549 cells. J Ethnopharmcol 2012; 141:803-809.
33. Maurya R, Handa SS. Tinocordifolin, a sesquiterpene from *Tinospora cordifolia.* Phytochem 1998; 49:1343-1346.
34. De-Oliveria AM, Conserva LM, De-Souza Ferro JN, De-Almeida Brito F, LyraLemos RP, Barreto E. Antinociceptive and anti-inflammatory effects of octacosanol from the leaves of sabiceagrisea var. Grisea in mice. Int J Mol Sci 2012; 13:1598-1611.
35. Wang T, Liu YY, Wang X, Yang N, Zhu HB, Zuo PP. Protective effects of octacosanol on 6-hydroxydopamine-induced Parkinsonism in rats via regulation of ProNGP and NGF signalling. Acta Pharmacol Sin 2010; 31:765-774.
36. Thippeswamy G, Sheela ML, Salimath BP. Octacosanol isolated from *Tinospora cordifolia* downregulates VEGF gene expression by inhibiting nucular translocation of NF<kappa>B and its DNA binding activity. Eur J Pharmcol 2008; 588:141-150.
37. Ghosh AK, Chapsal BD, Webar IT, Mitsuya H. Design of HIV protease inhibitors targeting protein backbone: An effective strategy for combating drug resistance. Acc Chem Res 2008; 41:78-86.
38. Mukherjee R, De-UK, Ram GC. Evaluation of mammary gland immunity and therapeutic potential of *Tinospora cordifolia* against bovine subclinical mastitis. Trop Anim Health Prod 2010; 42:645-651.
39. Sangeetha MK, Balaji HR, Gayathri V, Vasanthi HR. *Tinospora cordifolia* attenuates oxidative stress and distorted carbohydrate metabolism in experimentally induced type 2 diabetes in rats. J Nat Med 2011; 65:544-550.
40. Zinjarde SS, Bhargava SY, Kumar AR. Potent α-amylase inhibitory activity of Indian Ayurvedic medicinal plants. BMC Complement Altern Med 2011; 11:1.
41. Chougale AD, Ghadyale VA, Panaskar SN, Arvindekar AU. Alpha glycosidase inhibition by stem extract of *Tinospora cordifolia*. J Enzyme Inhib Med Chem 2009; 24:998-1001.
42. Umamaheswari S, Mainzen PPS. Antihyperglycaemic effects of 'IIogen-Excel' an ayurvedic herbal formulation in streptozotocin induced diabetes mellitus. Acta pol Pharma 2007; 64:53-61.
43. Tripathi YB, Sharma M, Manickam. Rubia 5 din, a new antioxidant from rubiacordifolia. Ind J Biochem Biophy 1997; 34:302-306.
44. Bishayi B, Roychowdhury S, Ghosh S, Sengupta M. Hepatoprotective properties of a *Tinospora cordifolia* in CCl4 intoxicated mature albino rats. J Toxic Sci 2002; 27:139-146.
45. Subramanian M, Chintawar GJ, Chattopadhyay S. Antioxidant properties of *Tinospora cordifolia* polysaccharide against iron-mediated lipid damage and gamma-ray induced protein damage. Redox Rep 2002; 7:137-143.
46. Sharma P, Parmar J, Sharma P, Verma P, Goyal PK. Radiation- induced testicular injury and its amelioration by *T. cordifolia* (An Indian Medicinal plant) extract. Evid based comp altern Med 2012; 643-647.
47. Upadhyay PR, Sharma V, Anita KV. Assessment of the multifaceted

immunomodulatory potential of the aqueous extract of *Tinospora cordifolia*. Res J Chem Sci 2011; 1:71-79.
48. More P, Pai K. *In vitro* NADH-oxidase and myeloperoxidase activity of macrophages after *Tinospora cordifolia* (guduchi) treatment. Immuno Pharma Immuno toxic. 2010; 34:368-372.
49. Sharma V, Pandey D. Protective role of *Tinospora cordifolia* against lead induced hepatotoxicity. Toxic Int 2010; 17:12-17.
50. Sharma V, Pandey D. Beneficial effects of *Tinospora cordifolia* on blood profiles in male mice exposed to lead Toxic Int 2010; 17:12-17.
51. Kalikae MV, Thawani VR, Varadpande UK, Santakke SD, Singh RP, Khiyani RK,. Immunomodulatory effect of *T. cordifolia* extract in HIV positive patients. Ind J pharmacol 2008; 40:107-110.
52. Akhtar S. Use of *T. cordifolia*in HIV infection. Ind J pharmacol. 2010; 42:57-63.
53. Diwanay S, Chitre D, Patwardhan B. Immunoprotection by botanical drug on experimental metastasis. J ethanopharmacol 2004; 90:223-237.
54. Jagetia GC, Nayak V, Vidyasagar MS. Evaluation of the antineoplastic activity of guduchi (*Tinospora cordifolia)* in cultured HeLa cells. Cancer let 1998; 127:71-82.
55. Narayanan AS, Raja SS, Ponmurugan K, Kandekar SC, Maripandi A. Antibacterial activity of selected medicinal plant against multiple antibiotic resistant uropathogens: A study from Kolli Hills, Tamilnadu, India. Benef Microbes 2011; 2:235-243.
56. Jayachandran R, Xavier TF, Anand SP. Antibacterial activity of stem extracts of *Tinospora cordifolia* (willd.) Hook. F. and Thoms. Anc Sci Life 2003; 22:40-43.
57. Ambekar DH, Khante BS, Chandak BR, Titare AS, Baralkar SS, Aghadte SN. Screening of antibacterial potential of some medicinal plants from Melghat forest in India. Afr J Trad Comp Altern Med 2009; 6:228-232.
58. Sengupta S, Mukherjee A, Goswami R, Basu S. Hypoglycemic activity of the antioxidant saponarin, characterized as alpha-glucosidase inhibitor present in *Tinospora cordifolia*. J Enzyme Inhib Med Chem 2009; 24:684-690.
59. Stanely P, Menon VP. Hypoglycaemic and hypolipidemic action of alcohol extract of *Tinospora cordifolia* roots in chemical induced diabetes in rats. Phytother Res 2003; 17:410-413.
60. Stanely P, Menon VP. Antioxidant action of *Tinospora cordifolia root* extract in alloxan diabetic rats", Phytother Res 2001; 15:213-218.
61. Rawal A, Muddeshwar M, Biswas S. Effects of *R. cordifolia, F. creticalinn., T. cordifolia*on free radical generation and lipid peroxidation during oxygen glucose deprivation in rat hippocampal slices. Biochem Biophy Res Com 2004; 324:588-596.
62. Kapur P, Wuttke W, Jarry H. Beneficial effects of beta-ecdysone on the joint epiphyseal cartilage tissue and trabecular bone in ovariectomized rats. phytomedecine 2010; 17:350-355.
63. Sarma DNK, Koul S, Khosa RL. Alkaloids from *Tinospora cordifolia* Miers. J Pharm Sci & Res 2009; 1(1):26-27.
64. Rao BR, Kumar DV, Amrutha RN, Jalaja N, Vaidyanath K, Rao AM *et al*. Effect of growth regulators, carbon source and cell aggregate size on berberine production from cell cultures of *Tinospora cordifolia Miers.* Curn Trends Biotech and Pharma 2008; 2 (2):269-276.
65. Gururaj HB, Giridhar P, Ravishankar GA. Micropropagation of *Tinospora cordifolia* (Willd.) Miers ex Hook. F and Thoms– a multipurpose medicinal plant. Cur Sci 2007; 92(1):23-26.
66. Khanapurkar RS, Paul NS, Desai DM, Raut MR, Gangawane AK. *In-Vitro* Propagation OF *Tinospora cordifolia (Wild.)* Miers ex

Hook. F. Thoms. J Bot Res 2012; 3(1):17-20.
67. Raghu AV, Geetha SP, Martin G, Balachandran I, Ravindran PN. *In vitro* Clonal Propagation through Mature Nodes of *Tinospora cordifolia* (WILLD.) HOOK. F. and THOMS: An Important Ayurvedic Medicinal Plant. In *vitro* Cell Dev Bio Plant 2006; 42:584–588.
68. Rana V, Thakur K, Sood R, Sharma V, Sharma TR. Genetic diversity analysis of *Tinospora cordifolia* germplasm collected from north-western Himalayan region of India. J Genet 2012; 91:99-103.
69. Ishnava K, Mohan JSS. Assessment of genetic diversity in medicinal climber of *Tinospora cordifolia* (willd.) Miers (Menispermaceae) from Gujrat, India. Asian Journal of biotech 2009; 14:114-118.
70. Ahmed SM, Verma V, Qazi PH, Ganaie MM, Bakshi SK, Qazi GN. Molecular phylogeny in Indian Tinospora species by DNA based molecular markers. Plant Syst E 2006; 256:75–87.
71. Rajathi K, Vijayaraj D, Anarkali J, Sridhar S. Green Synthesis, Characterization and *In-Vitro* Antibacterial Activity of Silver Nanoparticles By Using *Tinospora Cordifolia* Leaf Extract. Int J Green Chem and Biop 2012; 2(2):15-19.
72. Desai VR, Kamat JP, Sainis KB. An immunomodulator from *Tinospora cordifolia* with antioxidant activity in cell-free systems. Proc Ind Acad Sci (Chem Sci) 2002; 114(6):713–719.
73. Singh S, Srivastava R, Choudhary S. Antifungal and HPLC analysis of the crude extracts of *Acorus calamus*, *Tinospora cordifolia* and *Celastrus paniculatus.* J Agri Tech 2010; 6(1):149-158.
74. Singh N, Kumar A, Gupta P, Chand K, Samant M, Maurya R *et al*. Evaluation of antileishmanial potential of *Tinospora sinensis* against experimental visceral leishmaniasis. Parasitol Res 2007; 102:561–565.
75. Sharma A, Gupta A, Singh S, Batra A. *Tinospora cordifolia* (Willd.) Hook. F. and Thomson - A plant with immense economic potential. J Chem Pharm Res 2010; 2(5):327-333.
76. Sinha K, Mishra NP, Singh J, Khanuja SPS. *Tinospora cordifolia*, Guduchi, a reservoir plant for therapeutic application: A review. Ind. J of Trad Know 2004; 3(3):257-270.
77. Singh SS, Pandey SC, Srivastava S, Gupta VS, Patro B, Ghosh AC. Chemistry and medicinal properties of *Tinospora cordifolia* (guduchi). Ind J Pharma 2003; 35:83-91.
78. Shah S, Ghosh S. *Tinospora cordifolia*: One plant many role. Ancs Life of sci 2012; 31:151-159.
79. Sharma S, Rathi N, Kamal B, Pundir D, Kaur B, Arya S. Conservation of biodiversity of highly important medicinal plants of India through tissue culture technology- a review. Agri and Bio J North America 2010; 1(5):827-833.
80. Rout GR. Identification of *Tinospora cordifolia* (Willd.) Miers ex Hook F. & Thomas Using RAPD Markers. Z. Naturforsch 2006; 61:118-122.
81. Rose MF, Noorulla KM, Asma M, Kalaichelvi R, Vadivel K, Thangabalan B, and Sinha BN. *In vitro* antibacterial activity of methanolic root extract of *Tinospora cordifolia* (willd). IJPRD 2007; 2(5):1-5.
82. Devprakash, Srinivasan KK, Subburaju T, Gurav1 S, Singh S. *Tinospora cordifolia*: A Review On Its Ethnobotany, Phytochemical & Pharmacological Profile. Asian J Biochem and Pharma Res 2011; 1(4):291-302.
83. Maridass M, De-Britto AJ. Origins of Plant Derived Medicines. Ethno botanical Leaflets 2008; 12:373-387.
84. Sonaimuthu V, Krishnamoorthy S, Johnpaul M. Taxol producing endophytic fungus Fusarium culmorum SVJM072 from medicinal plant of Tinospora cordifolia - a first Report. J of Biotech 2010; 09:425.
85. Patel MB, Mishra SM. Magnoflorine from Tinospora cordifolia stem inhibits a-glucosidase and is antiglycemic in rats. J of Functional Foods 2012; 4:79–86.

86. Sangeethaa MK, Priya CDM, Vasanthia HR. Anti-diabetic property of Tinospora cordifolia and its active compound is mediated through the expression of Glut-4 in L6 myotubes. Phytomedicine 2013; 20:246–248.
87. Kapura P, Pereiraa BMJ, Wuttke W, Jarry H. Androgenic action of Tinospora cordifolia ethanolic extract in prostate cancer cellline LNCaP. Phytomedicine 2009; 16:679–682.
88. Mallick S, Prakash BS. Effects of supplementation of Tinospora cordifolia to crossbred cows peripartum. Animal Reproduction Science 2011; 123:5–13.
89. Jayaganthan P, Perumal P, Balamurugan TC, Verma RP, Singh LP, Pattanaik AK *et al*. Effects of Tinospora cordifolia supplementation on semen quality and hormonal profile in rams. Animal Repro Sci 2013; 140:47–53.
90. Nagarkar B, Kulkarni R, Bhondave P, Kasote D, Kulkarni O, Harsulkar A *et al*. Comparative Hepatoprotective Potential of Tinospora cordifolia, Tinospora sinensis and Neem-guduchi. British J of Pharma Res 2013; 3(4):906-916.
91. The anti-mycobacterial activity of Tinospora Cordifolia medicinal plant used for the treatment of leprosy and Tuberculosis. Int J of Sci & Eng Res 2013; 4(6):2953-2932.
92. Jayaseelan C, Rahuman AA, Rajakumar G, Kirthi KV, Santhoshkumar T, Marimuthu S *et al*. Synthesis of pediculocidal and larvicidal silver nanoparticles by leaf extract from heartleaf moonseed plant, Tinospora cordifolia Miers. Parasitol Res 2011; 109:185-194.
93. Tan RX, Zou WX. Endophytes: a rich source of functional metabolites. Nat Prod Rep 2001; 18:448-459.
94. Strobel G, Daisy B. Bioprospecting for Microbial Endophytes and Their Natural Products. Microbio Mol Biol Rev 2003; 67:4491-502.
95. Gaiero JR, Mc-Call CA, Thompson KA, Day NJ, Best AS, Dunfield KE. Inside the root micro biome: Bacterial root endophytes and plant growth promotion. Am J Bot 2013; 100(9):1738-1750.
96. Singh A, Sharma MM, Batra A. Synthesis of gold nanoparticles using Chick pea leaf extract using green chemistry. J of Optoelectronics and Biomed Maters 2013; 5(2):27–32.
97. Singh A, Jain D, Upadhyay MK, Khandelwal N, Verma HN. Green Synthesis of Silver Nanoparticles using *Argemone mexicana* Leaf Extract and Evaluation of their Antimicrobial Activities. Dig J of Nanomater and Biostr 2010; 5(2):483-489.
98. Thirumurugan T, Kaur K. Biological Synthesis and Characterization of Gold Nanoparticles from Pomegranate. Int J of Future Biotech 2013; 2(2):1-11.
99. Asghari G, Varshosaz J, Shahbazi N. Synthesis of silver nanoparticle using Portulaca oleracea L. extracts. Nanomedicine journal 2014; 1(2):94-99.
100. Pasca RD, Mocanu A, Cobzac SC, Petean I, Horovitz O, Cotisel MT. Biogenic Syntheses of Gold Nanoparticles Using Plant Extracts. Partic Sci and Tech An Int J 2014; 32(2):131-137.
101. Joladarash D, Chilkunda ND, Salimath PV. Glucose uptake-stimulatory activity of *Tinospora cordifolia* stem extracts in Ehrlich ascites tumor cell model system. J Food Sci Technol 2014; 51(1):178-182.