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Tinospora cordifolia: The Miracle plant

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Abstract
Traditionally, *Tinospora cordifolia* (Guduchi; family-Menispermaceae) used in the Ayurvedic system of medicine. Guduchi is a large, glabrous, perennial, deciduous, climbing shrub of weak and fleshy stem mostly found in tropical and sub-tropical areas of India, Myanmar and Sri Lanka. The isolated chemical constituent(s) belong to different classes, such as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides. Various properties of Guduchi described in ancient texts of Ayurveda, like Rasayana, Sangrahi, Balya, Agnideepana, Tridoshshamaka, Dahnashaka, Mehnashaka, Kasa-swasahara, Pandunashaka, Kasa-kushta-vataraktanashaka, Jwarhara, Krimihara, Prameha, Arshnashaka, Kricch-hridroganashak etc. are acquiring scientific validity through pharmacological approach. Potential medicinal properties reported by scientific research include immunomodulatory, anti-HIV, anti-allergic, anti-diabetes, anti-toxic, anti-arthritic, anti-osteoporotic, anti-cancer, anti-microbial, anti-oxidant, anti-pyretic, anti-inflammatory, analgesic, anti-stress, anti-neoplastic, radio protective, hepatoprotective, anti-leprotic, gastrointestinal, anti-ulcer, diuretic, cardio protective, anti-fertility, neuroprotective and effect on many other diseases. This review has genetic diversity, phytochemical and pharmacological reports.

Keywords: *Tinospora cordifolia*, Anti-pyretic, Guduchi, Giloy, Stem, Fruit and Bark

1. Introduction
Tinospora cordifolia also named as "Guduchi". It belongs to family Menispermaceae. It is a diversified plant having heart shaped leaves, greyish creamy and succulent bark, lenticels with deep clefts, cylindrically long root, yellow colour flowers, red fruits and most often grows on Neem and Jamun trees [1-3]. The male flowers are clustered and female flowers are present in solitary conditions. The flowering season expands over summer and winters. There are different kinds of active compounds and phytoconstituents including alkaloids, steroids, diterpenoid lactones, aliphatic and glycosides isolated from different type of parts [4]. Now a days this plant becomes more prominent because of its medicinal properties including immunomodulatory, anti-HIV, anti-allergic, anti-diabetic, anti-toxic, anti-arthritic, anti-osteoporotic, anti-cancer, anti-microbial, anti-oxidant, anti-pyretic, anti-inflammatory, analgesic, anti-stress, anti-neoplastic, radio protective, hepatoprotective, anti-ulcer, diuretic, cardio protective, anti-fertility, neuroprotective etc. [4-9]. In this review article we focus on the diversification, medicinal properties, biological roles, isolated phytoconstituents and reported activities in human and animals.

1.1 The genus *tinospora*
The *Tinospora* genus includes 34 species. Many species are used for traditional remedies out of 34 in the tropical and sub-tropical regions of Asia, Australia and Africa. A large, deciduous, glabrous and climbing type of shrubs are present in this genus. *Cordifolia* is medicinally very important specie also named as "Giloy" most often found at 300 m height of tropical region of India and some part of China [10].

1.1.1 Search criteria
Published literature on recent developments in research up to 2016 on *Tinospora cordifolia*, including original articles and papers in NCBI PubMed, PubMed Central Databases, PubChem, Science Direct, Wiley Online Library and AYU were taken into study for the report.

1.1.2 Inclusion criteria
All the reports of experiments on different model types (*in vitro*, *ex vivo*, and *in vivo*) were taken varying from animal and human model systems.

Reported data was analysed and represented in this current review. The figures of the compounds were obtained as reported in different journal sources.

2. *Tinospora cordifolia*: A genetically diverse plant

There are different plant markers which identified the morphological and physiological characters includes stem diameter, plant length, floral morphology, growth habit, stomatal density, flower colour, lenticels density, trichomal density, plant biomass, petiole length and some other characteristics of this specie, which indicates the diversity of this medicinal plant. This diversified information has its own importance for the effective management of plant genetic resources. There are many reports which shows the genetic variation among the plant population including amplified polymorphic DNA, inter-simple sequence repeat primer etc. but there are very few reports on the conservation and micro-propagation of this medicinally important plant with the help of plant tissue culture technology [3, 11].

3. Phytochemical characterization

A number of chemical compounds and phyto-constituents have been isolated from *T. cordifolia* belongs to different class. The plant leaves are very rich source of protein, calcium and phosphorus [12]. There are four clerodone furano diterpene glucosides (A, B, C and D) have been isolated from stem and the structures were elucidated with the help of spectroscopic methods [13]. There is an isolation of glycosyl component of polysaccharide from *T. cordofolia* and followed by purification, methylation, hydrolization, reduction and acetylation. There is partially methylated alditol acetate (PMAA) derivative has been obtained and subjected to GC-MS studies. There are many types of linkages have been reported including: Terminal glucose, 4-xylose, 4-glucose, 4, 6-glucose and 2, 3, 4, 6-glucose [14, 15]. There is an establishment of callus and cell suspension cultures from the explant (stem) of this plant. There is an accumulation of berberine and jatrorrhizine observed during callus and cell suspension cultures [16]. The signalling mechanism has been reported in macrophages for the evaluation of its immuno-stimulating properties of isolated novel (1,4)-alpha-D-glucan (RR1) compound [17]. There is an isolation of arabinogalactan from dried stem and examination is done by methylation, partial hydrolysis and carboxyl reduction. The polysaccharide showed the mitogenic activity against B-cells after purification [18].

3.1. Nutritive Composition of *Tinospora cordifolia*

T. cordifolia contains high fibre (15.9%), sufficient protein (4.5%-11.2%), sufficient 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 sufficient calcium (0.131%), important in various regulatory functions [19].

4. Traditional uses

Traditional uses of *T. cordifolia* are described in Table 1.

Table 1: Traditional uses of *T. cordifolia*

S. No.	Plant part	Traditional Uses	References
1.	Leaves	Treatment of gout and ulcer.	[20]
2.	Stem	Treatment of bitter stomach. As stimulant for bile secretions. As diuretic. To enrich the blood. Treatment of jaundice. Treatment of skin diseases. Treatment of diabetes. Treatment of vaginal infection and used for the proper vaginal and urethral discharge. Treatment of fever. Treatment of enlarged spleen.	[20]
		Treatment of worms in intestine. Treatment of sore eyes. Treatment of syphilitic sores. Treatment of malaria. Treatment of diarrhea. Treatment of dysentery. Treatment of indigestion.	[21]
3.	Stem & Root	Used as an antidote for snake and scorpion bite.	[22-24]
4.	Fruit	Treatment of jaundice and rheumatism.	
5.	Bark	Treatment of allergy, spasmosis and leprosy.	[25-27]

4.1 Alternative and complementary medicinal uses

Tinospora cordifolia is also used to cure the urinary diseases, syphilis, skin diseases, and bronchitis [28]. It also promotes longevity, increase the body's resistance and stimulate the immune system [29-31].

5. Morphology

As we discussed above in the introduction and the genus section that the *Tinospora cordifolia* has spreading and climbing nature with many coiling branches. The flowers on this plant are growing in lax racemes from nodes of old wood. The color of the fruits turned to red when they ripe [1].

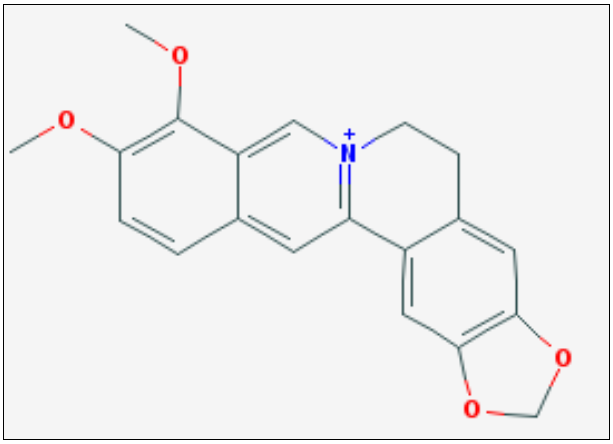
6. Phytoconstituents

Table 2: Phytoconstituents of *Tinospora cordifolia* and their biological roles

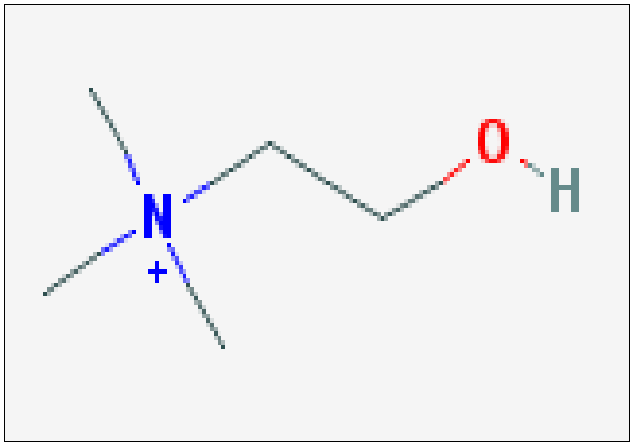
Active components type	Compounds	Source	Reported biological effect in animals	In human cell lines	References
Alkaloids	Berberine, Choline, Palmatine, Tembetarine, Magnoflorine, Tetrahydropalmatine, Tinosporin, Isocolumbin, Jatrorrhizine, N-formylasimilobine 2-0-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl (tinoscerside A, 1), Aporphine alkaloids N-acetylasimilobine 2-0-β-D- glucopyranosyl-(1→2)-β-D-glucopyranosyl (tinoscerside A, 2)	Stem, Root	Isoquinoline alkaloids have anti-cataract potential in roots. Anti-oxidant activity in mice, anti-cancer in ehrlich ascites carcinoma (EAC) mice, hypoglycaemia activity in RINm5F rat insulinona cell line.	Anti-cancer, anti-viral infection, inflammation and immuno-modulatory roles. Neurological, psychiatric conditions, anti-diabetes.	[4, 11, 32-37]
Glycosides	18-norclerodane glucoside, Furanoid diterpene glucoside, Tinocordifolioside, Cordioside, Palmatoside, Syringin, Syringin-apiosylglycoside	Stem	Cytotoxic action, protection against iron-mediated lipid peroxidation of rat brain homogenate, anti-oxidant activity and hydroxyl radical scavenging activities in Swiss albino rat.	Treats neurological disorders like ALS, Parkinson's, dementia, motor and cognitive deficits and neuron loss in spine and hypothalamus Immunomodulation: IgG increase and macrophage activation. Inhibits NF-Kb and act as nitric-oxide scavengers to show anti-cancer activities.	[10, 15, 38-47]
Diterpenoid lactones	Furanolactone, Clerodane derivatives [(5R, 10R)-4R-8R-dihydroxy-2S-3R:15, 16-diepoxy-cleroda-13(16)], Tinosporides, Tinosporon, Columbin	Whole plant	Chemo preventive potential in diethylnitrosamine (DEN) induced hepatocellular carcinoma (HCC) in rats.	Vasorelaxant: relaxes norepinephrine induced contractions. Inhibits Ca ++ influx. Anti-inflammatory, anti-microbial, anti-hypertensive, anti-viral. Induce apoptosis in leukemia by activating caspase-3 and bax, inhibits bcl-2.	[47-52]
Sisquiterpenoid, Aliphatic compounds	Tinocordifolin, Heptacosanol, Nonacosan-15-one dichloromethane, Tinosporidine, Cordifol, Cordifelone, N-trans-feruloyl tyramine as diacetate, Giloinin, Octacosanol	Whole plant, Stem, Root	Radiosensitizing activity in ehrlich ascites carcinoma mice. Modulating the pro-inflammatory cytokines. Inhibits proliferation of endothelial cells and ehrlich ascites tumor cells.	Anti-nociceptive and anti-inflammatory. Protection against 6-hydroxydopamine induced parkinsonism in rats. Down-regulate VEGF and inhibits TNF-α from binding to the DNA.	[10, 33, 53-55]
Steroids	B-sitosterol, 20 β-Hydroxy ecdysone, Ecdysterone, Makisterone A, Giloinsterol, Giloinsterol jateorine	Stem, Aerial parts	Beta-ecdysone shows anabolic and anti-osteoporotic effect in mammals.	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-1β, IL-6 and cox-2. Activates NF-kb.	[10, 56-59]
Others	Tinosporic acid, 3, (α, 4-dihydroxy-3-methoxy-benzyl)-tetrahydrofuran, Giloin,	Whole plant, Root	Insulin-mimicking and insulin-releasing effect. Enhanced phagocytic activity of milk polymorph nuclear cells in bovine subclinical mastitis.	Protease inhibitors for HIV and drug resistant HIV. Tyramine is a neuro-modulator. Used to treat anxiety and depression by inactivating neurotransmitters.	[10, 36, 60-63]
Miscellaneous compound	Nonacosan-15-one 3, (a,4-dihydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxy-benzyl)-tetrahydrofuran, Tinosporidine, 6 cordifol, 6 Cordifelone, 6 Jatrorrhizine	Whole plant	Radio sensitizing activity in ehrlich ascites carcinoma mice Modulating the pro-inflammatory cytokines. Inhibits proliferation of endothelial cells and ehrlich ascites tumor cells.	Anti-nociceptive and anti-inflammatory. Protection against 6-hydroxy dopamine induced parkinsonism in rats.	[10, 33, 53-55]

NF-kB= Nuclear factor Kappa-B, VEGF= Vascular endothelial cell growth factor
TNF= Tumor necrosis factor
IL= Interleukin
COX= Cyclooxygenase
ALS= Amyotrophic lateral sclerosis
IgG= Immunoglobulin G
IgA= Immunoglobulin A

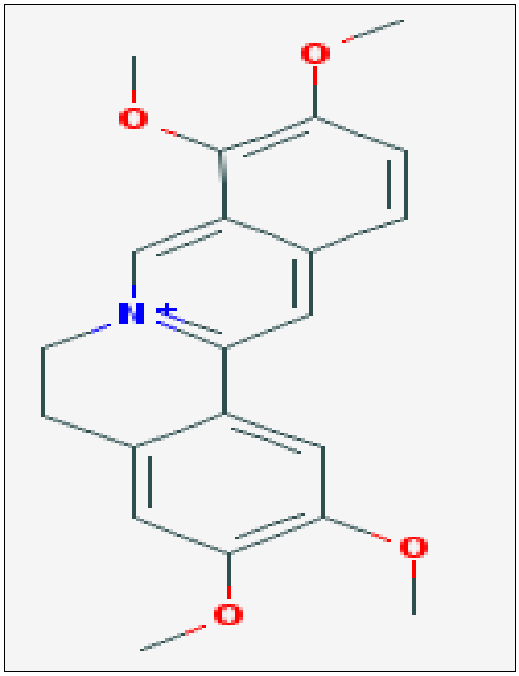
7. Structures of some major isolated compounds are mentioned below in fig. 1 (I TO XVIII)



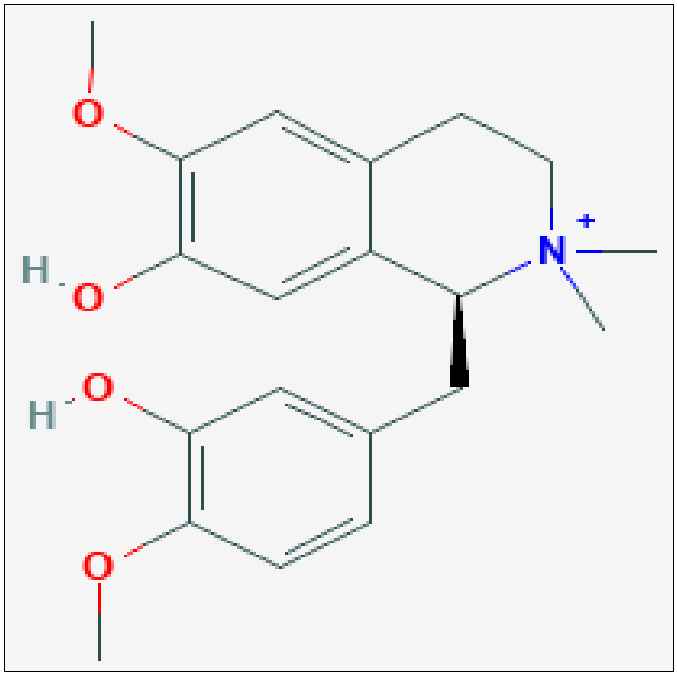
(i) Berberine



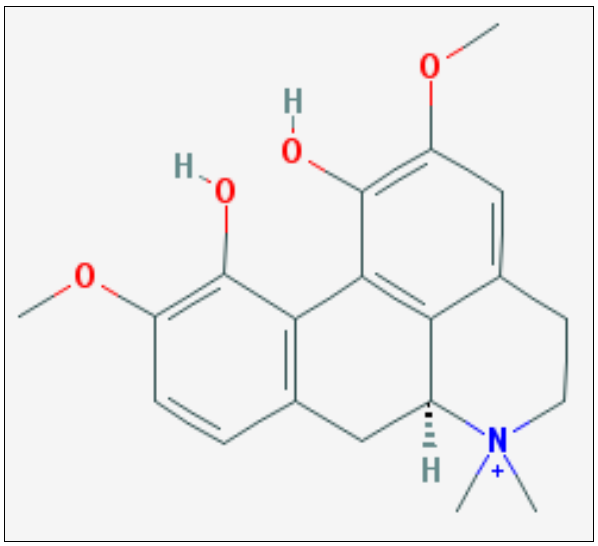
(ii) Choline



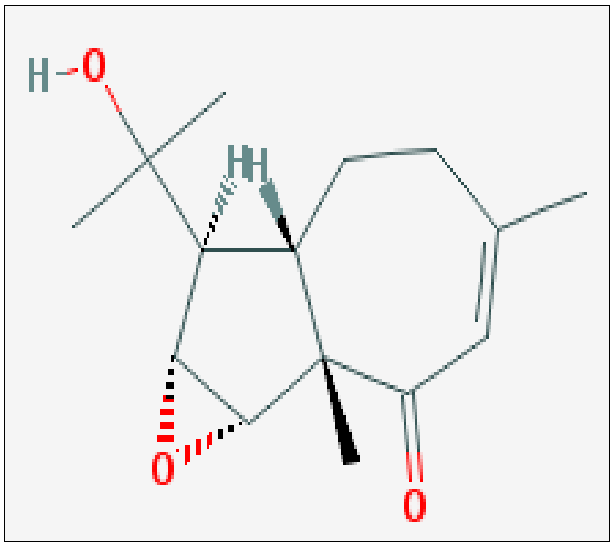
(iii) Palmatine



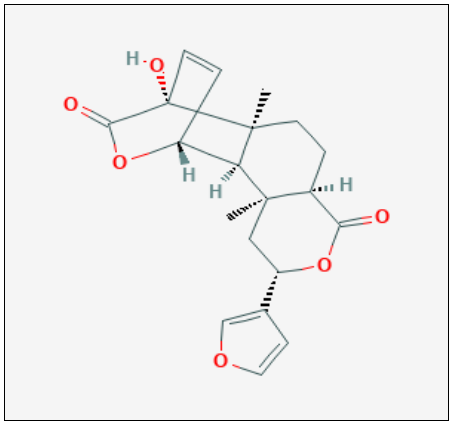
(iv) Tembetarine



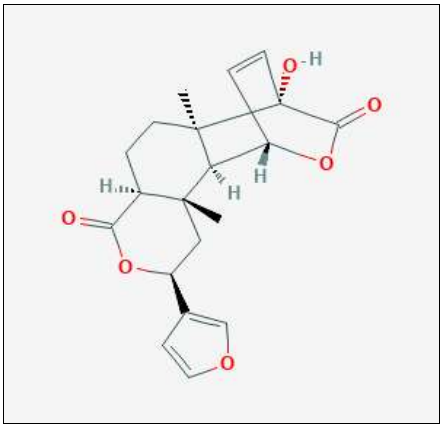
(v) Magnoflorine



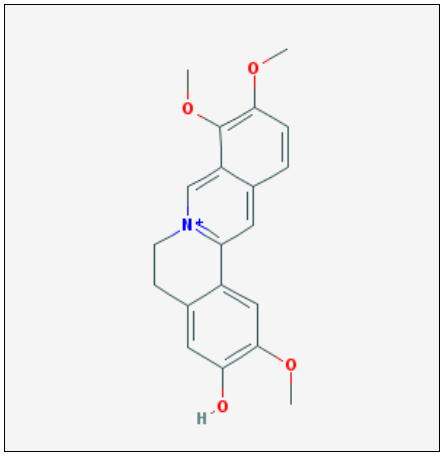
(vi) Tinocordifolin



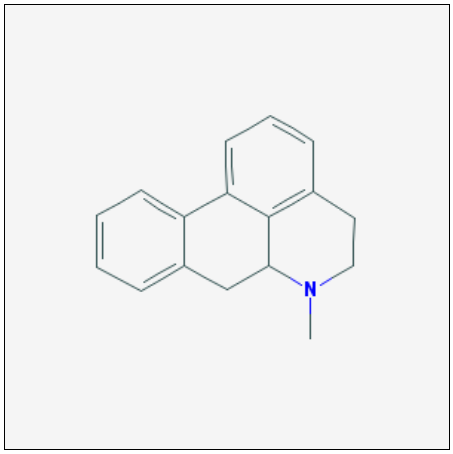
(vii) Tinosporin



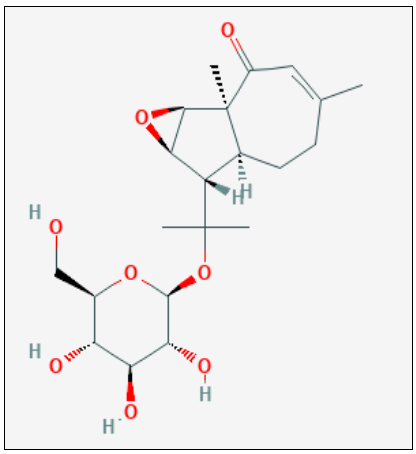
(viii) Isocolumbin



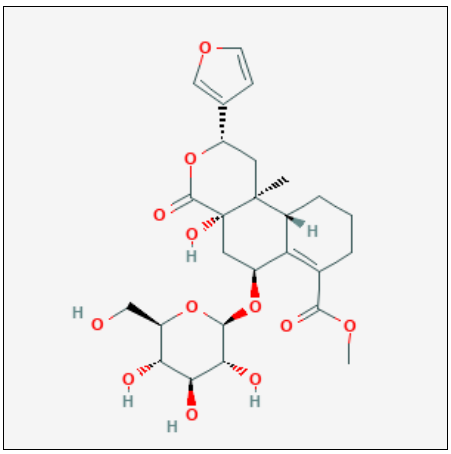
(ix) Jatrorrhizine



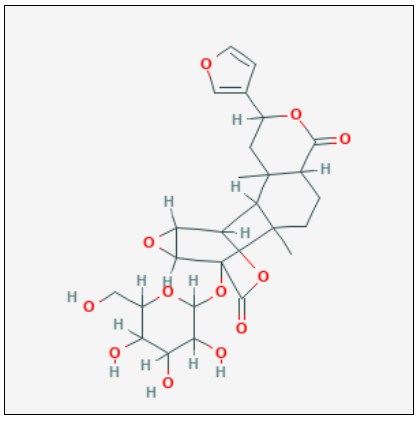
(x) Aporphine alkaloids



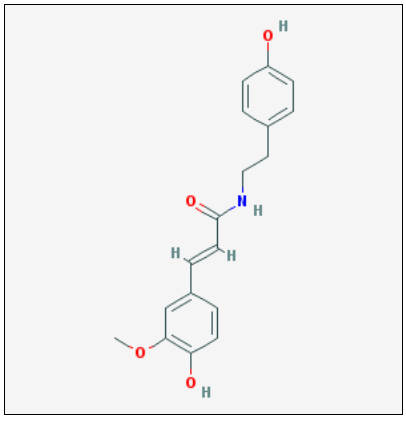
(xi) Tinocordifolioside



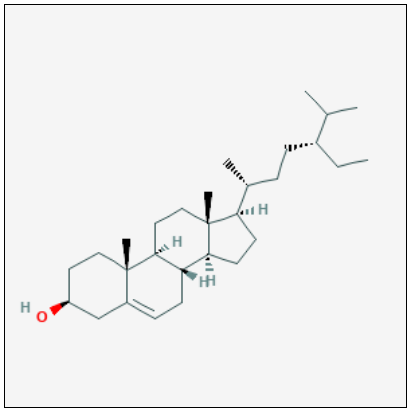
(xii) Cordioside



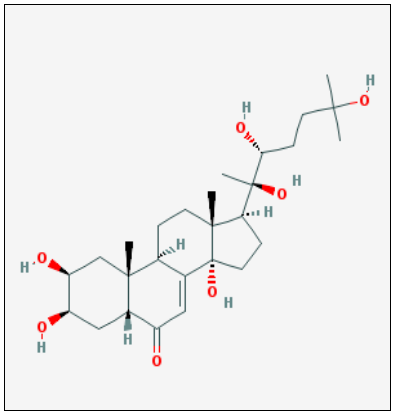
(xiii) Palmatoside



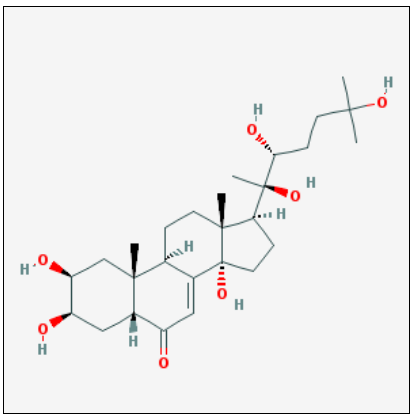
(xiv) N-trans-feruloyl tyramine



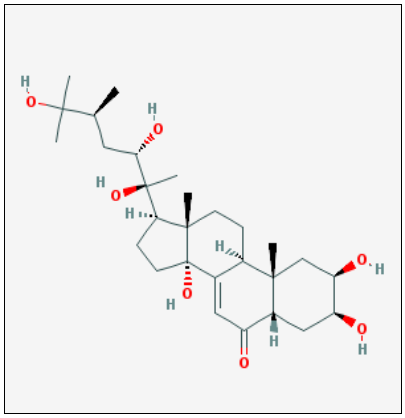
(xv) Beta sitosterol



(xvi) 20 beta hydroxy ecdysone



(xvii) Ecdysterone



(xviii) Makisterone A

Source: From PubChem Compound – NCBI

8. Some important phytochemicals and their action

Table 3: Mechanism of action of some important phytochemicals

Phytochemicals	Activity	Mechanism of action	References
Quinones	Antimicrobial	Binds to adhesions, complex with cell wall, inactivate enzymes.	[24, 64-75]
Flavonoids	Antimicrobial	Complex with cell wall, binds to adhesins Inhibits release of autacoids and prostaglandins.	
	Antidiarrheal	Inhibits contractions caused by spasmogens, stimulates normalization of the deranged water transport across the mucosal cells, Inhibits GI release of acetylcholine.	
Polyphenols and Tannins	Antimicrobial	Binds to adhesions, enzyme inhibition, substrate deprivation, complex with cell wall, membrane disruption, metal ion complexation.	
	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 diarrhoea, astringent action.	
	Anthelmintic	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.	
Coumarins	Antiviral	Interaction with eukaryotic DNA.	
Terpenoids and essential oils	Antimicrobial and Antidiarrheal	Membrane disruption and Inhibits release of autocoids and prostaglandins.	
Alkaloids	Antimicrobial	Intercalates into cell wall and DNA of parasites.	
	Antidiarrheal	Inhibits release of autocoids and prostaglandins.	
	Anthelmintic	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 helminths, acts on CNS causing paralysis.	
Lectins and Polypeptides	Antiviral	Blocks viral fusion or adsorption, forms disulphide bridges.	
Glycosides	Antidiarrheal	Inhibits release of autocoids and prostaglandins.	
Saponins	Antidiarrheal	Inhibits histamine release *in vitro*.	
	Anticancer	Possesses membrane permeabilizing properties.	
	Anthelmintic	Leads to vacuolization and disintegration of teguments.	
Steroids	Antidiarrheal	Enhance intestinal absorption of Na+ and water.	

Table 4: Source for some of the above chemicals

Part	Chemical type	Active principle	Reference
Stem	Alkaloids	Berberine, Palmatine D, Choline D, Tinosporine, Magnoflorine, Tetrahydropalmatine, Isocolumbin	[10]
Stem	Glycosides	18-norclerodane glycoside, Furanoid diterpene Glycoside, Tinocordiside, Syringin, Syringin-apiosylglycoside, Tinocordifolioside, Cordioside, Cordifolioside A, Cordifolioside B, Palmatoside C31, Palmatoside F31, Cordiofoliside B2, Cordifoliside D2, Cordifoliside	
Stem	Sesquiterpenoid	Tinocordifolin	
Root	Alkaloid	Palmatine	
Aerial parts	Steroids	B-sitosterol, D-sitosterol, g-sitosterol B-hydroxyecdysone, Ecdysterone, Makisterone, Giloinsterol jateorine, Columbin	
Whole plant	Diterpenoid lactones	Furanolactone, Tinosporon, Columbin	
Whole plant	Aliphatic compound	Octacosanol, Heptacosanol	
Whole plant	Miscellaneous compound	Nonacosan-15-one 3, (a, 4-dihydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxy-benzyl)-tetrahydrofuran, Tinosporidine, 6 Cordifol, 6 Cordifelone, 6 Jatrorrhizine	

Using above mentioned potent chemical compounds from this plant species, various pharmaceutical market products have been produced by different companies are mentioned in table 5.

Table 5: Pharmaceutical products of *Tinospora cordifolia* and their biological roles

Name of market products	Biological Roles	Reference
Tinospora cordifolia pellets	To treat a number of diseases	[1]
Guduchi	For the immune system	
Safe herb	To Cure the anaemia and sexual disabilities	
Brave heart capsule	For lipid and cholesterol level in body	
Cirrholiv capsule	For Hepato-protective	
Cirrholiv syrup	For Hepato-protective	
Mussafen	To purify the Blood and for Anti-allergic	
Madhumehari	For urinary problems, maintain blood sugar, fatigue	
Tonples	To Increase the immunity	
Rebuild	For Anti- stress and Anti-oxidant	

8.1 Ayurvedic Pharmacology (Dravya Guna-Karma) of *Tinospora cordifolia* (Guduchi)

Ayurvedic pharmacology is based on biophysical, experiential, inferential and intuitional mechanisms. The action of a substance is based on five mechanisms of action or attributes of a substance namely *rasa* (taste appreciation of the substance by the chemical receptors on the tongue — Six tastes are described namely sweet (*madhura*), sour (*amla*), salty (*lavana*), bitter (*tikta*), pungent (*katu*)and astringent (*kasāya*), *guna* (10 pairs of opposite or mirror image attributes; attribute or property of any substance), *vipaka* (intestinal digestion and tissue metabolism; *madhura*-neutral, *amla*- acidic, *katu*- alkaline), virya (potency; *ushna*-hot, *sheeta*- cold) and *prabhav* (specific action through specialized receptors). All these mechanisms related to drug action are biophysical in nature. *Karma* is the action that involves the activity or performance. It is the final effect of the drug. The properties, action (pharmacodynamics) and uses (indication) of *T. cordifolia* are given in Table 6.

Table 6: Ayurvedic properties (dravya-guna) of *Tinospora cordifolia* (Guduchi)

Rasa	Guna	Virya	Vipaka	Prabhava	References
Tikta, Kasaya	Laghu, Guru, Snigdha	Ushna	Madhura	Vishaghna	[76, 77]

9. Pharmacological reports

The Survey of literature was revealed that *T. cordifolia* has been investigated for various pharmacological activities which are mentioned in the Table 7. The different crude extracts, fractions of plant and isolated compounds from the plant have been employed for the scientific studies.

The literature of plant included pharmacological activities, plant part used, extracts, fractions, isolates, tested doses of samples and positive controls along with their route of administration, *in vivo* and *in vitro* experimental models, animals used in *in vivo* experimental models, experimental studies, designs, parameters assessed during studies, sort of mechanism and inference concerned with activity and references.

Table 7: Pharmacological activities reported for *T. cordifolia*

S. No.	Pharmacological Activity	Plant part / Extract / Fraction / Isolate / Compound / Formulation	Doses tested / Route of administration	Positive control	Subjects	Experimental studies / Design / Model / Parameters assessed during studies / Some sort of mechanism action	Inference in concern with activity	References
1.	Neuroprotective effect	Aerial parts/Ethanol extract	200/400 mg/kg orally	Levodopa 6 mg/kg intracerebral	Rat	6-hydroxy dopamine lesion rat model of Parkinson's disease	Shown significant effect	[6]
2.	Antiulcer activity	Whole plant/Ethanol and Aqueous extract	250/500 mg/kg orally	Ranitidine 50 mg/kg orally	Rat	Pylorus ligation induced ulcer	Shown significant activity	[78]
3.	Antidiarrhoel activity	Whole plant/Ethanol and Aqueous extract	250/500 mg/kg orally	Loperamide 3 mg/kg orally	Rat	Castor oil and magnesium sulphate induced diarrhea	Shown significant activity	[78]
4.	Analgesic activity	Whole plant/Ethanol extract	300 mg/kg orally	Rentazocine 10 mg/kg I.P.	Rat	Hot plate and abdominal writhing method	Shown significant activity	[5]
5.	Aphrodisiac property	Aqueous and hydro alcoholic extract	200/400 mg/kg orally	Sildenafil citrate 4.5 mg/kg orally	Rat	Assessed the sexual behavior	Shown significant moderate activity at lower and higher activity at higher dose	[79]
6.	Immunomodulatory activity	Whole plant / Aqueous Extract	40 mg/kg orally	Isotonic saline 0.1 ml I.P.	Mice	CCl4 intoxicated mice	Shown significant activity	[80]
7.	Antidyslipidemic activity	Stem extract	500 mg/kg orally	Glibenclamide 0.6 mg/kg orally	Rat	Alloxan induced diabetic adult rat	Shown significant activity	[81]
8.	Antioxidant activity	Whole plant/Ethanol Extract	300 mg/kg orally	Normal saline 0.9% orally	Rat	n-nitrosodiethylamine induced liver cancer	Shown significant activity	[82]
9.	Anti-inflammatory activity	Stem/Aqueous extract	50 mg/kg orally	Tap water 1 ml/100g Orally	Rat	Carrageenan induced paw edema model	Shown significant activity	[7]
10.	Gastro protective activity	Whole plant	400/600 mg/kg orally	Rantidine 20 mg/kg orally	Rat	Aspirine and ethanol induced gastric mucosal lesions	Shown significant activity	[83]
11.	Nootropic effect	Stem/Ethanol extract/n-butanol Fraction	100/200 mg/kg orally	Piracetam 250 mg/kg orally	Mice	Elevated plus maze model	Shown significant activity	[84]
12.	Radio protective and Cytoprotective activity	Stem/Ethanol extract	80/120 mg/kg I.P.	Tocopheryl acetate 300 mg/kg I.P.	Mice	4 G-γ radiation and cyclophosphamide induced genotoxicity	Shown significant activity at higher dose	[85]
13.	Antifeedant activity	Whole plant/Chloroform extract	15/30 µg/cm2 of Disc	Azadirachtin- A 0.5 µg/cm2 of disc	Microbes	Microbial biological assay	Shown efficacy	[86]
14.	Ameliorative effect	Root/Ethanol extract	50/100/200 mg/kg orally	Normal saline 0.9%	Mice	Animal exposed to aflatoxin B1	Shown significant improvement	[33]
15.	Cardio protective effect	Whole plant/Alcohol extract	150/300/450 I.V.	Verapamil 5 mg/kg I.V.	Rat	Calcium chloride induced arrhythmia	Shown significant activity	[87]
16.	Hepatoprotective effect	Whole plant/Ethanolic Extract	200 mg/kg orally	Silymarin 25 mg/kg orally	Rat	CCl4 induced hepatotoxicity	Shown significant activity	[88]
17.	Hypoglycemic activity	Stem/Aqueous extract	50/100/200 mg/kg orally and 10/20/40 mg/kg orally	-	Rat pancreatic cell lines	Insulin released effect was assessed in cell lines	Shown significant activity	[36]
18.	Antipsychotic activity	Aqueous/Ethanol extract	250/500 mg/kg orally	Haloperidol 1 mg/kg I.P.	Mice	Amphetamine challenged mice model	Shown no activity	[89]
19.	Antidepressant activity	Pet. Ether extract	50/100/200 mg/kg orally	Imipramine 15 mg/kg orally, Sertraline 20 mg/kg orally	Mice	Tail suspension test and forced swim test	Shown no activity	[90]
20.	Antiosteoporotic activity	Stem/Ethanol extract	10/50/100 mg/kg S.C.	E(2) 1µg/day S.C.	Rat	Female Sprague dawley rat model	Shown mild activity	[28]
21.	Antineoplastic activity	Aerial parts/DCM extract	25/30/40/50/100 mg/kg I.P.	-	Mice	Ehrlich ascites carcinoma induced model	Shown significant activity	[57]
22.	Antifertility effect	Stem/Methanol extract	100 mg/kg orally	-	Male rat	Assessed the Sexual behavior parameters	Shown significant activity	[91]

23.	Antiasthamatic activity	Stem/Hydro-alcoholic extract	100 mg/kg orally	Dexamethasone 1 mg/kg orally	Mice	Intranasal oval bumin in vivo asthma model	Shown protective effect	[92]
24.	Antitumor activity	Aqueous alcoholic extract	10-1000 µg/ml	-	-	Reduction the cell proliferation	Shown significant activity	[93]
25.	Diabetic neuropathy	Stem/Aqueous extract	100/200/400 mg/kg orally and 5/10/25/50/100/200 µg/ml	Glibenclamide 5 mg/kg + Metformin 25 mg/kg orally	Rat	Streptozotocin induced diabetes and Aldose reductase inhibition assay	Shown significant activity	[94]
26.	Hepatocellular carcinoma	Aerial parts/Ether extract	10 mg/kg orally	-	Rat	Diethyl nitrosamine induced hepatocellular Carcinoma	Shown significant activity	[95]
27.	Antimalarial activity	Stem/ Ethanolic extract	500 mg/kg orally	Chloroquine 4 mg/kg orally	Mice	Microbe used *Plasmodium berghei* on white Swiss mice Model	Shown significant activity	[96]
28.	Antibacterial activity	Stem/Aqueous and Ethanolic/Chloro-form extract	0.2 ml	-	Microbes	Microbial inhibition assay	Shown significant high, moderate, less and low activity against different selected microbes	[97]
29.	Anticancer activity	Aqueous and Ethanolic extract	-	-	-	IMR 32 human neuro-blastoma cell lines as a model	Shown significant activity	[98]
30.	Antipyretic activity	Formulation *guduchi ghrita*	900/1800 mg/kg orally	Paracetamol 100 mg/kg S.C.	Rat	Yeast induced pyrexia model	Shown significant activity	[99]
31.	Antipyretic activity	Whole plant/Aqueous extract	-	-	Mice	Yeast induced pyrexia model	Shown significant activity	[100]
32.	Allergic rhinitis	Aqueous extract	-	-	-	Double blind placebo controlled trial	Shown significant activity	[101]
33.	Anti HIV activity	Whole plant/aqueous extract	-	-	HIV Patient	Immunomodulatory effects were assessed in HIV patients	Shown significant activity	[102]

CCl4: Carbon tetra chloride; HIV: Human Immuno deficiency Virus; Route of administration: I.P.: Intraperitoneal, I.V.-Intravenous, S.C.: Subcutaneous

10. Effects on other diseases

Tinospora cordifolia inhibits the proliferation of endothelial cells and Ehrlich ascites tumor cells due to the octacosanol which is one of the important isolated chemical constituent from this herb, inhibits neovascularization induced by angiogenic factors in chick chorioallantoic membrane and in rat cornea *in vivo* angiogenesis assays and also inhibits secretion of ascites fluid in the growing tumor cells *in vivo* by inhibiting activity of matrix metalloproteinases (MMPs) and translocation of transcription factor nuclear factor-kappa-B (NF-KB) to nucleus [94]. The 70% methanolic extract of *Tinospora cordifolia* stem reduces the sperm motility and density, lowering of serum testosterone, protein, sialic acid, glycogen contents, and depletion of vesicular fructose of testes leading to reduction of male fertility in rats through Oral administration [24].

11. Discussion

Tinospora cordifolia has been used in traditional Ayurvedic medicine used for the treatment of many diseases from ancient times. Recent reports have shown the isolated chemical constituent(s) from *Tinospora cordifolia* extract and their biological roles their medicinal properties may be exploited for the production of new formulations, which may be better, safer and promising one over the allopathic drugs. Effective conservation strategies of the germplasm for such an economically important medicinal plant with many biological role remains yet to be accomplished.

12. Conclusions

The medicinal properties of the *Tinospora cordifolia* in Ayurvedic texts have been validated by a remarkable body of modern evidence suggesting that this drug has immense potential in modern pharma-co-therapeutics.

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