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Brief Review On Tinospora Cordifolia, Its Phytochemical, Pharmacological Properties And Ayurvedic Formulation Of Tinospora Species

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Abstract: In the india, traditional indian system of medicine AYUSH (Ayurveda, Yoga, Unani, Siddha and Homeopathy) is widely used from ancient time. Ayurveda is a comprehensive, natural health care system that originated in the ancient vedic times of india. Tinospora Cordifolia is used as ayurvedic formulation from ancient time. The aim of this review article explore about various phytochemical, pharmalogical activities and ayurvedic formulation of Tinospora Cordifolia. Tinospora Cordifolia also called as heart leaved moonseed, amrita, gurbel, giloy or guduchi(in Sanskrit) is a herb of the family Menispermaceace. It is native torrid areas of India, Srilanka, Myanmar, Australia and Africa. It is attracted attention in the last few 10 years becaue whole part of plant like roots, stems and leaves are used in folk medicine and the ayurvedic system of medicine alonen and use in combination with other plant for treating several diseases. Tinospora cordifolia is broadly acknowledge as a important plant in the indian system of medicines due to its biological active componds and has been therapeutic used in disease like diabetes, jaundice, stomachache, urinary promblems, cancer, fever, helminthiasis, leprosy, skin aliments dysentery, prolonged diarrhea and many more. T. cordifolia has a rich sources of phytochemicals that extract used as medicnal properties. Phytochemical present in T. cordifolia is alkaloids, steroids, glycosides, diterpenoid lactones, phenloics, aliphatic compound and polysaccharides.

Keywords: Pharmacognosy, Cultivation, Phytochemistry, Pharmacological activity, Ayurvedic formulation

Introduction: History of T. cordifolia is when Ravana, the majesty of Lanka and the god of the rakshasa, capture Rama's wife, Sita from the forest, driven by lust, the powerful Rama is surrounded by monkey soldiers, destroyed that enemy who had theft is wife, on the battleground. With the proud Ravana, the enemy of the gods, Indra, the majesty of gods, was pleased with Rama. The majesty of gods, Indra revived the monkeys who had been distroyed by the rakshasa in battleground, by sprinkling nectar showers. Those places nectars drop fell from monkeys bodies, T. cordifolia plant were born[1].

Plant medicine is also called phytomedicine. 70-80% of individuals still use herbal medication for primary care because it is more palatable to the human body and has fewer side effects. The rich understanding of traditional herbal medicine system like Siddha, Ayurveda and Unani, along with India's biodiversity offer a strong basis for the genral healthcare application of a wide range of species and common illnesses.

Pharmacognosy of Tinosporia cordifolia

Tinospora cordifolia, also referred to as Guduchi, Amrita or Giloy, has a number of botanical synonyms, one of which is Tinospora mahajanii. Tinospora mahajanii was reduced to synonymy with Tinospora cordifolia, indicating that they pertain to the same species, and this synonymy was established. Furthermore, Tinospora cordifolia belongs to a wider group of species in the Tinospora genus that are known for their therapeutic

qualities, including T. bakis, T. crispa, T. malabarika, and T. rumpii. Tinospora cordifolia is a Menispermaceae family member that climbs deciduous trees[2], [3].

Table 1: Common names of Tinospora cardifolia[3]

Hindi	Giloy
Marathi	Gulavel
English	Heart-leaved Moonseed
Kannada	Amrta balli
Tamil	Amrda valli
Telgu	Tippatige
Malayalam	Chittamrtam
Bengali	Gulancha

Fig. 1.2: Tinospora cordifolia

Geographical disribution of Tinosporia cordifolia

The deciduous climbing shrub Tinospora cordifolia is primarily found in tropical and subtropical climates. Its range include sections of tropical Africa, Southeast Asia, the Indo-Malaya area, including India, Myanmar, Sri Lanka, and China. This plant is used in many traditional treatments and is known to have a wide range of medical benefits. It is present in Assam, Bihar, Kokan, Kuman, Sri Lanka, and Myanmar in addition to other parts of India[5], [6].

Cultivation Details

Climate: It does not thrive in humid or wet climates and typically thrives in tropical dry regions. It can be grown in a variety of climates[4].

Altitude: It is inhabited throughout tropical India, reaching a height of 5,000 meters[4].

Temperature and Rainfall: Temp. requried 25 to 40^0C and even distributed of rainfall[4].

Type of soil: It grows well in practically every kind of soil. High crop yields have been discovered to be possible with sandy loam soil that has good drainage and a high organic matter content[4].

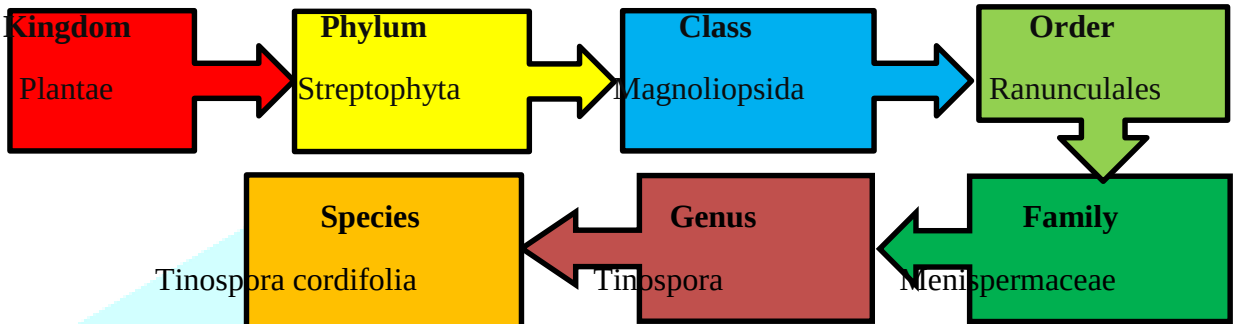
Strong stem cuttings were used for propagation. It is grown between May and June, at the beginning of the monsoon season. Nursery plantations use the stem cuttings. This crop is perennial. An agricultural crop grown on well-prepared soil yields a good crop because it grows well in a variety of agroclimatic conditions. Deep ploughing is used two or three times to prepare the land. After the field is cleared of weeds, a little amount of compost manure or FYM is mixed in. Pits are dug and ploughed at an appropriate distance of roughly 60 cm by 60 cm. Stem cutting is used to propagate the plants. Stems of high grade are selected in order to prepare stem cuttings. In April and May, these cuttings are planted in nursery beds that have been prepared with a blend of soil, sand, and farmyard manure. One could apply the irrigation on different days. Water stagnation and excessive irrigation are prevented. Plant the raised rooted cuttings or rooting suckers two suckers at a time into the prepared pits. Water can't stand still because of the channels designed to let extra water go. After the climbers have taken root in the fields, they need assistance and improved crop medicinal value. As an alternative, wire supporters are offered[4].

It might need to be watered once a week since it is an intercrop. if the primary crop receives weekly irrigation. Giloe doesn't require additional irrigation if the main crop is already receiving it. In order to keep the soil moist during the summer, mulch made of straw or dried leaves is applied. Compost manure is used for the crop at the nursery level. When ploughing, a base dose of farmyard manure is administered after the fields have been transplanted. Since it's a perennial crop, it's best to apply composted or organic manure again. If necessary, an NIK fertiliser dose can be administered. It is simple to intercrop with coconut, mango, and neem. Since it is a perennial crop, regular weeding is necessary to keep the crop clear of weeds. In the initial stages of crop growth, one manual weeding should be performed to control weeds. However, after 20 to 30 days and over the remaining crop growth period, three or four weedings may be enough to control weeds. The stem and leaves of the plant are harvested. When the plants are old enough, the leaves are harvested, and the sturdy stems are harvested by cutting. The gathered stems are diced into tiny bits. After removing any adherent contaminants, the leaves and stem cuttings are shade-dried and stored in dry environments. Nine to ten quintals of stem are produced on average per hectare of land. Dried stem is priced between Rs. 20 and Rs. 25 per kg[4].

Table 2: Parts of Tinospora cordifolia

Parts of plants	Descrption	Refre[n]
Stem 	The stem is fibrous, grey in colour, and has a deep fissure that runs longitudinally and spirally and contains lenticels. The wood is soft, porous, and white.	[5],[6]
Leaves 	Petioles are 2.5–7 cm long, while leaves are simple, heart-shaped, alternating, membrane, and venation with reticulation, measuring 5–10 cm.	[5],[6]

Flower	Its flower are yellow-green in color. The inflorescence of the unisexual, racemes-type flowers is about 5cm long. Male flowers bloom in bunches whereas female blooms are solitary.	[5],[6]
Fruits	The fruits are fleshy, single-seeded, and crimson in colour. The seeds have a curved form.	[5],[6]

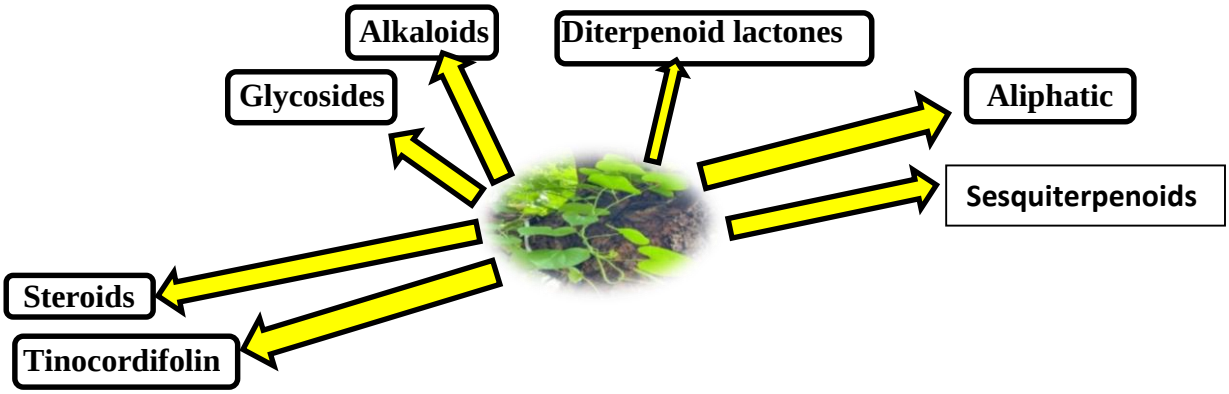


Taxonomic Classification of Tinospora cardifolia[7]

Alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoids, phenolics, aliphatic chemicals, and polysaccharides are among the chemical components found in Tinospora cordifolia. Many conditions, including fevers, jaundice, diabetes, dysentery, urinary tract infections, and skin disorders, can be treated with the diverse medicinal qualities of T. cordifolia. Numerous chemical, pharmacological, pre-clinical, and clinical investigations have been conducted on this molecule, and several new therapeutic potential effects have been revealed. possess additional properties that include anti-diabetic, anti-cancer, immune-modulatory, antiviral, antioxidant, antibacterial, and hepatoprotective.

Table 3: Phytoconstituents of Tinospora cordifolia

Sr. no.	Parts of Tinospora cordifolia	Phytoconstituents	Reference
1	Leaves	Alkaloids, anthracene, coumarins, flavonoids, glycosides, polyphenols, reducing sugar, saponins, terpenoids, amino acids, carbohydrates, proteins, calcium, phosphorus	[6], [8]
2	Stem	Berberine, palmatine D, choline D, tinosporine, magnoflourine, tetrahydropalmatine, isocolumbin, 18-norclerodane glycoside, furanoidditerpene glycoside, tinocordiside syringin, syringin-apiosylglycoside, tinocordifolioside, cordioside, cordifolioside A, cordifolioside B, palmatoside F31, cordiofoliside B2, cordiofoliside D2, cordiofoliside sesquiterpenoid, Tinocordifolin	[9]
3	Fruits	Palmatine, barberine, furanoid diterpene glucosides, tinocordisides, tinocordifolins, giloinsterol, hydoxyl ecdysone, ecdysterone, octacosanol, heptacosanol, nonacosan-15-one, cordifolide, cordifol, tinosporide, beta-sitosterol, clerodane furano diterpine, tinosporaside, columbin	[7]
4	Flower	Diterpenoids lactones and steroids	[7][8]



Active compounds of Tinospora cordifolia

Phytochemistry:

Alkaloids, glycosides, steroids, sesquiterpenoid, aliphatic molecule, essential oils, and a combination of fatty acids and polysaccharides are the primary constituents of the plant. Berberine, bitter gilonin, and non-glycoside giloningilosterol are examples of alkaloids[10].

Tinosporine, tinosporide, tinosporaside, cordifolide, cordifol, clerodanefuranoditerpene, diterpenoidfuranolactonetinosporidine, columbin, and b-sitosterol are the principal phytoconstituents of Tinospora cordifolia. Its stem has been shown to contain berberine, palmatine, tembertarine, magnesium, choline, and timosporin. From the immunomodulatory aqueous fraction of the Indian medicinal plant Tinospora cordifolia, a rearranged cadinanesesquiterpene glycoside known as tinocordiside—which consists of a tricyclic skeleton with a cyclobutane ring—has been isolated. From the stems of Tinospora cordifolia, a novel clerodanefurano-diterpene2 with the molecular formula C20H20O8 has been discovered. We studied this plant because of the local medicinal herbs, and we discovered a novel clerodanefurano-diterpene after extracting the stems with a hot CHCI3.It turns out that 6-hydroxyarcangelisin is its epimer[9].

Tinocordifolin, a novel daucane-type sesquiterpene, has been extracted from Tinospora cordifolia stems. N-trans-feruloyltyramine, tinocordifolin, and tinocordifolioside are the names of the new sesquiterpenes. Four new and seven recognised compounds were isolated from the methanol extract of Tinospora cordifolia Miersaerial portions using phytochemical analysis[9].

Pharmalogical activity:

Because of its general tonic, antiperiodic, anti-spasmodic, anti-inflammatory, antipyretic, anti-arthritic, anti-lepritic, anti-allergic, and anti-diabetic qualities, Tinospora cordifolia is a commonly used medicinal herb in the Ayurvedic system.

The plant is used to strengthen the body's defences against infections and the immune system. This plant's roots are well-known for its anti-stress and anti-malarial properties. The stem is diuretic, bitter, stomachic, and increases bile secretions in addition to quelling thirst, enhancing blood quality, and treating jaundice. For skin issues, the stem extract is helpful. As an antidote against scorpion and snakebite, Tinospora cordifolia root and stem are used in combination with other medications. In addition, the herb is used to cure cough, asthma, pneumonia, and wounds. Tinospora cordifolia possesses properties that protect the liver, decrease cholesterol, stimulate the immune system, shield nerve cells, and prevent cancer. Additionally, tinospora cordifolia is in charge of reducing radiation-induced tissue damage, lessening the negative effects of various chemotherapy treatments, and accelerating the healing of diabetic foot ulcers[11], [12].

Anti-cancer activity

Most research on Tinospora cordifolia's anti-cancer properties uses animal models. In male Swiss albino mice, TCE has been demonstrated to have a radioprotective role by dramatically increasing body weight, tissue weight, testes-body weight ratio, and tubular diameter. It has also been shown to block the deleterious effects of sub-lethal gamma radiation on testes. TCE dramatically impacted the radiation-induced elevation in lipid peroxidation and the subsequent decrease in GSH concentration in the testes of pre-irradiating animals. It has been demonstrated that pre-treating HeLa cells with TCE reduces GSH S-transferase activity, increases LDH, and decreases cell viability. It has been observed that dihydrotestosterone (DHT) in TCE promotes the expansion and development of human LNCaP cells, or androgen-sensitive human prostate cancer cells. The androgen receptor is how androgenic chemicals in TCE work. In rats with diethylnitrosamine (DEN)-induced hepatocellular carcinoma (HCC), newly isolated compounds such as (R, R)-R, R-dihydroxy-S, R:, -diepoxycleroda-(),, S:,S-dilactone (ECD), a diterpenoid from Tinospora cordifolia have been reported to have chemopreventive potential by decreasing anti-oxidant activities via SOD, CAT and detoxification enzymes like GSH, GPx. This was followed by an increase in the activities of the hepatic markers (Serum glutamic oxaloacetic transaminase) SGOT, (Serum Glutamic Pyruvate Transaminase) SGPT, LDH), and a decrease in serum transaminase level, confirming its anti-tumor effects and suggesting a promising use as a powerful chemopreventive drug for HCC.

In Ehrlich ascites carcinoma (EAC) mice, the DCM extract of Tinospora cordifolia has been shown to have radiosensitizing activity, enabling tumor-free survival through depletion of GSH and glutathione-S-transferase by elevated levels of lipid peroxidation and DNA damage to tumour cells. TCE hexane fraction has been shown to block the G phase in EAC mice and cause apoptosis through the formation of apoptotic bodies, nuclear condensation, activation of caspase-, decreased cell number and ascites volume, increased expression of pro-apoptotic gene Bax, and decreased expression of anti-apoptotic gene Bcl-. In animal models of skin cancer, TCE may cause a decrease in papillomas, tumour production, tumour burden, and tumour weight while increasing phase II detoxifying enzymes. When Swiss albino mice were exposed to a hydroalcoholic (% ethanol:% distilled water) extract of Tinospora cordifolia aerial roots, the livers of the mice showed a notable increase in acid-soluble sulfhydryl (-SH), cytochrome P () contents, and enzyme activities of cytochrome P () reductase, cytochrome b reductase, GST, DT-diaphorase (DTD), SOD, catalase, GPX, and GR activity. This suggests that Tinospora cordifolia may have chemoprevent cancerous effects.

Increased levels of pro-inflammatory cytokines, such as IL-β, IL-, TNF-α, granulocyte monocyte-colony stimulating factor (GM-CSF), and vascular endothelial cell growth factor (VEGF), as well as increased production of anti-angiogenic agents, such as IL- and tissue inhibitor of metalloprotease- (TIMP-), in the animals treated with B-F extract, were indicative of TCE's in vivo anti-angiogenic activity in B-F melanoma. It was discovered that the polysaccharide component of Tinospora cordifolia was highly effective in lowering the ability for B-F melanoma cells to metastasise. When comparing the treated mice to the untreated control animals, there was a significant decrease in markers associated with neoplastic growth. The majority of synthetic chemotherapy drugs have harmful side effects. Guduchi extracts had an equivalent or superior impact to doxorubicin therapy.

Anti-microbial activity

It has been suggested that Tinospora cordifolia methanol extracts may be effective against microbial infections. Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Proteus vulgaris, Salmonella typhi, Shigella flexneri, Salmonella paratyphi, Salmonella typhimurium, Pseudomonas aeruginosa, Enterobacter aerogene, and Serratia marcesenses have all been tested for the antibacterial activity of Tinospora cordifolia extracts.– TCE has been shown to enhance neutrophil phagocytic and intracellular bactericidal abilities in mice models by clearing microorganisms. It has been found that TCE stimulates macrophage immunity. In cows with mild mastitis, intra-mammary infusion of hydro-methanolic extracts of Tinospora cordifolia therapy increased polymorphonuclear cells' phagocytic activity.

Immunomodulatory Property

There is ample evidence supporting Tinospora cordifolia's immunomodulatory ability.– It has been reported that the active ingredients hydroxymustakone, N-methyl-pyrrolidone, N-formylannonain, cordifolioside A, magnoflorine, tinocordiside, and syringin may have cytotoxic and immunomodulatory effects.According to reports, they work by increasing the phagocytic activity of macrophages, causing human neutrophil cells to produce reactive oxygen species (ROS), and stimulating splenocytes and macrophages to produce more nitric oxide (NO), which is indicative of anti-tumor activities. It has also been observed that aqueous Tinospora extracts affect immunological effector cell stimulation, activation, mitogenicity, and cytokine generation. It has been demonstrated that extracts from Tinospora cordifolia cause mice's IL-cytokine to be overexpressed, which causes inflammation, acute responses to damage, activation of cytotoxic T cells, and B cell differentiation. Alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic chemicals, and polysaccharides are examples of active ingredients in aqueous extracts whose cytotoxic effects have been documented in an experimental rat model. Dry stem crude extracts of Tinospora cordifolia have been shown to improve immunological response in mice by eliciting the release of IL- and activating macrophages upon binding to a polyclonal B cell mitogen, G-A. There are numerous reports on the use of Tinospora cordifolia to reduce oxidative damage. In vitro, it has been demonstrated that the (,)-alpha-d-glucan (alpha-d-glucan) produced from Tinospora cordifolia activates human cells, causing the creation of pro- and anti-inflammatory cytokines downstream. It has been discovered that certain substances have synergistic effects on Tinospora cordifolia's immunomodulatory function.

Anti-HIV activity

It has been demonstrated that TCE reduces the HIV virus's recurrent resistance, increasing the therapeutic success. TCE's anti-HIV effects were demonstrated by a decrease in the eosinophil count, an increase in B cells, macrophages, polymorphonuclear leucocytes, and haemoglobin percentage, all of which suggested that the treatment of the illness could benefit from its use.

Anti-osteoporotic activity

Tinospora cordifolia has the potential to be used as an anti-osteoporotic agent because it has been shown to influence the mineralisation, differentiation, and proliferation of bone-like matrix on osteoblast model systems in vitro. It has been demonstrated that the alcoholic extract of Tinospora cordifolia increases the differentiation of cells into osteoblastic lineage, promotes osteoblast development, and increases the mineralisation of bone-like matrix. It has been claimed that ecdysteroids extracted from the plant have anti-osteoporotic and protein anabolic actions in mammals. It has been shown that beta-Ecdysone (Ecd) from extracts of Tinospora cordifolia can significantly thicken joint cartilage, stimulate osteogenic differentiation in mouse mesenchymal stem cells, and alleviate osteoporosis in animal models of osteoporosis. Additional reports of -OH-β-Ecd isolated from Tinospora cordifolia have indicated its anti-osteoporotic properties, underscoring the plant's potential use in the management of osteoporosis and osteoarthritis.

Anti-diabetes activity

In Indian traditional folk medicine, the stem of Tinospora cordifolia is frequently used to treat diabetes by controlling blood sugar levels. Its anti-diabetic properties are said to be mediated via reducing oxidative stress (OS), increasing insulin production, and blocking the processes of gluconeogenesis and glycogenolysis, which in turn controls blood sugar levels. The primary phytoconstituents of Tinospora cordifolia, including alkaloids, tannins, cardiac glycosides, flavonoids, saponins, and steroids, have been shown to have anti-diabetic properties.

Research has demonstrated that the isoquinoline alkaloid-rich fraction from stem, which includes palmatine, jatrorrhizine, and magnoflorine, has the ability to mimic and release insulin in both vitro and vivo settings. It has been observed that administering root extracts orally can control blood sugar, improve insulin production, and reduce OS indicators. Studies conducted in vitro documented the initiation and restoration of cellular defence anti-oxidant markers, such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and glutathione (GSH), the inhibition of glucose phosphatase and fructose, diphosphatase, and the restoration of glycogen level in the liver. Tinospora cordifolia crude stem ethyl acetate, dichloromethane (DCM), chloroforms, and hexane extracts inhibited pancreatic and salivary amylase and glucosidase, raising postprandial glucose levels and perhaps helping treat diabetes mellitus.

It has been claimed that the root extract reduces the levels of vitamin E, ceruloplasmin, hydroperoxides, plasma thiobarbituric acid reactive compounds, and glycosylated haemoglobin in diabetic rats. It has been reported that oral administration of Tinospora cordifolia extract in the "Ilogen-Excel" formulation (an Ayurvedic herbal formulation) reduces GSH and vitamin C in blood and urine glucose and lipids in the serum and tissues in alloxan diabetic rats. The formulation comprises eight medicinal plants: Curcuma longa, Strychnos potatorum, Salacia oblonga, Tinospora cordifolia, Vetivelia zizanioides, Coscinium fenestratum, Andrographis paniculata, and Mimosa pudica. Rats with diabetes have been shown to have lower levels of SOD, GSH, GPx, and catalase activity in their hearts and brains. In diabetic rats, T. cardifolia root extract (TCE) has been shown to have a hypoglycemic and hypolipidemic effect by increasing body weight, total haemoglobin, and hepatic hexokinase while lowering hepatic glucose-phosphatase, serum acid phosphatase (ACP), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH). There have been reports of TCE's protective benefits when anti-oxidant molecules and enzyme levels are higher. Through a considerable reduction in malondialdehyde and ROS levels and a rise in GSH and total thiols, TCE has been demonstrated to significantly counterbalance the diabetes-associated OS in the maternal liver.

Anti-diarrhoea and Anti-ulcer Activity:

The in vivo antidiarrheal activity of extracts was evaluated using castor oil and magnesium sulfate-induced diarrhoea by evaluating the onset of diarrhoea, frequency of wet and total stools, weight of wet stool, and total weight of stools. Castor oil (a hydrolytic metabolite, i.e., ricinoleic acid) causes diarrhoea by releasing nitric oxide (NO), which stimulates prostaglandin synthesis and increases peristalsis. On the other hand, magnesium sulphate inhibits water reabsorption and encourages the release of cholecystokinin (CCK) from the duodenal mucosa. Because pretreatment with extracts provides significant protection against castor oil and magnesium sulfate-induced diarrhoea, the extracts may be assumed to have antisecretory and preventive action towards CCK release.

Pylorus ligation and ethanol-induced ulcers were used to test the plant extracts' in vivo antiulcer efficacy. The buildup of pepsin and acid caused by pylorus ligation results in ulceration and auto-digestion of the stomach mucosa. Ethanol causes vascular permeability, inflammatory mediator expression, and a decrease in the amount of stomach mucus.

A drop in the ulcer index, acidity, and volume of gastric content, as well as a rise in the pH of gastric content, demonstrate that extracts significantly prevent ulcers in both models. The production of reactive oxygen species (ROS) is another aspect of the pathophysiology of ethanol-induced ulcers and pylorus ligation. Strong free radical scavenging capabilities against superoxide anion, hydroxyl radicals, NO radical, and peroxynitrite anion have been documented for T. cordifolia. In both ulcer models, extracts significantly raised the levels of antioxidant enzymes such as catalase and GSH, which serve as the first line of defence against ROS-induced damage to the stomach mucosa.

Neuroprotective activity:

The second most prevalent neurodegenerative illness is Parkinson's disease (PD), which mostly affects individuals over 55 (1.5–2%), young adults, and even children. 50–70% of dopaminergic neurones in the substantia nigra (SN) are lost in Parkinson's disease (PD).Alkaloids, glycosides, saponins, tannins, flavonoids, steroids, carbohydrates, and proteins were found in the initial phytochemical analyses, but quinones were not. After a preliminary phytochemical investigation, HPTLC was used to standardise TCEE.Berberine, one of the main marker compounds found in T. cordifolia, was used by HPTLC to standardise TCEE. The quality of the extract was shown by the 0.28% w/w berberine content of TCEE. The findings show that, in comparison to the 6-OHDA group, animals administered with TCEE at 200 ($P < 0.01$) and 400 ($P < 0.001$) had much less catalepsy.

Analgesic activity:

Tinospora cordifolia's alcoholic and aqueous extracts have antioxidant and calcium-attenuating properties that help reduce sciatica pain brought on by sciatic nerve root ligation.T. cordifolia's petroleum ether extract has been shown to raise monoamine levels, including dopamine, serotonin, and noradrenaline, which may account for its anti-nociceptive properties.The aerial portion of T. cordifolia contains terpenoids, alkaloids, flavonoids, glycosides, and steroids. Therefore, any of these phytoconstituents may be responsible for the analgesic action that has been observed. Flavonoids have also been reported to have analgesic properties that

work by preventing prostaglandin synthesis.Peripheral nerve terminals become sensitive to prostaglandins. Furthermore, during inflammation, chemicals like substance P and bradykinin—potent mediators of pain—are released. NSAIDs and other anti-inflammatory drugs are used as analgesics and reduce pain by lowering inflammatory mediators, including PG.

Antioxidant activity:

When Tinospora cordifolia stem methanol extracts were taken orally, their antioxidant properties enhanced the erythrocyte membrane lipid peroxide and catalase activity. In alloxan-induced diabetic mice, it also reduced the activities of SOD and GPx. Extracts from Tinospora cordifolia Willd. (Menispermaceae) may be aldose reductase and antioxidant inhibitors, which reduces chemotoxicity brought on by free radicals. Strong free radical scavenging capabilities of TCE against superoxide anion (O-), hydroxyl radicals (OH), NO radical, and peroxynitrite anion (ONOO-) have been documented. By reducing the production of free radicals, the extract was also reported to lessen the harmful side effects of CP in mice. Tinospora cordifolia increases GSH and total thiols while lowering malondialdehyde and ROS levels. Even in the foetal environment, Tinospora cordifolia's protective benefits were evident due to increased levels of antioxidant molecules and enzymes.

Free radicals produced during aflatoxicosis can be scavenged by Tinospora cordifolia. Because of the presence of alkaloids such choline, tinosporin, isocolumbin, palmatine, tetrahydropalmatine, and magnoflorine, Tinospora cordifolia demonstrated protection against aflatoxin-induced nephrotoxicity. Diabetic rats have shown a substantial rise in TBARS concentration in the brain and a decrease in the heart. Additionally, it improved the liver's production of SOD, GPx, and GSH. Additionally, treatment with Tinospora cordifolia inhibited fructose and glucose phosphatase and restored the liver's glycogen content. It has been demonstrated that Tinospora cordifolia controls blood sugar.

A diterpenoid from Tinospora cordifolia, (R, R)-R, R-dihydroxy-S, R:, -diepoxycleroda-(),, S:,S-dilactone (ECD), has been demonstrated to have chemo-preventive potential in rats with DEN-induced HCC. In both preventive and curative DEN-induced mice, ECD treatment raised the concentration of antioxidants and detoxifying enzymes. Mice are more likely to survive a sub-lethal dose of gamma radiation when exposed to an aqueous extract of Tinospora cordifolia because it exhibits radioprotective properties. Tinospora cordifolia was successful in increasing the expression of the Cu-Zn SOD and gamma-glutamylcysteine ligase genes as well as GSH levels. Tinospora cordifolia's aqueous extract provided radioprotective benefits by preventing the development of the (Fe+)-bipiridyl complex, which in turn prevented radiation-mediated -deoxyribose degradation.The TBARS and lipid hydroperoxide (LOOH) tests demonstrated that the arabinogalactan polysaccharide (TSP) that was isolated from Tinospora cordifolia provided good protection against iron-mediated lipid peroxidation of rat brain homogenate. Additionally, Tinospora cordifolia has components that enhance the effectiveness of antiretroviral therapy (ART) and reduce the HIV virus's recurring resistance to it. Swiss albino mice's livers have been used to test the effects of a hydroalcoholic (% ethanol:% distilled water) extract of Tinospora cordifolia aerial roots on phase-I and phase-II enzymes that metabolise carcinogens and drugs, antioxidant enzymes, GSH concentration, LDH, and lipid peroxidation. Tinospora cordifolia's chemo-preventive effectiveness is suggested by the increased GSH level and enzyme activities involved in xenobiotic processing and preserving the antioxidant status of cells.

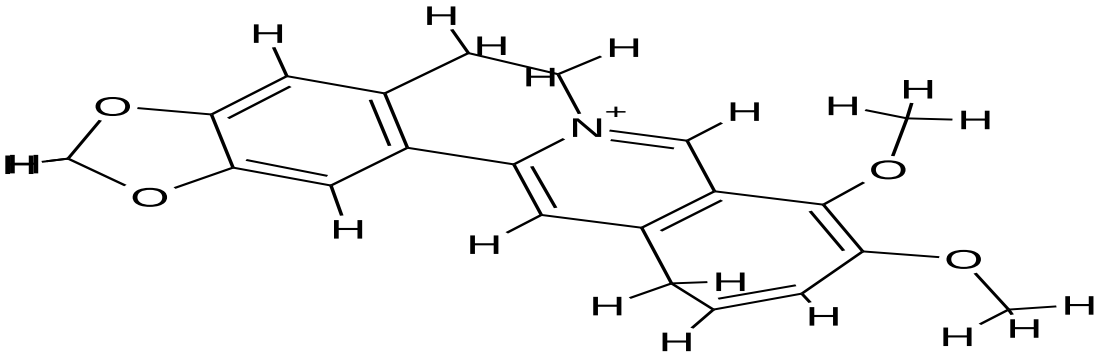
It has been reported that the alpha-glucosidase inhibitor saponarin (apigenin--C-glucosyl--O-glucoside) is present in Tinospora cordifolia. Significant antioxidant and hydroxyl radical scavenging properties were exhibited by the leaf extract. In rats, Pepticare, an Ayurvedic herbomineral formulation made of the herbal medications Glycyrrhiza glabra, Emblica officinalis, and Tinospora cordifolia, exhibits anti-oxidant and anti-ulcer properties.

Table3: Therapeutic activities of Tinospora cordifolia

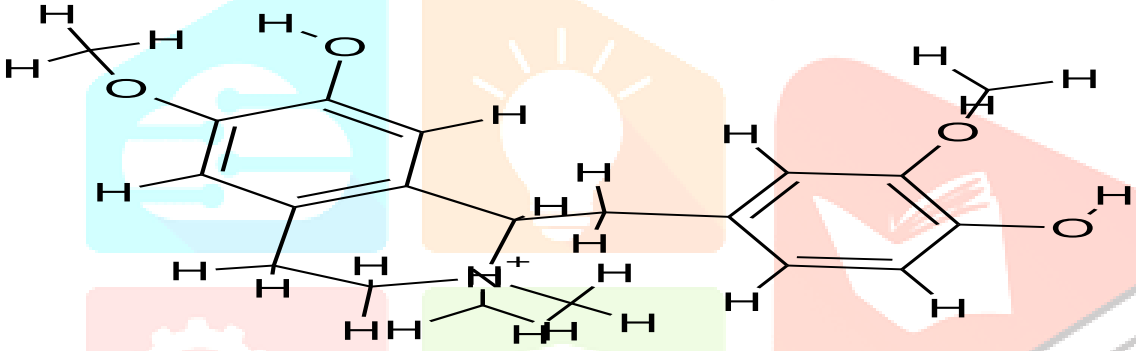
Parts of T. cordifolia	Therapeutic activity	Chamical constituent	Extraction	Refⁿ
Whole plant	Antioxidant activity	(-)Epicatechin, Tinosporin, Isocolumbin, Palmatine	Ethanol extract	[13]
	Antiulcer activity			[14]
	Antidiarehoea activity			[14]
	Analgesic activity			[15]
	Gastroprotective activity	Epoxyclerodane diterpene		[16]
	Hepatoprotective activity	Magnoflorine, Palmatine, Tinosporin, Isocolumbin, Tetrahydropalmatine	Alcohol extract	[17]
	Cardioprotective activity	Furanolactone, Tinosporin, Tinosporide, Jateorine, Columbin, Clerodane derivatives	Aqueous extract	[18]
	Immunomodulatory activity	Cordifolioside A, Syrigin, Tinocordiside		[19]
Stem	Anti-inflammatory activity	Furanolactone, Tinosporin, Tinosporide, Jateorine, Columbin, Clerodane derivatives		[20]
	Radioprotective and Cytoprotective	Cordifolioside A	Alcohol extract	[21]
	Hypoglycemic activity		Aqueous extract	[22]
	Antiosteoprotective		Ethanolic extract	[23]
	Antimalarial activity		Ethanolic extract	[24]
	Antimicrobial activity	Furanolactone, Tinosporon, Jateorine, Columbin	Ethanolic and Aqueous extract	[25]
	Anticancer activity	Magnoflorine, Palmatine, Tinocordiside, Cordifolioside A		[26]
	Antidiabetic	Berberine,Choline,Tembetarine, Palmitine, Jatrorrhizine	Aqueous extract	[27]
	Antiasthamic activity		Hydroalcholic extract	[28]
Aerial	Neuroprotective activity	Berberine,Choline,Tembetarine, Palmitine, Jatrorrhizine	Ethanol extract	[29]
	Antineoplastic activity		Dichloromethane extract	[30]

The active principle structure:

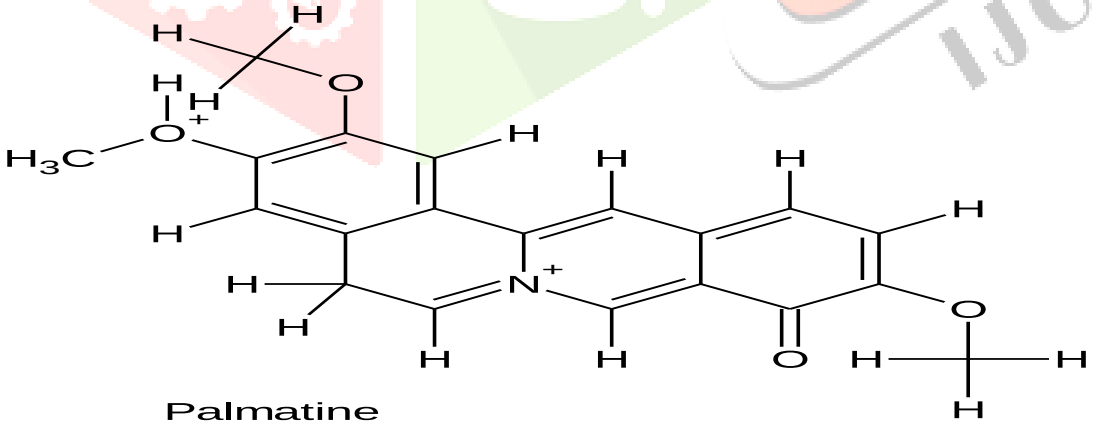
Akaloids



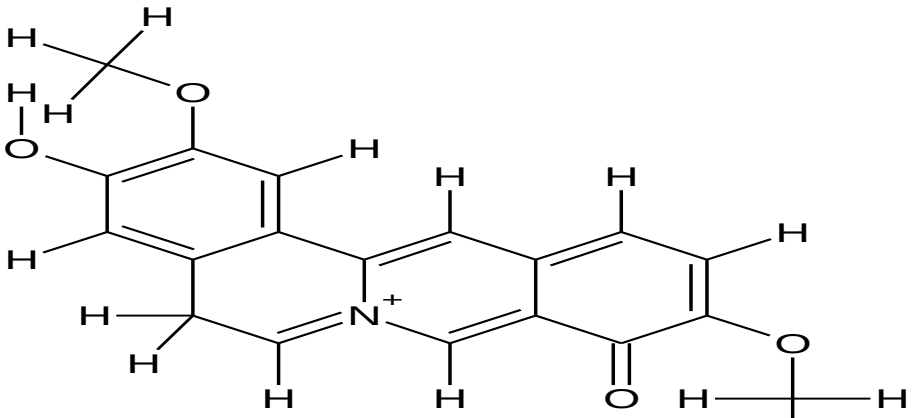
Berberine



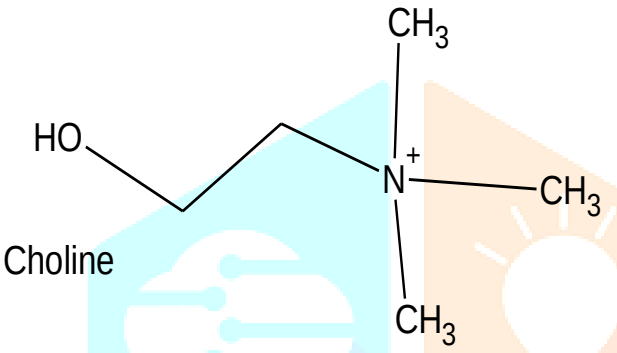
Tembetarine



Palmatine

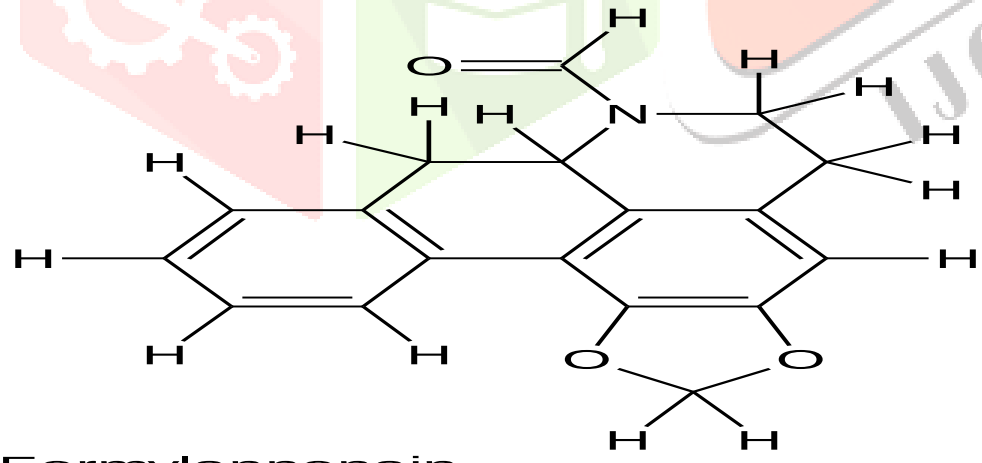


Jatrorrhizine

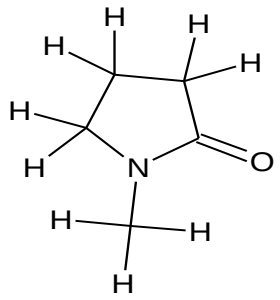


Choline

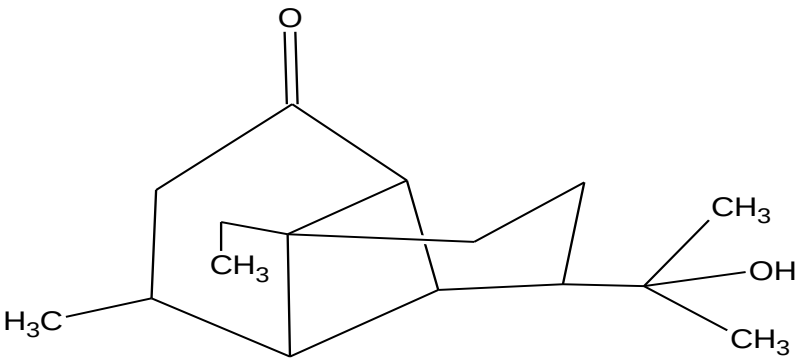
Gylcoside



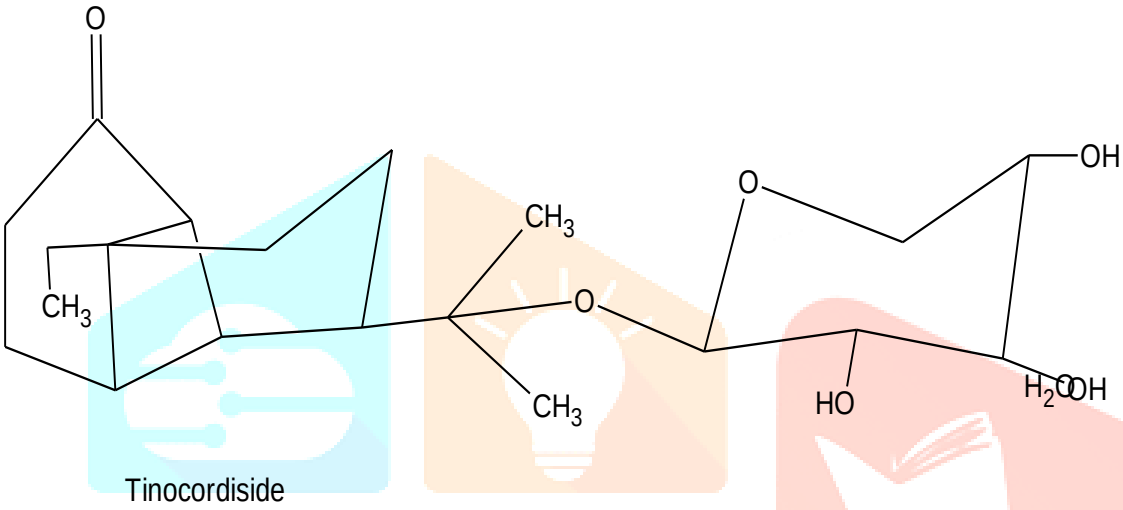
N-Formylannonain



N-Methyl-2-pyrrolidine

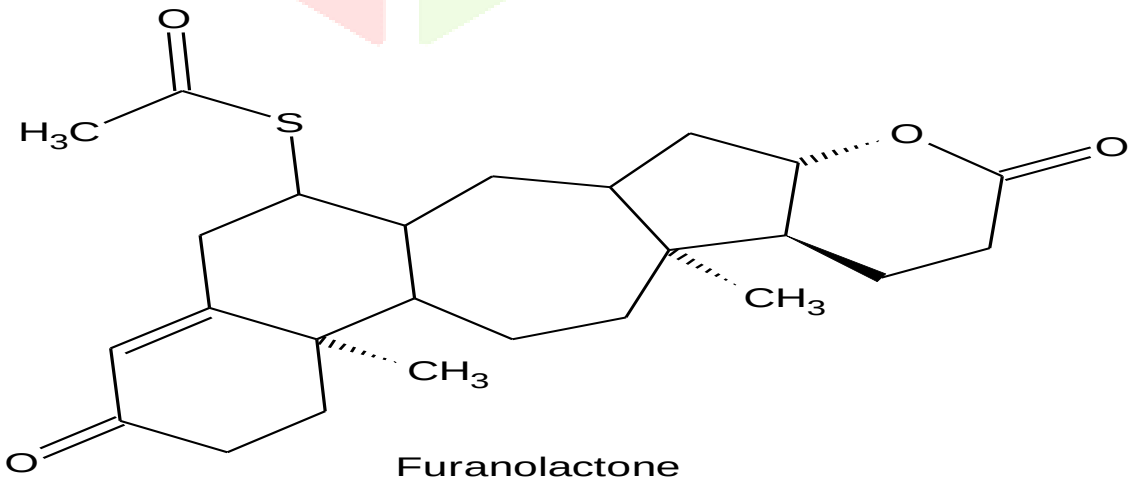


H-droxymustakone



Tinocordiside

Diterpenoids



Furanolactone

Table 4: Ayurvedic Formulation

Ayurvedic formulation	Treatment of diseases	Refrⁿ
Guduchi Tablets	General infection, immune disease, Hepatitis, Arthritis and anticancer	[31], [32]
Shilpa Pravang	Sexual Vitality	[32]
Madhu Mehari	Dryness of mouth, relives frequent urination and maintains the normal sugar levels	[32]
Mussaffen	Blood purifier and skin diseases	[32]
Rebuild	Antistress and antioxidant activity	[32]
Septilin	Respiratory infection	[32]
Tonplex	Increase the immunity and vitality	[32]
Joint Muscle Excellence Tablets	Excreate the toxins of joints	[32]
Natadadrol	Androgen builder	[32]
Trisama	Indigestion, constipation and flatulence	[33]
Hyponidd	Antioxidant and antihyperglycaemic	[34]
Ghana Tablet	Antidepressant and antixiolytic	[35]
Naga bhasma	Antidiabetic activity	[36]
Dihar	Antihyperglycemic, antihyperlipidmic and antioxidant	[37]

Conclusion:

Several members of the Tinospora genus, including Tinospora cordifolia, are acknowledged as therapeutic and ethnopharmacologically valuable medicinal herbs. It is frequently seen in a variety of clinical settings throughout Indian medical systems. T. cordifolia is a multipurpose medicinal plant that contains a wide range of bioactive substances, such as steroids, glycosides, alkaloids, sesquiterpenoids, and aliphatic compounds. Numerous bioactive chemicals found in the plant are responsible for its anticancer, antidiabetic, analgesic, immunomodulatory, antioxidant, antiulcer, antibacterial, antipyretic, and nephroprotective properties.

Future aspects:

Tinospora species are utilised as chemopreventive and therapeutic agents for a variety of illnesses. They can also be used as supplements to existing medications to treat diabetes or, through bioactivity-guided isolation, to identify significant and intriguing physiologically active chemicals from these herbs. The authors hope the review would yield useful information for Tinospora species explorations and further studies.

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