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TINOSPORA SINENSIS: A REVIEW ON ITS TRADITIONAL VALUE TO ITS UTILIZATIONS IN CURRENT THERAPEUTICS

Dibyajyoti Das*[1], Dr. Jun Moni Kalita[1], Ankita Kashyap[1], Abhishek Parasar[2], PankajBasumatary[1], Debabrata Nath[1], Hrishikesh Bhagawati[1] and Aminul Islam[1]

[1]Dept. of Pharmaceutical Chemistry, Girijananda Chowdhury Institute of PharmaceuticalScience (GIPS), Azara, Guwahati, Assam 781017.
[2]Dept. of Pharmaceutics, Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS),Azara, Guwahati, Assam 781017.

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***Corresponding Author**
Dibyajyoti Das
Dept. of Pharmaceutical Chemistry, Girijananda Chowdhury Institute of PharmaceuticalScience (GIPS), Azara, Guwahati, Assam 781017.

ABSTRACT

Plants are biologically valuable to humans and animals around the world, providing food, fodder, and medicine. Based on the online survey, information on *Tinospora sinensis* (Linn) journey from traditional applications to scientific validation was acquired. According to the outcomes of the review, the herb is utilised by various tribes around the world to cure individuals suffering from various diseases. *Tinospora sinensis* (Linn) is a plant in the Menispermeace family that has traditionally been used to cure jaundice, liver disease, and skin problems. Aside from its traditional uses scientific investigation reported that the plant has a significant pharmacological activity, viz. Rheumatoid Arthritis, antioxidant, antimicrobial activity, Anti-inflammatory activity, Hyperlepidemic activity, Anthelmintic activity, Anti- ulcer activity, Antiurolithiatic activity, Adaptogenic activity, Analgesic activity, Lieshmanial activity, Hypoglycemic activity, Hepatoprotective activity, anti-cancer ativity, immunomodulatory activities. In conclusion, the outcome of this review will be useful for: (a) Establishing a comprehensive plant profile, (b) assisting investigators in improving their study, (c) To fulfil the gaps lacking in terms of clinical investigation.

KEYWORDS: *Tinospora sinensis*, Menispermeace, phytoconstituents, pharmacological activities, antiurolithiatic activity, Honguni lota.

1. INTRODUCTION

Assam is home to a wide variety range of medicinal plants. Man has used diverse parts of plants in the treatment and prevention of many illnesses since the ancient period. Because of the highcost of modern medical care, which is out of reach for the poor, side effects of synthetic drugs, and the development of resistance to currently used drugs for infectious diseases, the use of traditional herbal medicine for the treatment of common ailments has a lot of relevance today. Plants utilised for medical purposes, on the other hand, have been proven to have few or no adverse effects. Plant-based medicines have been used to treat a variety of disorders for millennia, ranging from the common cold to cancer.[1] Plants have been utilised by ancient societies to treat a variety of diseases, but they keep no records and the knowledge is mostly passed down orally from generation to generation.[2] Traditional ethnomedical knowledge has been passed down the generations, with constant updates based on trial and error. The World Health Organization (WHO) is very active in recording the usage of medicinal plants by cultures all over the world.[3] Traditional herbal medicine is an important component of primary health care system in developing countries like India. They are considered to be safe, effective and inexpensive, for which there is a global trend for the revival of traditional herbal medicine. Screening of medicinal herbs used by different ethnic groups or communities has now become a potential source for isolation of bioactive compound.

Tinospora is a genus of herbs utilised by the Indians for medicinal purposes. Among four species in India two Tinospora species are found in South India, one is located in North Eastern India, and another is found in the Andaman Islands. The North-eastern part of India is the wealthiest reservoir of various plant species where altogether more than 200 tribes.[4] along with other communities protect the forest and sacred groves. Assam, one of the states in Northeast India, comprises different tribal and non-tribal communities, which use numbers of plant species both identified and unidentified ones for the treatment of health disorder.[5] *Tinospora sinensis* is also used by different tribes in assam namely the Karbi tribe in Karbi Anglong for the treatment of diabetes,[6] the tea tribes of Morigaon district for the treatment of jaundice,[7] tea-tribes in Nagaon.[8] district and different tribes Arunachal Pradesh.[9] for the treatment of malaria. Many research has been conducted based on the literature to validatethe scientific featues of

traditional claims and the use of *Tinospora sinensis* in the treatment of diseases. Furthermore, as many studies have shown, the plant's phytochemical profile is well established, with a range of isolated active constituents contributing to its pharmacological actions. To the best of our knowledge, and based on a thorough assessment of the literature, no attempt has been made to compile the data in the form of a review or overview that covers all of the relevant aspects of *Tinospora sinensis*. Thus, the current study aims to document and critically evaluate current information on *Tinospora sinensis* based on botanical description, traditional practice, phytoconstituents, toxicity, and pharmacological properties. The review also intends to fill in important research gaps so that *Tinospora sinensis* and its active phytoconstituents might be used in clinical context.

2. Methodology for Conducting Literature Survey

The information In this review was collected and published using a variety of sources, including research and review publications including databases like Pubmed, Ovid, Embase, Scopus, Sci- hub, Google scholar, scifinder, science direct, ACS publications, Taylor and Francis and Wiley online library. The review comprised articles that focused on the *Tinospora sinensis* and its potency.

3. Plant Botanical Profile

Tinospora sinensis plays a larger role in Ayurvedic and Homeopathic medicine, especially in the treatment of jaundice, fever, rheumatism, gonorrhea, diabetes, and other ailments. Tinospora is a genus of herbs utilized by the Indians for medicinal purposes.[10] Two Tinospora species are found in South India, one is located in Northeastern India, and another is found in the Andaman Islands.[11]

3.1. Taxonomical Classification

Tinospora belongs to the family Menispermaceae and are large woody climbers having ovate to cordate leaves with pulvinus leaf base. According to APG III system of classification *Tinospora sinensis* falls under following classification:

Kingdom: Plantae **Clade:** Angiosperms**Clade:** Eudicots
Superorder: Rananculanae**Order:** Rananculales
Genus: *Tinospora*
Species: *Tinospora sinensis* (Lour.) Merr.[12]

3.2. Morphological Description

Plant is found in India's tropical zone, up to 800-1200 metres above sea level, ranging from the Himalayas to the southern tip of peninsular India.[13]

- **STEM:** A yellowish wood with radially oriented wedge-shaped wood bundles, containing large vessels, separated by narrow medullary rays is fibrous and the transverse section reveals wedge shaped wood bundles, containing large vessels.[14]
- **BARK:** Warty, creamy white to grey brown, spirally deep left, with huge rosette-like lenticels sprinkled between the gaps.[15-16]
- **ROOT:** Succulent with long filiform fleshy aerial roots from the branches.[15]
- **LEAVES:** Petioles up to 15 cm long, simple, alternating, estipulate, cordate, roundish, pulvinate. Both at the base and apex, with the base one being slightly longer and twistedhalfway around.[17]
- **LAMINA:** Ovate or ovate cordate, 10-20 cm long, 8-15 cm broad, 7 nerved and deeply cordate base, membranous, whitish tomentose with prominent reticulum beneath.[17]
- **FLOWERS:** Unisexual, small on separate plants and appearing when plant is leafless, greenish yellow on axillary and terminal racemes. Male flower clustered and female usually solitary. Flowers grow during summer.[14,17]
- **SEPALS:** Six, free in two series of three each, the outer one is smaller than the inner.[17]
- **PETALS**: Six, free smaller than sepals, obovate and membranous.[17]
- **FRUITS:** Aggregates of 1-3 ovoid smooth drupelet on thick stalk with sub terminal style scars, scarlet or orange red colour. Fruits grow during winter.[14,17]
- **SEEDS:** White, bean shaped, curved.[17]

Fig. A: Leaf of *Tinospora sinensis.*

Fig. B: Fruits of *Tinospora sinensis.*

Fig. C: Flowers of *Tinospora sinensis.*

Fig. D: Stems of *Tinospora sinensis.*

3.3. Local Names

- Assamese: শগুনীলতা (hoguni -lota)
- Hindi: गिलोय giloy, गुलंचा gulancha, gurch
- Kannada: Sudarsana balli
- Malayalam: Pee-amerdu, Kattu amirthu
- Marathi: gulvel, vhadli-amrutvel
- Nepali: गुरुज Guruj
- Sanskrit: Vatsadani, Sudarsana, Amrta
- Tamil: potchindil
- Telugu: tippatega

3.4. Synonyms

Campylus sinensis Lour.; *Tinospora malabarica Lam.; Cocculus tomentosus Colebr.; Menispermum cordifolium Willd.; Menispermum malabaricum Lam.; Menispermum tomentosum (Colebr.) Roxb.; Tinospora cordifolia (Willd.) Miers.* ; Tinospora tomentosa (Colebr.)[18]

3.5. Geographical Distribution

Tinospora sinensis is distributes in South and Southeast Asia from countries like India, China, Nepal, Sri Lanka, Bangladesh, Myanmar to Thailand, Vietnam and Cambodia. In India it is distributed in the states like Assam, Orissa, Bihar, Maharashtra, Andhra Pradesh, Karnataka and Kerela.[12]

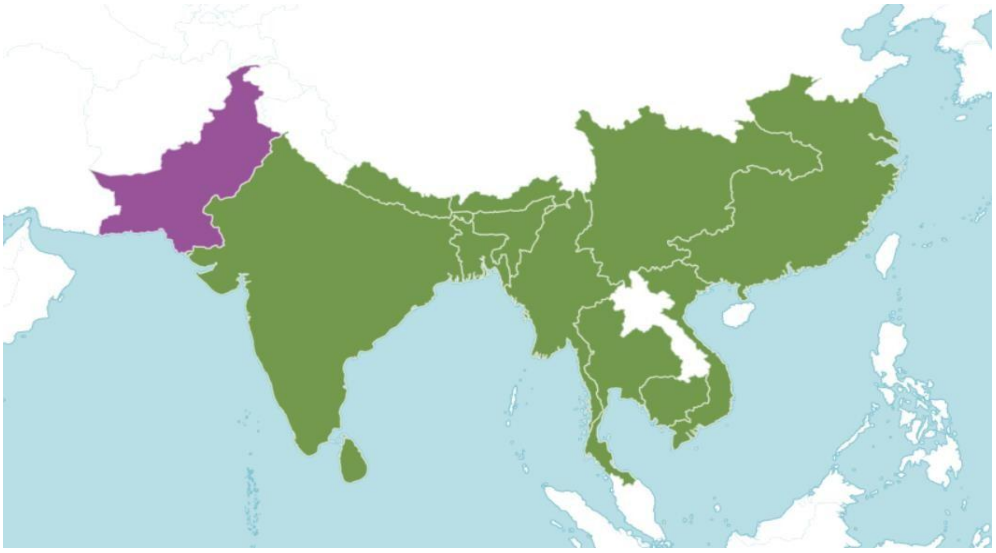

Fig: Showing the distribution of *Tinospora Sinensis* (Linn) in South and Southeast Asia.

4. Traditional Use

- **Anti-malarial property**

A study was conducted in southern part of Assam of North-east India and found that the Chorei tribes used numerous plants for treatment of various diseases. It also reported that the bark extract of *Tinospora sinensis* was given 2-3 times a day for 5-7 days to cure malaria.[19] An Ethnobotanical study also reported the traditional practices of Khiamniungan tribe of Tuensang district of Nagaland where they used different parts of numerous plants to cure various diseases. It was reported that the juice obtained from the grinded stem of *Tinospora sinensis* was used to cure malarial fever.[20]

- **Anti-diabetic property**

An ethno-medical survey was conducted among the the Karbi tribe in Bichikri and Harlong sacred groves of West Karbi Anglong district of Assam. The study reported that the juice extracted from the stem of *Tinospora sinensis* was administerd orally to cure diabetes.[6] A similar ethnomedicinal study was conducted at Kumaun Himalaya in 2013, based on information collected from *vaidyas,* local and rural persons through oral communication and interview. It was reported that the juice from stem and leaves was used to treat diabetes.[21] An ethno medical survey was conducted among the newar community of Pharping village of Kathmandu district, Nepal which reported that the rhizome juice and powder was used to cure diabetes.[22]

- **Anti- gonorrhoea and treatment of impotency**

In 2004–2005, a comprehensive ethnobotanical survey was conducted about the Folklore medicinal uses of some plant species growing wild in Assam of North-East India where the juice of root, stem and bark is administered orally in the treatment of gonorrhoea , It has also been reported that the plant extract possessed antiviral activity.[23] A study was conducted during the period 2017 – 2018 in the Tuensang district of Nagaland, describing the ethno medical practices of Khiamniungan tribe where they used different parts of numerous plants to cure various diseases. It was reported that the juice obtained from the grinded stem of *Tinospora sinensis* was used to cure impotency.[20]

- **To treat Jaundice:**

In June 2016 to July 2017, an ethnomedicinal field investigation was conducted to document the ethnomedicinal plants used against jaundice by the tea tribes of Morigaon district of Assam, India. The tea tribes of Morigaon district uses the infusion extract from the stems of *Tinospora sinenensis* in the treatment of Jaundice.[24] An Ethnobotanical study also reported the traditional practices of Khiamniungan tribe of Tuensang district of Nagaland where they used different parts of numerous plants to cure various diseases. It was reported that the juice obtained from the grinded stem of *Tinospora sinensis* was used to cure jaundice.[20]

- **Treatment of Rheumatisim, Piles and wounds**

P.L.Rajagopal et al., 2013 reported that the Fresh leaves and stems of this plant are employed in the treatment of

chronic rheumatism in China and Tong kong, and fumigations are recommended in piles and ulcerated wounds.[25] A study was conducted during the period 2017 – 2018 in the Tuensang district of Nagaland, describing the ethno medical practices of Khiamniungan tribe where the juice obtained from the grinded stem of *Tinospora sinensis* wasused to cure piles.[20]

- **Treatment of Body-ache**

A comprehensive ethnobotanical survey conduted in the year 2011, data was gathered by observation, interview, and a concrete case study method. The Sonowal Kacharis of bhekulajan village, Dibrugarh district, Assam, have a traditional knowledge of ethnomedicinal plants that they use for primary healthcare. The juice of grounded twigs of *Tinospora sinensis/cordifolia* is applied on the body which relieved the body ache.[26] A similar ethnobotanical survey reported the use of plants by Bantar one of the dominant ethnic groups of Bhaudaha, Morang, Nepal. The whole plant was used to treat tiredness.[27]

- **Treatment of Fever, Cough and Cold**

A study of the ethnomedicinal use and sacred value of some important Kumaun Himalayan plants was carried out during the year 2013. Juice from the Stem and leaves from *Tinospora sinensis* is used in fever, body heat, burning sensation. The information was collected based on oral communication and interview with local people, rural persons, and *vaidyas*.[21] A similar ethnobotanical survey reported the use of different plants by Khiamniungan tribe of Tuensang district of Nagaland. It was reported that the stem of *Tinospora sinensis* was crushed and the juice obtained was used in the treatment of cough, cold and bronchitis.[20] During the years 2010-2011, an ethno medical study of medicinal plants from Assam and Manipur was conducted. The study was done among 84 plant species which are commonly used by people of both the states for curing several diseases. It was reported that the roots, stems and leaves of the plant *Tinospora sinensis* was used to cure chronic fever, irregular fever and cough.[28]

- **Treatment of Disease Related to Gastrointestinal Tract**

A study reported the use of ethno-medicinal Plants by the People of Nawalparasi District, Central Nepal during the year 2004-2008. It was reported that about 500 g root from *Tinospora sinensis* is pounded and mixed with two cups of water and boiled for some time. Half a cup of decoction is drunk twice a day for diarrhoea, dysentery, stomach-ache or diuretic until recovery.[29] An ethnobotanical study also reported the traditional practices of Khiamniungan tribe of Tuensang district of Nagaland where the juice obtained from the grinded stem of *Tinospora sinensis* was used to cure indigestion, diarrhoea and acidity.[20] According to an ethnomedical survey conducted among the newar community of Pharping village in Kathmandu district, Nepal. The powder and juice obtained from the rhizome of *Tinospora sinensis* was used to curegastritis.[22]

- **Treatment of diseases related to skin**

An ethno botanical study was conducted during the period 2017 – 2018 in the Tuensang district of Nagaland, describing the ethno medical practices of Khiamniungan tribe where they used different parts of numerous plants to cure various diseases. It was reported that the juice obtained from the grinded stem of *Tinospora sinensis* was used to cure skin diseases and eruptive boils.[20] A similar ethno medical survey conducted in two states namely Assam and Manipur, which also reported that the stems, leaves and roots of *Tinospora sinensis* was used to cure diferrent skin diseases.[28]

- **To treat Arthritis**

During the years 2010-2011, an ethnomedicinal study of medicinal plants utilised among the different ethnic groups living in remote areas of Assam and Manipur was conducted. A total of 84 species of plant was reported to have several medicinal importance, including *Tinospora sinensis* where the stems, leaves and roots were used to cure Arthritis.[28]

- **Diuretic Property**

A study was conducted in the Tuensang district of Nagaland between 2017 and 2018, describing the ethno medicinal customs of the Khiamniungan tribe, who employed various parts of several plants to cure various illnesses. The juice derived from the crushed stem of *Tinospora sinensis* was used as a diuretic.[20]

- **Treatment of Bone Fracture**

A semi-structured ethnomedical study was conducted in North Central Western Ghats in India. The purpose of the study was to collect and analyse traditional knowledge on the practise and usage of plants in the treatment of bone fractures. It reported that the paste made from the leaves and stem of *Tinospora sinensis* was admimistered both internally and externally in the treatment of bone fracture and strengthening of bones.[30]

5. Pharmacological Activity

- **Adaptogenic activity**

Sharma et al., (2007) documented the adaptogenic activity of *Tinospora sinensis* stem utilising petroleum ether, alcohol, and aqueous extract of stem against various animal models such as anoxia stress tolerance test in mice, forced swimming, and cold induced stress in rats in 2007. Petroleum ether extract was shown to be non-toxic up to a dose of 2000 mg/kg, while aqueous and alcohol extracts were found to be non-toxic up to a dose of 5000 mg/kg. Pre-treatment with aqueous and alcoholic extracts significantly increased anoxia stress tolerance at the end of the first, second, and third weeks of treatment with both doses, i.e., 500 mg/kg ($p<0.05$) and 1000mg/kg ($p<0.01$), while petroleum ether extract significantly increased anoxia stress tolerance time ($p<0.01$). The rat swam for 139±11.2 minutes in an aqueous extract swimming endurance time test on the eighth day, but not

in the alcohol or petroleum ether extracts treatment groups, which showed a significant ($p<0.05$) increase in swimming endurance time. Swimming stress caused ulcers in the stress control group, but pre-treatment with standard and aqueous extracts of *Tinospora sinensis* (but not alcoholic or petroleum ether extracts) greatly reduced the ulceration. In forced swimming and cold induced stress models in rats, biochemical parameters such as glucose, cholesterol, triglycerides, BUN, and cortisol were found to be elevated, which were reduced after pre-treatment with a standard drug (Withania somnifera), whereas aqueous and alcoholic extracts only reduced glucose, cholesterol, and cortisol. In both stress models, the weight of organs such as the liver and spleen rose, whereas the spleen shrank. In the forced swimming stress model, pre-treatment with standard drug, aqueous and alcoholic extracts, but not petroleum ether extract, significantly reduced the weight of the liver, adrenal gland, and spleen while increasing the weight of the spleen. However, alcoholic extract did not significantly reduce the weight of the adrenal gland. In any of the stress models, there was no substantial change in the weight of the kidney. The haematological parameters were considerably affected by forced swimming and cold stress, with increased RBC, WBC, and DLC levels. The stress-induced alterations in these parameters were considerably decreased by pre-treatment with conventional medication, aqueous and alcoholic extracts, but not petroleumether extracts.[31]

- **Analgesic activity and Toxicity studies**

As documented by ***Sandhyrani et al., (2014),*** the analgesic activity was evaluated from ethanolic extract of leaves of *Tinospora sinensis* (Lour.) Merr. Using tail flick test and acetic acid induced Writhing test. Extract tested at the dose level of 250 mg/kg and 500 mg/ kg; the reference used is diclofenac sodium at the dose of 10 mg/kg in tail flick tests. This experiments the extract showed the highest significance at the dose of 500 mg/kg than 250mg/kg and maintained for longer period of time when compared with the standard drug diclofenac sodium which showed significant activity at 60th min. and reduced after 90th min. The results of acetic acid induced writhing test showed highest percentage of protection at the dose level of 500 mg/kg (32.74 %) than in 250 mg/kg (25.27 %) but the standard drug diclofenac sodium showed most prominent reduction at the dose of 10 mg/kg and the percentage protection was 69.94 %. The Acute Toxic Class Method, as stated in OECD (Organization for Economic Co-operation and Development) Guidelines No.423, was used to conduct an acute oral toxicity research for an ethanolic extract of *Tinospora sinensis* leaves. When tested for 14 days at a starting level of2000 mg/kg, the extract was shown to be nontoxic.[32]

- **Anthelmintic activity**

As documented by ***Aruna Devi M. et al., (2014),*** reported the anthelmintic activity of different extracts of leaves of *Tinospora sinensis* using petroleum ether, ethyl acetate methanol and water as solvents against *Pherithima posthuma* and and albendozol was taken as standard and normal saline as control. The anthelmintic activity of a methanolic extract of *Tinospora sinensis* was dosage dependent, with the 50mg/ml concentration taking the shortest time for paralysis (P) and death (D). Even though chloroform and ethyl acetate extracts were not accomplished with anthelmintic property when compared to control and standard group, whereas methanolic extract was found to be more potent than the other three extracts (petroleum ether, ethyl acetate, and water).[33]

- **Anticancer activity**

The anticancer activity was reported by ***Punitha et al., (2012),*** by using the MTT assay, ethanolic extract of *Tinospora sinensis* leaves reduced the growth of malignant cell lines such as human melanoma cancer cell lines (A 375) and skin cancer cell lines (A 431). The extract reduced cell viability, inhibited cell growth, and caused cell death in a dose-dependent manner, with IC50 values of 49.87 g/ml and 112.54 g/ml being significant in the effect of cytotoxicity on A 375 and A 431 cell lines, respectively. 50 milligrammes per kilogramme. The optimum anticancer efficacy of *Tinospora sinensis* leaf extract provided after 1,3,9,12, and 15 days of tumour inoculation was recorded for 1,3 and 9 days of tumour inoculation. NMR data identified isolated substances such as 4-hydroxylheptadec- 6-enoic acid ethyl ester, -sitosterol, and lirioresino—dimethyl ether by analysing spectroscopic data. 4-hydroxyl-heptadec-6-enoic acid ethyl ester and β-sitosterol were shown to inhibit new protein thyrosine phosphatase 1B with IC50 values of 61.1µM and 74.2µM, respectively, while sodium vandate was used as standard inhibitor. The first two chemicals inhibited the novel protein tyrosine phosphatase 1B by 86.0±0.56 percent and 69.0±5.61 percent, respectively, whereas the sodium vandate showed a 56.4 percent inhibitory effect.[34]

- **Antioxidant avtivity:**

As documented by ***Barik et al., (2010),*** reported the aqueous and ethanolic extracts of the species *Tinospora sinensis* were subjected to in vitro antioxidant activity screening models such as DPPH, ABTS, nitric oxide and superoxide radical scavenging activity, inhibition of lipid peroxidation, reduction of ferric ions and total antioxidant capacity. Ascorbic acid was used as the standard. The aqueous and ethanolic extracts showed almost nearer values for all the above said parameters. The total antioxidant activity of the extracts was estimated using spectrophotometric measurements of the production of phosphomolybdenum complex. Lipid peroxidation is induced by free radicals in polyunsaturated lipid-rich tissues such as the liver and brain. Lipid peroxidation was generated in vitro in this work, and the extracts showed concentration-dependent inhibition of lipid peroxide formation. According to the findings, *Tinospora sinensis* is a potential medication for reducing radicals to corresponding hydrazine as they react with hydrogen donors in antioxidant principles.[35]

- **Anti-inflammatory activity**

As documented by ***Punitha et al., (2013),*** reported the anti-inflammatory activity of various concentration of diosgenin isolated from *Tinospora sinensisis* was investigated in chemically induced inflammation rodents' model. At 3 hours after carrageenan injection, it exhibited a considerably (P<0.01) reduced mean paw edema volume. When compared to the control group,these extracts showed anti-inflammatory efficacy in a dose-dependent manner, with a percent reduction of paw edema. All the animals were sorted into five groups, each with five animals. Acute inflammation was induced in all groups by injecting 0.1ml freshly made 1 percent suspension of carrageenan in normal saline into the rats' right hind paws, and paw volume was quantified plethysommetrically from 0 to 180 minutes following carrageenan injection. Two hours before infection, all the animals were given indomethacin (10 mg/kg b.wt.) orally. The average increase in paw volume was calculated as a percentage. Acute toxicity tests were performed on all the extracts, and 1/10th of the LD50 dose was chosen for pharmacological activity. The following formula was used to compute the percentage inhibition of paw volume.

% inhibition = Vc-Vt/Vc x 100; where,
Vc = means increase in paw volume in control group of mice.
Vt = means increase in paw volume in mice treated with test compounds
When compared to the reference drug, indomethacin (82.01 percent), the described chemical, diosgenin, demonstrated a maximal anti-inflammatory activity of 82.25 percent at a dose of 400g/kg.b.wt.[37]

- **Anti-microbial activity**

As documented by ***Mahesh Aruna Devi et al., (2014),*** reported the The antimicrobial activity of ethanolic, methanolic, aqueous, and chloroform extracts of *Tinospora sinensis* leaves, stems, and flowers was investigated using the agar well diffusion method against E. coli, Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans, Aspergillus niger, and Aspergillus fumigatus. *Tinospora sinensis* ethanolic leaf extract exhibited antibacterial efficacy against Candida albicans, Pseudomonas aeruginosa, and Aspergillus niger (zone of inhibition 14, 13 mm, and 8 mm, respectively). Ethanolic stem and flower extracts were found to have antibacterial action against the gram-positive bacterium Staphylococcus aureus and the fungus strain Aspergillus niger (with zones of inhibition of 19, 6 mm and 8, 10 mm for stem and flower extracts, respectively). The presence of alkaloids could explain the antibacterial activity. *Tinospora sinensis* methanolic leaf, stem, and flower extract exhibited no antibacterial action against gramme positive or gramme negative bacteria, however it was efficient against Candida albicans. Methanolic flower extract of *Tinospora sinensis* had the highest antifungal activity (18 mm zone of inhibition), followed by methanolic leaf extract (13 mm zone of inhibition), and methanolic stem extract (11 mm zone of inhibition). Candida albicans was inhibited by all plant parts in a methanolic solution.[38]

- **Hepatoprotective activity**

As documented by ***Narendra Naik D. et al., (2013),*** evaluate the hepato-protective effect of the ethanolic root extract of *Tinospora sinensis* on carbon tetrachloride induced hepatotoxicity. Using rat liver, the extract was evaluated for hepatoprotective efficacy against CCl_4-induced hepatotoxicity. Hepatic enzymes studied include Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and alkaline phosphatase (ALP). Hepatic injuries may have resulted in necrosis, which could have contributed to a rise in hepatic enzyme levels. *Tinospora sinensis* root extract was dissolved in water and taken orally. The root extract was screened for oral toxicity studies according to OECD guidelines 423. LD_{50} was calculated for selection of dose. The liver was excised, and a histopathological investigation was performed using 10% formalin. They were photographed after being stained with haematoxylin and eosin. When compared to Silymarin, results demonstrated that treatment with ethanolic root extract of *Tinospora sinensis* normalised cells and reduced sinusoidal dilation as well as mild inflammagens. This was evident from significant reduction in P<0.05, P<0.01, P<0.001 in serum enzyme levels. The alcoholic fraction of *Tinospora sinensis* showed a drop in SGOT, SGPT, and ALP enzymatic activity, as well as a reduction in increased liver weight in treated groups and was substantially lower (P<0.001) than silymarin, which was employed as a control. As a result, the alcoholic extract of *Tinospora sinensis* roots has a high potency, which can beattributed to its hepatoprotective properties.[39]

- **Anti-ulcer activity**

As documented by ***Khayu et al., 2009*** *Tinospora malabarica* a synonym of *Tinospora sinensis* was evaluated for anti-ulcer activity. The dried stems of the plant were ground into a coarse powder and extracted in a soxhlet apparatus for 18 hours using petroleum ether and absolute alcohol. The same marc was macerated with water for 48 hours to obtain an aqueous extract, with percentage yields of 2.43, 4.53, and 6.5 g for all three extracts, respectively. Adult Swiss albino mice (20-25g) and Wistar rats (160-200g) were used for the entire study including the toxicity and anti-ulcer activity. All animals were kept in standard husbandry parameters (light/dark cycle of 12 hours day/night, temperature of 240°C 20°C) with ample access to foodand water. OECD guiding lines No. 425 were followed to test the acute toxicity of petroleum ether, alcoholic, and aqueous extracts of the plant in 3 h fasting female albino mice. The test extracts' LD50 was determined using AOT 425 software from the Environmental Protection Agency in the United States. After a single dosage administration of all the extracts, aqueous and alcohol extracts were found to be nontoxic up to a dose of 5000 mg/kg, whereas petroleum ether extract was determined to be safe up to a dose of 2000 mg/kg. Rats of either sex weighing 150–170 g are starved for 48h having access to drinking water ad libitum. The

rats were divided into five groups, each with six animals. Group I received vehicle (tween 80), Group II received standard (ranitidine 20 mg/kg), Group III received aqueous extract (500mg/kg), Group IV received alcoholic extract (500mg/kg) and Group V received petroleum ether extract (500mg/kg). All the drugs were administered by oral route. A midline abdominal incision was done under ether anaesthesia. The pylorus was ligated with caution to avoid damaging the blood supply or causing traction on the pylorus. Sutures were used to seal the abdominal wall. Gavage was used to provide the test compounds orally. The animals were kept in plastic cylinders with an inner diameter of 45mm and wire mesh at both ends for 6 hours. The animals are then sacrificed under ether anaesthesia. A ligature was placed around the oesophagus closeto the diaphragm after the abdomen was opened. The contents of the stomach were drained in a centrifuge tube after the stomach was removed. The stomach was opened and pinned on a cork plate along the greater curvature. A dissection microscope was used to examine the mucosa. In pylorus ligated rats, there was a significant reduction in the ulcer index with aqueous and alcoholic extracts, but less significant with petroleum ether, and there was also a significant reduction in free and total acidity. Ulcer index parameter was used for the evaluation of anti-ulcer activity since ulcer formation is directly related to factors such as gastric volume, free and total acidity. This research has revealed that the plant extracts, particularly the aqueous extract, has a potential anti-ulcer activity.[40]

- **Anti-urolithiatic activity**

Urinary stone problem is a common disorder that affects roughly 12% of the global population, with a recurrence rate of 70-81 percent in males. Females make about 47-60% of the population. Raw drugs were exposed to 'Suddhi' (purification procedure) during the production of the drug from the plant *Tinospora sinensis*, as per Classical Siddha scripture. The drug is used to treat renal calculi (Kalladaippu), and it is quickly prepared every day and given orally by gastric intubation. The filtered solution was then directly administered to animals to test antiurolithiatic activity and toxicity study. As per the OECD guidelines 425 the acute oral toxicity study was carried out, the doses were chosen for experiments according to the results of the acute toxicity test. The goal of the study was to find out the effect of *Tinospora sinensis* on therapeutic usage against Ethylene glycol induced Urolithiasis model. Animals were divided into five groups. Each group contains six animals. Group I served as control, groups ranging from II-IV was fed with Ethylene glycol (0.75%) in drinking water for induction of renal calculi till 28th day. Group III received *Tinospora sinensis* (TS - 1ml/kg body weight) and Group IV received *Tinospora sinensis* (TS - 2ml/kg body weight) from 15th day till 28thday, Group V received standard antiurolithiatic drug, Cystone (750mg/kg body weight) from 15th day till 28th day. All doses were administered once daily by oral route. Serum was separated by centrifugation at 10,000 x g for 10 min and analyzed for creatinine, uric acid and urea nitrogen. Blood was collected from the animals via retro-orbital puncture after the experimental period. The both kidneys from each animal, extraneous tissue was removed from both isolated kidneys and stored in 10% neutral formalin. The content of calcium, phosphate, and oxalate in kidney homogenate was measured. Electrolyte estimation in urine and electrolyte estimation in kidney homogenate were investigated. The levels of urinary oxalate, calcium, and phosphorus were significantly lower in the trial drug-treated rats as compared to the control group. Urinary excretion of oxalate, calcium and phosphorus were also significantly decreased in standard group as compared to the control, test drug demonstrated a greater response at a dose of 2 ml/kgthan at a dose of 1 ml/kg, indicating that *Tinospora sinensis* activity is dose dependent. The results reveal that *Tinospora sinensis* at a dose of 2ml/kg reduced urinary stone-forming constituents in a dose-dependent manner.[41]

- **Comparative-Hepatoprotective Activity**

From the year 2011 to 2012, a study to evaluate the hepato-protective activity of *Tinospora sinensis* was done by ***Nagarkar et al., 2013.*** The purpose of this study was to compare the efficacy of *Tinospora cordifolia* (Willd.) Miers ex Hook. F., *Tinospora sinensis* (Lour.) Merrill, and *Tinospora cordifolia* growing on Neem (Azadirachta indica A. Juss.) called Neem- guduchi.z. Guduchi Satwa was made from fresh stems of three Tinospora sp. varieties. Guduchiis one of the most widely prescribed herbs for a variety of ailments due to its therapeutic and preventative properties. The Ayurvedic literature defines the preparation as sediment extract, which is primarily starchy in nature.[42] Male Wistar rats weighing 150–250 g were used in the experiment. All animal studies were carried out in accordance with the National Research Council's international guidelines for the care and management of laboratory animals (1996). The CPCSEA rules (Committee for the Purpose of Control and Supervision of Experimental Animals) were followed in this investigation. According to *Sadashivan et al., 2006* technique the hepatoprotective potential of *T. cordifolia*, *T. sinensis*, and Neem-guduchi was investigated against paracetamol-induced hepatotoxicity.[43] Standard kits (Merck Specialties Pvt. Ltd. India) were used to determine the activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and total bilirubin. The activities of blood enzymes AST, ALT, ALP, and total bilirubin were used to compare the hepatoprotective properties of *T. cordifolia, T. sinensis*, and Neem-guduchi Satwa. When compared to the healthy control group, the paracetamol-treated animals had significantly higher levels of AST, ALT, ALP, and bilirubin. When compared to Neem-guduchi, both T. cordifolia and T. sinensis Satwa significantly reduced paracetamol-induced raised levels of serum ALT, AST, ALP, and BIL at a dose of 200 mg/kg, i.p. The current study revealed that giving Satwa of *T. cordifolia* and T. sinensis at a dose of 200 mg/kg, i.p. reduced the elevated activities of serum marker enzymes AST, ALT, ALP, and total bilirubin level considerably. According to the

results of a hepatoprotective study, Satwa of *T. sinensis* has a better hepatoprotective efficacy than T. cordifolia, however both formulations may provide considerable protection against paracetamol-induced hepatic toxicity.[44]

- **Immunomodulatory Activity**

P.N. Manjrekar et al., 2000, reported the comparative immunomodulatory activity *Tinospora. Sinensis* and *Tinospora cordifolia.* The water and ethanol extracts of the stems of *Tinospora sinensis* and *Tinospora cordifolia* was used to investigate the immunomodulatory activity of cyclophosphamide induced immunosuppression. Fresh stems of *T. cordifolia* and *T. sinensis* were collected and subjected to hot continuous extraction by soxhlet. Separate Soxhlet extractions of sun-dried, powdered stems yielded aqueous extracts of 12.2% wrw. and 22.2 percent yield, and ethanol extracts of 5.6 and 8.2 percent yield, respectively, from *T. cordifolia* and *T. sinensis*. On phytochemical screening, all extracts were positive for alkaloids, glycosides, tannins, and free sugars. Swiss albino mice of either sex, weighing 25-30 g was used to perform the study. Animals were separated into eight groups, each with eight water extracts or seven ethanol extracts. The test extracts were administered to the animals in the treatment groups daily for 14 days, at a dose of 100 mgrkg p.o. in 0.1 percent wrv. carboxymethylcellulose (CMC). Animals in both the positive and negative control groups were given 0.1 percent CMC. 0.3 mlrkg every day, p.o., for 14 days Except for the negative control group, all animals were given with cyclophosphamide 30 mgrkg, i.p., 1 hour after the extracts were administered. On the first day, blood samples were taken, followed by those on the 10th and 14th days. A haemocytometer was used to determine the total white blood cell (WBC) count and haemoglobin. There was a considerable rise in the total count of leucocytes after oral treatment of mice with water and ethanol extracts of *Tinospora cordifolia* and *Tinospora sinensis* stems, with the water extract of *T. sinensis* being the most active. Cyclophosphamide-induced immunosuppression was suppressed by all of the extracts examined. Experiments revealed that both *Tinospora cordifolia* and *Tinospora sinensis* stems had immunomodulatory properties and the ability to prevent cyclophosphamide-induced anaemia, with *T. sinen*sis water extract exceeding *T. cordifolia* water extract in boosting WBC count in mice. As a result, replacing *T. cordifolia* with *T. sinensis* might improve immunomodulatory effects.[45]

- **Hypolipidaemic Activity**

The aqueous extract from the flowers of *Tinospora sinensis* in hydrogenated groundnut oil wasstudies on the hyper cholesterol emic rats with increase in total cholesterol, LDL, PL, Triglycerides and decrease in HDL. Male wistar rats were used for the study and they were categorised into IV groups. Group I received normal diet and water, Group II received Cholesterol 1% + Hydrogenated Ground nut oil (orally), Group III received Cholesterol 1% +HGNO and aqueous extract of *Tinospora sinensis* flowers (100mg/kg Bw/day), Group IV received Cholesterol 1% + HGNO and standard drug (Atorvastatin 3mg/kg Bw/day). The animals were sacrificed via cervical decapitation on the 31st day of the experiment, which lasted 30 days. Blood was drawn and the liver was removed immediately. For further investigation, the latter were rinsed with ice-cold saline and kept at 20°C. For the test of lipoprotein lipase (LPL) activity, liver was homogenised (10% W/V) in cold 100 mm phosphate buffer, pH 7.2. The lipids were extracted from tissues of liver using a chloroform – methanol mixture (2:1 v/v) technique. Using a potter Elvehjam homogenizer, a known weightof tissue was homogenised in 7.0 ml of chloroform – methanol. Total cholesterol, triglycerides, phospholipids, high density lipoprotein (HDL), low density lipoprotein (LDL), and lipoprotein lipase were all measured in the serum and liver (LPL). Zak's approach was used to determine serum cholesterol levels. The usual method was used to compute triglycerides, phospholipids, HDL, LDL, and LPL, LPO, SOD, CAT, and GSH. Supplementing with *Tinospora sinensis* flowers reduced total cholesterol, LDL, TG, and PL levels while increasing HDL levels. Furthermore, supplementation with *Tinospora sinensis* flowers lowered total cholesterol, TG, and PL accumulation in the liver and other peripheral organs, emphasising its powerful hypolipidemic characteristics. *Tinospora sinensis* flowers also reduced oxidative stress significantly by reducing serum and LPO levels. *Tinospora sinensis* flowers supplementation to HFD-fed rats had a significant effect on serum, liver, lipids, and lipoprotein levels, accordingto this study. The activity of lipoprotein lipase was found to be reduced. A high-fat diet also reduced SOD, CAT, and reduced glutathione levels, resulting in a rise in lipid peroxidation. *Tinospora sinensis* flowers (100 mg/kg b.wt./day) changed the rearranged metabolic profile and effectively produced hypolipidemia. The results from the study revaled that the cholesterol-lowering efficiency of *Tinospora sinensis* flowers, which act on a potential modification of cellular lipid homoeostasis and antioxidant state, and could serve as a baseline for the development of an effective antihyperlipidaemic medication with antioxidant efficacy.[36-46]

6. Phytochemistry

Compound no.	Phytoconstituents	Solvent	Percentage yield/ Yield	References
1	Tinosposinenside A	95% Ethanol	0.233	[47]
2	Tinosposinenside B	95% Ethanol	2.666	[47]
3	Tinosposinenside C	95% Ethanol	0.366	[47]
4	1-Deacetyltinosposide A	70% Acetone	1.88	[48]
5	Tinosineside A	Ethanol	0.0000070992	[49]
6	Tinosineside B	Ethanol	0.0000032443	[49]
7	Penta-*O*-acetyl-tinosineside A	Methanol	120 mg	[49,50]
8	Hexa-*O*-acetyl-tinosineside A	Methanol	2.5 mg	[49,50]
9	Palmatrubine	Methanol	0.290	[51]
10	Palmatine	70% Acetone	0.14	[48]
11	3-Hydroxy-2,9,11-trimethoxy-5,6-dihydroisoquino3,2-a-isoquinolinylium	Ethanol	338.117	[51]
12	Lirioresino-β-dimethyl ether	Methanol	2.580	[51]
13	(−)-Pinoresinol-4-*O*-β-D-glucopyranoside	70% acetone	0.32	[48]
14	8'-Epitanegool	70% acetone	0.36	[48]
15	Dehydrocorydalmine	Methanol	6.76	[52]
16	Tinosporafuranol	Ethanol 95%	0.033	[53]
16	ß-sitosterol	Ethanol 95%	0.014	[53]
17	Jatrorrhizine	Methanol	6.76	[52]
18	Tinocordifolioside	70% acetone	0.6	[48]
19	Syringin	70% acetone	0.7	[48]
20	Daucosterol	70% acetone	0.026	[48]
21	Vanillin	70%Methanol	9.7	[54]
22	Dodecanoic acid, methyl ester	70% Methanol	33.46	[54]
23	n-Hexadecanoic acid	70% Methanol	33.46	[54]
24	Oleic acid	70% Methanol	33.46	[54]
25	Octadecanoic acid	70% Methanol	33.46	[54]
26	Docosanoic acid	Hexane	33.46	[54]
27	Ethyl isoallocholate	Hexane	42.23	[54]
28	Vitamin E	Hexane	1.69	[54]
29	Betulin	Hexane	3.35	[54]
30	Campesterol	Hexane	42.23	[54]
31	Stigmasterol	Hexane	42.23	[54]
List of compounds identified by sophisticated analytical instrumentation (HPLC-LTQ-Orbitrap)Diterpenoids				
Compound no.	Phytoconstituents	Empirical Formula	Experimental Mass m/z	References
32	Cordioside	$C_{26}H_{33}O_{12}$	537.19592	[55]
33	Cordifoliside D	$C_{26}H_{33}O_{12}$	537.19623	[55]
34	Tinospinoside D	$C_{27}H_{35}O_{13}$	567.20660	[55]
35	Borapetoside B	$C_{27}H_{35}O_{12}$	551.21204	[55]
36	Amritoside C	$C_{27}H_{35}O_{13}$	567.20612	[55]
37	Tinospinoside B	$C_{27}H_{35}O_{12}$	551.21298	[55]
38	Palmatoside F	$C_{26}H_{31}O_{12}$	535.17987	[55]
39	Rumphioside A	$C_{27}H_{35}O_{13}$	567.20685	[55]
40	Furanoid diterpene glycoside	$C_{26}H_{33}O_{11}$	521.20099	[55]
41	Rumphioside F	$C_{27}H_{35}O_{13}$	567.20642	[55]
42	Amritoside A	$C_{26}H_{35}O_{13}$	555.20624	[55]
43	Rumphioside D	$C_{37}H_{49}O_{17}$	765.29431	[55]
44	Sagittatayunnanoside D	$C_{26}H_{35}O_{11}$	523.21667	[55]
45	Borapetoside H	$C_{33}H_{45}O_{17}$	713.26588	[55]
46	Isocolumbin a	$C_{20}H_{21}O_6$	357.13321	[55]
47	Tinoside	$C_{26}H_{31}O_{11}$	519.18542	[55]

48	Tinocapilactone B	$C_{22}H_{25}O_8$	417.15411	[55]
49	Tinoscorside C	$C_{27}H_{33}O_{12}$	549.19586	[55]
50	Rumphioside I	$C_{27}H_{35}O_{12}$	551.21210	[55]
51	Borapetoside C	$C_{27}H_{35}O_{11}$	535.21637	[55]
52	Borapetoside A	$C_{26}H_{33}O_{12}$	537.19604	[55]
53	8-Hydroxycolumbin	$C_{20}H_{21}O_7$	373.12759	[55]
54	6-Hydroxycolumbin	$C_{20}H_{21}O_7$	373.12759	[55]
55	Boropetoside G	$C_{27}H_{37}O_{11}$	537.23218	[55]
56	Tinocrisposide	$C_{27}H_{35}O_{11}$	535.21600	[55]
57	Cordifolide A	$C_{28}H_{37}O_{12}S$	597.19922	[55]
58	Tinosposinenside C	$C_{26}H_{35}O_{12}$	539.21155	[55]
59	6’-O-Lactoylborapetoside B	$C_{30}H_{39}O_{14}$	623.23434	[55]
60	Columbin	$C_{20}H_{21}O_6$	357.13297	[55]
61	Tinospinoside E	$C_{26}H_{29}O_{11}$	517.16986	[55]
62	Tinosporaside	$C_{25}H_{31}O_{10}$	491.19087	[55]
63	Sagittatayunnanoside B	$C_{33}H_{47}O_{17}$	715.28030	[55]
64	Tinospinoside C	$C_{27}H_{35}O_{12}$	551.21155	[55]
65	Sagittatayunnanoside C	$C_{32}H_{47}O_{15}$	671.28912	[55]
66	Tinosponone	$C_{19}H_{21}O_5$	329.13791	[55]
67	Sagittatayunnanoside A	$C_{26}H_{37}O_{10}$	509.23792	[55]
68	2-O-Lactoylborapetoside B	$C_{30}H_{39}O_{14}$	623.23334	[55]
69	Tinotufolin D	$C_{20}H_{25}O_4$	329.17441	[55]
70	Tinotufolin C	$C_{21}H_{31}O_5$	363.21662	[55]
List of compounds identified by sophisticated analytical instrumentation (HPLC-LTQ-Orbitrap)Non-Diterpenoid				
71	Lotusine	$C_{19}H_{24}NO_3$	314.17507	[56]
72	Tembetarine	$C_{20}H_{26}NO_4$	344.18563	[56]
73	Magnoflorine	$C_{20}H_{24}NO_4$	342.16998	[56]
78	Trans-syringin a	$C_{18}H_{25}O$	417.13913	[56]
79	Tinosinen	$C_{22}H_{32}O_{13}Na$	527.17351	[56]
80	Menisperine	$C_{21}H_{26}NO_4$	356.18563	[56]
81	Cyclanoline	$C_{20}H_{24}NO_4$	342.16998	[56]
82	Colletine b	$C_{20}H_{26}NO_3$	328.19072	[56]
83	Tanegoside	$C_{27}H_{35}O_{14}$	583.20213	[56]
84	Tetrahydropamatine	$C_{21}H_{26}NO_4$	356.18563	[56]
85	Stepharanine	$C_{19}H_{18}NO_4$	324.12303	[56]
86	Dehydrodiscretamine	$C_{19}H_{18}NO_4$	324.12303	[56]
87	Demethyleneberberine	$C_{19}H_{18}NO_4$	324.12303	[56]
88	13-Hydroxypalmatine	$C_{21}H_{22}NO_5$	368.14924	[56]
89	Icariside D1	$C_{19}H_{28}O_{10}Na$	439.15746	[56]
90	Columbamine	$C_{20}H_{20}NO_4$	338.13868	[56]
91	Sagitiside A	$C_{26}H_{34}O_{11}Na$	545.19933	[56]
92	80-Epitanegool	$C_{20}H_{24}O_7Na$	399.14142	[56]
93	Berberine [a]	$C_{20}H_{18}NO_4$	336.12317	[56]
94	Pinoresinol-O--D-glucopyranoside	$C_{26}H_{31}O_{11}$	519.18608	[56]
95	Tinocordifolin	$C_{15}H_{22}O_3Na$	273.14611	[56]
96	Syringaresinol-O--D-glucopyranoside	$C_{28}H_{36}O_{13}Na$	603.20481	[56]
97	Lyoniresinol-2a-O--D-glucopyranoside	$C_{28}H_{38}O_{13}Na$	605.22046	[56]
98	13-methylberberine b	$C_{21}H_{20}NO_4$	350.13868	[56]
99	N-Formylannonain	$C_{18}H_{16}NO_3$	294.11246	[56]
100	Ursolic acid	$C_{30}H_{47}O_3$	455.35197	[56]
101	Oleanic acid	$C_{30}H_{47}O_3$	455.35197	[56]
102	β-Sitosterol glycoside	$C_{36}H_{61}O_8$	621.43609	[56]

7. DISCUSSION

Tinospora sinensis, distributed in South and Southeast Asia, from countries like India, China, Nepal, Sri Lanka, Bangladesh, Myanmar, Thailand, Vietnam and Cambodia. In India it is distributed in the states like Assam, Orissa, Bihar, Maharashtra, Andhra Pradesh, Karnataka and Kerala which is used for its therapeutic activity. As previously said in this study, the plantis well-known for its usage in traditional medicine, which is used to treat disease conditions varying in severity from modest to major. This article has presented a summary of the actions related to plant botany, ethno medicinal value, phytoconstituents, pharmacology, and toxicology that have been recorded to date. This review of *Tinospora sinensis*, on the other hand, highlighted the reported data and the existing research gap, both of which are importantwhen considering *Tinospora sinensis* as an ethnopharmacological and medicinal plant. The preliminary phytochemical investigation in different extracts reported the presence of glucoside, glycoside, terpenoids, diterpenoids, non diterprnoids, polyphenols, alkaloids, steroids, saponins, tannins and lignans. Numerous phytoconstituents were isolated and identified, of which few major compounds, viz., tinosposineside A. tinosposineside B, tinosposineside C, tinosineside A, tinosineside B, β-sitosterol and possesses significant pharmacological activities.

Ethanolic leaf extract of *Tinospora sinensis* exhibited antibacterial efficacy against *Candida albicans*, *Pseudomonas aeruginosa*, and *Aspergillus niger*. The plant extracts, particularly the aqueous extract, has a potential anti-ulcer activity. The alcoholic extract of *Tinospora sinensis*roots has a high potency, which can be attributed to its hepatoprotective properties. The methanolic extract of *Tinospora sinensis* leaves has more potential activity than chloroform and ethyl acetate extract. The methanolic extract of flowers of *Tinospora sinensis* has a great potency in immunity, resulting in hypolipidemia.

8. CONCLUSION

The aim of this review is to summarize the progress of *Tinospora sinensis* from its traditional use to its utility in modern therapeutics. *Tinospora sinensis* is distributed in South and Southeast Asia, from countries like India, China, Nepal, Sri Lanka, Bangladesh, Myanmar, Thailand, Vietnam and Cambodia. In India, it is distributed in the states like Assam, Orissa, Bihar, Maharashtra, Andhra Pradesh, Karnataka and Kerala as per extensive literature survey. Many significant phytochemical components are found in the plant and they are responsible for a variety of pharmacological activities. As a result of this research, we can conclude that the study of this plant can be extended for future scientific investigation in the area of core pharmacology and phytochemistry to unveil hidden novel entity for safe therapeutic uses.

Conflict of Interest

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