

Menispermaceae Family of Plants and its Action against Infectious Diseases: A Review

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Abstract

India is a country where traditional medicines play a huge role in primary health care. Ayurveda, Siddha, Unani are some of the well-known traditional practices which has been in use for centuries and these traditional systems are greatly dependent on medicinal plants. India's rich bio-diversity assures various plants species with high medicinal values. The Western Ghats of peninsular India is known for its rich diversity and presence of uncommon endemic species. Menispermaceae family consists of more than 400 species; all are reported to have high medicinal values. Different classes of alkaloids present may be the major reason for these biological potentials, which are of great interest for various research groups. Benzyloquinoline alkaloids, protoberberine alkaloids, aporphine alkaloids, etc are some examples for the alkaloids present in menispermaceae family. This review deals with the phytochemistry and pharmacological study of menispermaceae family and the action of these plants

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against various infectious diseases described in Ayurveda.

Keywords: Menispermaceae family, alkaloids, benzyloisoquinoline alkaloids, protoberberine alkaloids.

1. Introduction

Conventional medicines otherwise called the well-known traditional medicines are an imperative part of Indian culture and fortunately, we have a huge repository of medicinal plants that are used in these traditional systems. These ethnomedicinal species and their uses are well accepted in ethnic traditional systems like Unani Ayurveda, Siddha, and Allopathy. Medicinal plants are the backbone of customary medicines in most of the developing countries, which means that majority of the world relies on these medicinal plants as a basis of their primary medication, especially in rural areas. For centuries, plants have remained the foremost source of medicine. They provide a storehouse of remedies to almost all ailments of humankind. Tribal communities are also using plants in different forms like crushed, powders, or mixtures for this purpose. However, the term Natural products mainly focus on organic and inorganic scaffolds from nature, in which the main attraction is towards the organic moieties with structural diversities. Isolation, identification of structure, and biological evaluation of these secondary metabolites are the major processes involved in Natural product chemistry. It has been estimated that over 3,00,000 secondary metabolites exist¹ which comprises alkaloids, flavonoids, terpenoids, sterols, etc. Most of these are reported to have excellent medicinal properties, which are subject to extensive studies. Also, secondary metabolites have often attracted the curiosity of researchers because of their biological effect on other organisms.

Natural products, especially secondary metabolites, have great potential for developing novel therapeutic agents and are usually stated as keystones of the drug discovery process. The diverse chemical structure of natural products can serve as a lead for novel drugs. Earth, which is a rich source of flora and fauna, consists of around 75,000 plant species, but only 10% of it is utilized for their

medicinal properties and 1-5% are validated scientifically.² Due to this reason, there has been an endlessly budding interest of drugs originating from plants, which have been found to form an important class for disease control. Aspirin, morphine, paclitaxel, etc. are some examples of plant-derived drugs in modern medicine.

These NPs are found in abundance in different natural sources like medicinal plants, microbes, etc. In this group, medicinal plants are found to be more important due to their availability and rich reservoir of bioactives, which can be utilized for the development of new pharmaceuticals. Greater side effects and costs offered by synthetic drugs has made the exploration of new drugs from natural sources more valid.

Alkaloids have a major role in modern medicine. The renowned drugs vinblastine, vincristine, morphine, codeine, nicotine, strychnine, etc. are nitrogen-containing compounds still in medicinal use (Figure 1). These categories of compounds hold a wide range of pharmacological properties like antimalarial, anti-inflammatory, anticancer, analgesic, anti-bacterial, etc. Family menispermaceae is very much prominent for its alkaloid contents. It covers different classes of alkaloids like protoberberine alkaloids, benzyloisoquinoline alkaloids, atropine alkaloids, aporphine alkaloids, etc. The present study intends a comprehensive review of the phytochemistry of the menispermaceae family and its alkaloid contents.

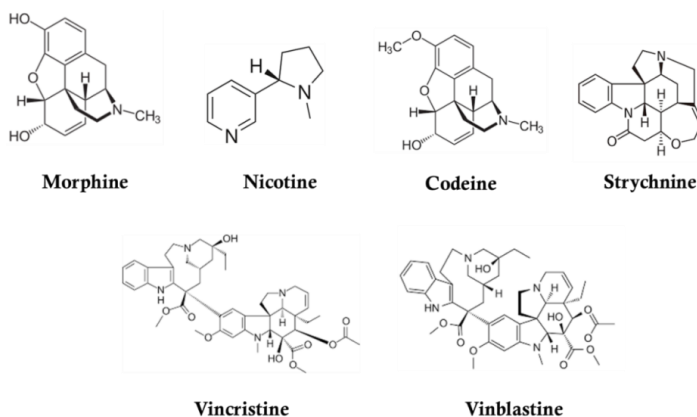


Figure 1: Alkaloids in medicine

2. Menispermaceae Family

In 1789, A. L. de Jussieu named the Menispermaceae family, which is also renowned as the Moonseed family due to the half-moon shaped seeds. It was later renamed as Menispermoidees by Ventenat and Menispermées by Jaume. Later A.P. de Candolle in 1824 made another classification into Schizandreae, Menispermeeae, Lardizabaleae tribes. Schizandreae and Lardizabaleae were further contained within Berberidaceae and Magnoliaceae family correspondingly.

Miers carried out a classification based on embryo structure in 1851, which described six tribes: Anomospermeae, Tiliacoreae, Heterocinaceae, Pachygoneae, Leptogoneae, and Platygoneae. After several such classifications, finally, Diels put out a novel partition based on Mier’s work in 1910, which consists of 8 tribes: Anomospermeae, Cocculeae, Anamirteae, Peniantheae, Tricliseae, Fibraureae, Hyperbaeneae, and Tinosporeae.³

Ranunculales is the super order of menispermaceae family, composed of eight tribes and three sub-tribes. 72 genera and nearly 400 species are present in this family and the species are dispersed all over the world, but predominantly in the temperate, tropical, subtropical regions. 19 genera and 77 species are found in China where 43 are endemics⁴. *Stephania* is the largest genus with 43 species, trailed by *Tinospora* with 35 species, 30 species from genus *Abuta* or *Cocculus*, 22 species from genus *Tiliacora*, and 19 species for both *Cissampelos* and *Cyclea*. The position of the family according to Dahlgren’s classification is:

Table 1: Scientific classification

Kingdom	Plantae
Class	Magnoliopsidae
Sub-Class	Magnoliidae
Super Order	Ranunculiflorae
Order	Ranunculales
Family	Menispermaceae

The genera of menispermaceae family include;

Albertisia, Abuta, Anamirta, Anomospermum, Anisocycla, Antizoma, Aspidocarya, Arcangelisia, Beirnaertia, Burasaia, Borismene, Calycocarpum, Caryomene, Carronia, Cebatha, Chlaenandra, Chasmanthera, Chondrodendron, Cocculus, Cissampelos, Coscinium, Cyclea, Curarea, Dioscoreophyllum, Disciphania, Dialythea, Diploclisia, Echinostephia, Eleutharrhena, Elephantomene, Fibraurea, Hypserpa, Hyperbaena, Jateorhiza, Kolobopetalum, Limacia, Leptoterantha, Limaciopsis, Menispermum, Orthogynium, Odontocarya, Orthomene, Parabaena, Pachygone, Parapachygone, Pericampylus, Penianthus, Pycnarrhena, Perichasma, Rhigiocarya, Rhaptonema, Sciadotenia, Spirospermum, Sinomenium, Stephania, Syrrheonema, Synclisia, Syrrhonema, Tiliacora, Telitoxicum, Tinomiscium, Triclisia, Tinospora, Ungulipetalum.

The benzyltetrahydroisoquinoline class of alkaloids can be taken as marker compounds of this family because these bioactives are found to occur mostly in Magnoliiflorae and Ranunculiflorae orders. The well-known dart poisons “curare” is made by using these classes of compound which make them medicinally important. These type of poisons are widely used by South Americans for immobilizing birds and animals, and they work effectively as drugs, such as “atracurium” which is used for treating anesthesia.³ Among the 22 different class of alkaloids reported from the family, benzylisoquinoline types are the most abundant present, atropine alkaloids are in the second place and protoberberine alkaloids are the third most abundant.

2.1 Medicinal Importance

The menispermaceae family plants possess a huge role in traditional and folk medicine. They are an integral part of many Ayurvedic preparations. For example, *Cycleapeltata* otherwise padakizhangu in Malayalam, is widely recognized in Ayurveda, which is the main component of various polyherbal combinations like Panchagavyagritham, Mahatikthakagritham, Gulguluthikthakagritham, Saraswathamgritham, etc.⁵ *Tinosporacordifolia*, another plant from the family, otherwise called Guduchi, finds a special place in folk and tribal medicine. The stem

is bitter, helps to stimulate bile secretion, acts as a diuretic, causes vomiting, constipation, burning sensation, cures jaundice, and also enriches the blood. The stem is useful in treating skin diseases. Mixture of stem and root are recommended as an antidote for snakebite and scorpion sting.⁶

Stephaniaglabra is another well-recognized plant of this family. The tuber is ethnobotanically used to cure tuberculosis, fever, dysentery, diabetes, sleep disturbances, intestinal troubles, cancer, inflammation, mental disorders, and asthma in many Asian countries. The plant is widely used as a veterinary medicine also.⁷

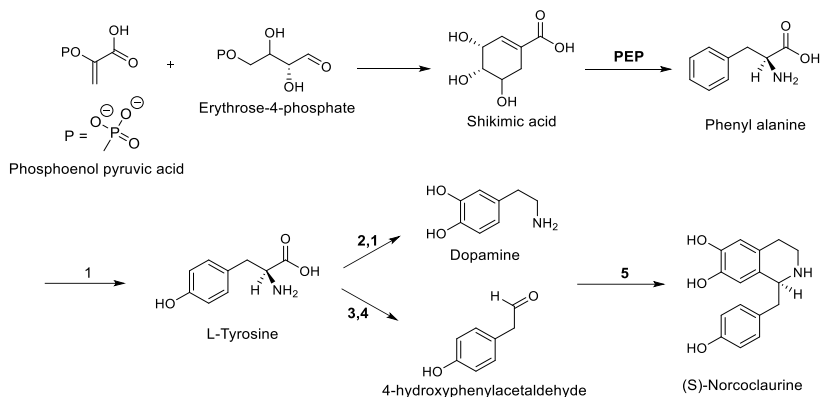
Internationally also, menispermaceae family is widely used. The folk medicines of Bangladesh mainly depend on these plants for dealing with various disorders. Six species of this family mainly *Tinosporacrispa*, *Cocculushirsutus*, *Stephania japonica*, *Tinosporasinensis*, *Stephaniaglabra* and *Tinosporacordifolia* were found to be used by the Kavirajes of Bangladesh and *T. cordifolia* and *S. japonica* were most frequently used for curing gastrointestinal disorders, tuberculosis, diabetes, edema, respiratory tract disorders, urinary tract problems, bone fracture, helminthiasis, hepatic disorders, malaria, etc. This information has also been validated through scientific studies.⁸

2.2 Biosynthetic pathway of alkaloids of Menispermaceae family

Biosynthesis is a multi-step process usually taking place in almost all living organisms, where substrates are converted into more complex products via an enzyme-catalyzed process. It occurs via a series of chemical reactions where simple compounds are converted into other compounds with more complex structure, or hinged together to form macromolecules.

Biosynthesis of the most commonly reported benzylisoquinoline alkaloids of menispermaceae family starts from the synthesis of shikimic acid. Phosphoenolpyruvic acid and erythrose-4-phosphate undergo reaction to form the shikimic acid, which is a source and a large precursor for wide variety of secondary metabolites. It further reacts with phosphoenolpyruvic acid (PEP), trailed by a sequence of reactions to produce phenylalanine, which undergo decarboxylation and deamination simultaneously to produce two important intermediates phenylethylamine and phenylacetaldehyde

respectively. These two monomers combine to form the benzyltetrahydroisoquinolinecore, which is a crucial intermediate in the construction of most of the benzyloisoquinoline compounds reported from the family and these compounds can be accounted as worthy markers for this family since they occur customarily in the super-orders Ranunculiflorae and Magnoliiflorae.³



Scheme 1. Biosynthetic pathway of alkaloids

2.3 The plant list

The family includes;

Abuta – 34 accepted species

Abuta acutifolia, *Abuta chiapasensis*, *Abuta colombiana*, *Abuta chocoensis*, *Abuta dwyeriana*, *Abuta grandifolia*, *Abuta fluminum*, *Abutagrisebachii*, *Abuta longa*, *Abuta imene*, *Abuta mycetandra*, *Abuta pahni*, *Abuta obovata*, *Abuta panamensis*, *Abutaplatyphylla*, *Abuta panurensis*, *Abuta racemosa*, *Abuta sandwichiana*, *Abuta rufescens*, *Abuta schomburgkii*, *Abuta seloana*, *Abuta seemannii*, *Abuta solimoesensis*, *Abuta spicata*, *Abutasoukupii*, *Abuta steyermarkii*, *Abuta velutina*, *Abuta vaupesensis*.

Albertisia – 20

Albertisia capituliflora, *Albertisia apiculate*, *Albertisia cordifolia*, *Albertisia cuneata*, *Albertisia crassa*, *Albertisia exelliana*, *Albertisia delagoensis*, *Albertisia ferruginea*, *Albertisialaurifolia*, *Albertisia glabra*, *Albertisia manganotii*, *Albertisia megacarpa*, *Albertisia mecistophylla*,

Albertisia papuana, *Albertisia puberula*, *Albertisia porcata*, *Albertisia scandens*, *Albertisia undulata*, *Albertisia triplinervis* Forman, *Albertisia villosa*.

Anamirta - 1

Anamirta cocculus

Anisocycla - 5

Anisocycla linearis, *Anisocycla blepharosepala*, *Anisocycla cymosa*, *Anisocycla jollyana*, *Anisocycla grandidieri*.

Anomospermum - 8

Anomospermum chloranthum, *Anomospermum andersonii*, *Anomospermum bolivianum*, *Anomospermum grandifolium*, *Anomospermum reticulatum*, *Anomospermum matogrossense*, *Anomospermum steyermarkii*, *Anomospermum solimoesianum*.

Antizoma - 3

Antizoma angolensis, *Antizoma miersiana*, *Antizoma angustifolia*.

Arcangelisia - 3

Arcangelisia flava, *Arcangelisia tympanopoda*, *Arcangelisia gusanlung*.

Aspidocarya - 1

Aspidocarya uvifera

Beirnaertia - 1

Beirnaertia cabindensis

Borismene - 1

Borismene japurensis

Burasaia - 4

Burasaia australis, *Burasaia gracilis*, *Burasaia congesta*, *Burasaia madagascariensis*.

Calycocarpum - 1

Calycocarpum lyonii

Carronia - 4

Carronia multiselepala, *Carronia protensa*, *Carronia pedicellata* Forman, *Carronia thyrsoflora*.

Caryomene - 5

Caryomene foveolata, *Caryomene grandifolia*, *Caryomene olivascens*,
Caryomene glaucescens, *Caryomene prumnoides*.

Cebatha - 1

Cebatha sagittifolia

Chasmanthera - 2

Chasmanthera welwitschii, *Chasmanthera dependens*.

Chlaenandra-1

Chlaenandra ovata Miq.

Chondrodendron- 6

Chondrodendron iquitianum, *Chondrodendron microphyllum*,
Chondrodendron tomentocarpum, *Chondrodendron platyphyllum*,
Chondrodendron tomentosum, *Chondrodendron limaciiifolium*.

Cissampelos-21

Cissampelos capensis, *Cissampelos glaberrima*, *Cissampelos andromorpha*,
Cissampelos friesiorum, *Cissampelos fasciculata*, *Cissampelos grandifolia*,
Cissampelos hispida, *Cissampelos hirta*, *Cissampelos laxiflora*,
Cissampelos nepalensis, *Cissampelos mucronata*, *Cissampelos ovalifolia*,
Cissampelos nigrescens, *Cissampelos owariensis*, *Cissampelos rigidifolia*,
Cissampelos pareira, *Cissampelossympodialis*, *Cissampelos torulosa*,
Cissampelos verticillata, *Cissampelos tropaeolifolia*, *Cissampelos tenuipes*.

Cocculus-9

Cocculus carolinus (L.) DC., *Cocculus balfourii* Schweinf. ex Balf.f.,
Cocculus diversifolius DC., *Cocculus hirsutus* (L.) W.Theob, *Cocculus carolinus*,
Cocculus laurifolius, *Cocculus orbiculatus*, *Cocculus madagascariensis*,
Cocculus prainianus (Diels) A.Pramanik & Thoth
Cocculus pendulus.

Coscinium - 2

Coscinium fenestratum (Goetgh.) Colebr., *Coscinium blumeanum*.

Curarea - 5

Curarea cuatrecasatii, *Curarea crassa*, *Curarea candicans*, *Curarea toxicofera*,
Curarea tecunarum.

Cyclea- 36

Cyclea gracillima Diels, *Cyclea aphylla*, *Cyclea acuminatissima*, *Cyclea barbata*,
Cyclea apoensis, *Cyclea atjehensis*, *Cyclea bicristata*, *Cyclea*

cauliflora, *Cyclea caudata*, *Cyclea ciliata*, *Cyclea densiflora*, *Cyclea debiliflora*, *Cyclea elegans*, *Cyclea fissicalyx*, *Cyclea fansipanensis*, *Cyclea hypoglauca*, *Cyclea hainanensis*, *Cyclea kinabaluensis*, *Cyclea insularis*, *Cyclea laxiflora*, *Cyclea meeboldii*, *Cyclea longgangensis*, *Cyclea merrillii*, *Cyclea peltata*, *Cyclea migoana*, *Cyclea pendulina*, *Cyclea polypetala*, *Cyclea peregrina*, *Cyclea racemosa*, *Cyclea scyphigera*, *Cyclea robusta*, *Cyclea sutchuenensis*, *Cyclea varians*, *Cyclea wattii*, *Cyclea wallichii*.

Dialythea - 1

Dialythea gossweileri

Dioscoreophyllum -3

Dioscoreophyllum gossweileri, *Dioscoreophyllum cumminsii*,
Dioscoreophyllum volkensisii.

Diploclisia -2

Diploclisia glaucescens (Blume) Diels, *Diploclisia affinis* (Oliv.) Diels,

Disciphania-26

Disciphania cardiophylla, *Disciphania calocarpa*, *Disciphania convolvulacea*, *Disciphania contraversa*, *Disciphania cubijensis*, *Disciphania domingensis*, *Disciphania dioscoreoides*, *Disciphaniaaernstii*, *Disciphania heterophylla*, *Disciphania hernandia*, *Disciphania inversa*, *Disciphania killipii*, *Disciphania juliflora*, *Disciphania lobata*, *Disciphania modesta*, *Disciphania mexicana*, *Disciphania moriorum*, *Disciphania remota*, *Disciphania nesiotetes*, *Disciphania sagittaria*, *Disciphania smithii*, *Disciphania sarcostephana*, *Disciphania spadicea*, *Disciphania tricaudata*, *Disciphania tessmannii*, *Disciphania unilateralis*.

Echinostephia -1

Echinostephia aculeata

Elephantomene-1

Elephantomene eburnea

Eleutharrhena -1

Eleutharrhena macrocarpa

Fibraurea -3

Fibraurea tinctoria Lour, *Fibraurea recisa* Pierre, *Fibraurea darshanii* Udayan & K.Ravik.,.

Hyperbaena -13

Hyperbaena axilliflora, *Hyperbaena allenii*, *Hyperbaena columbica*,
Hyperbaena domingensis, *Hyperbaena cubensis*, *Hyperbaena hassleri*,
Hyperbaena jalcomulcensis, *Hyperbaena ilicifolia*, *Hyperbaena laurifolia*,
Hyperbaena winzerlingii, *Hyperbaena oblongifolia*, *Hyperbaena*
mexicana, *Hyperbaena tonduzii*.

Hypserpa - 3

Hypserpa decumbens, *Hypserpa nitida*, *Hypserpa laurina*

Jateorhiza -2

Jateorhiza palmata (Lam.) Miers, *Jateorhiza macrantha*

Kolobopetalum - 2

Kolobopetalum chevalieri, *Kolobopetalum auriculatum* Engl.

Leptoterantha - 1

Leptoterantha mayumbensis.

Limacia - 1

Limacia blumei

Limaciopsis - 1

Limaciopsis loangensis

Menispermum 2

Menispermum dauricum, *Menispermum canadense*

Odontocarya - 30

Odontocaryamonandra, *Odontocarya diplobotrya*, *Odontocarya*
micrantha, *Odontocarya arifolia*, *Odontocarya petiolaris*, *Odontocarya*
acuparata, *Odontocarya asarifolia*, *Odontocarya dielsiana*, *Odontocarya*
deminuta, *Odontocarya hastata*, *Odontocarya floribunda*, *Odontocarya*
integrifolia, *Odontocarya krukoviana*, *Odontocarya klugii*, *Odontocarya*
echinus, *Odontocarya mexicana*, *Odontocarya magnifolia*, *Odontocarya*
perforata, *Odontocarya mallosperma*, *Odontocarya steyermarkii*,
Odontocarya rusbyi, *Odontocarya tamoides*, *Odontocarya truncata*,
Odontocarya tripetala, *Odontocarya ulei*, *Odontocarya emarginata*,
Odontocarya zuliana, *Odontocarya vitis*, *Odontocarya uva-alba*,
Odontocarya wullschlaegelii.

Orthogynium - 1

Orthogynium gomphioides

Orthomene - 3

Orthomene verruculosa, *Orthomene schomburgkii*, *Orthomene hirsuta*.

Pachygone - 5

Pachygone ovata, *Pachygone yunnanensis*, *Pachygone sinica* Diels.,
Pachygone valida Diels., *Pachygone plukenetii*.

Parabaena - 1

Parabaena sagittata Miers

Parapachygone - 1

Parapachygone longifolia

Penianthus - 2

Penianthus zenkeri, *Penianthus longifolius* Miers.

Pericampylus - 2

Pericampylus incanus, *Pericampylus glaucus*.

Perichasma - 1

Perichasma laetificata Miers

Pycnarrhena - 3

Pycnarrhena lucida (Teijsm. & Binn.) Miq, *Pycnarrhena longifolia*
(Decne. ex Miq.) Becc., *Pycnarrhena poilanei* (Gagnep.) Forman.

Rhaptonea - 2

Rhaptonea thouarsiana (Baill.) Diels, *Rhaptonea densiflora* (Baker)
Diels.

Rhigiocarya - 1

Rhigiocarya racemifera Miers

Sciadotenia - 10

Sciadotenia cayennensis, *Sciadotenia peruviana*, *Sciadotenia amazonica*,
Sciadotenia nitida, *Sciadotenia mathiasiana*, *Sciadotenia paraensis*,
Sciadotenia ramiflora, *Sciadotenia sagotiana*, *Sciadotenia toxifera*,
Sciadotenia sprucei.

Sinomenium - 1

Sinomenium acutum

Spirospermum - 1

Spirospermum penduliflorum

Stephania - 40

Stephania abyssinica, *Stephaniabrevipedunculata*, *Stephania brachyandra*, *Stephania capitata*, *Stephania chingtungensis*, *Stephaniacephalantha*, *Stephania cyanantha*, *Stephania dentifolia*, *Stephania delavayi*, *Stephania dicentrinifera*, *Stephania dinklagei*, *Stephania dielsiana*, *Stephania dolichopoda*, *Stephania elegans*, *Stephania ebracteata*, *Stephania epigaea*, *Stephaniaglabra*, *Stephania excentrica*, *Stephania gracilentata*, *Stephania herbacea*, *Stephania hainanensis*, *Stephania viridiflavens*, *Stephania intermedia*, *Stephania kuinanensis*, *Stephania kwangsiensis*, *Stephania longa*, *Stephania longipes*, *Stephania merrillii*, *Stephania mashanica*, *Stephaniamicrantha*, *Stephaniaofficinarum*, *Stephania miyiensis*, *Stephania sinica*, *Stephania yunnanensis*, *Stephania lincangensis*, *Stephania japonica*, *Stephania succifera*, *Stephania subpeltata*, *Stephania sutchuenensis*, *Stephaniatetrandra*.

Synclisia - 1

Synclisia scabrida

Syrrhonema - 1

Syrrhonema fasciculatum

Syrrhonema - 1

Syrrhonema welwitschii

Telitoxicum - 5

Telitoxicum krukovii, *Telitoxicum inopinatum*, *Telitoxicum peruvianum*, *Telitoxicum duckei*, *Telitoxicum minutiflorum*.

Tiliacora - 8

Tiliacora funifera, *Tiliacora chrysobotrya*, *Tiliacora gossweileri*, *Tiliacoragabonensis*, *Tiliacora macrophylla*, *Tiliacoraleonensis*, *Tiliacora klaineana*, *Tiliacora acuminata*

Tinomiscium - 1

Tinomiscium petiolare Hook. f. & Thomson

Tinospora - 13

Tinospora uviforme, *Tinospora caffra*, *Tinospora bakis*, *Tinospora cordifolia*, *Tinospora dentata*, *Tinospora crispa*, *Tinospora fragosa*, *Tinospora hainanensis*, *Tinospora quangxiensis*, *Tinospora oblongifolia*, *Tinospora sinensis*, *Tinospora sagittata*, *Tinospora tenera*.

Triclisia - 8

Triclisia calopicrosia, *Triclisia subcordata* Oliv., *Triclisia saeleuxii*, *Triclisia dictyophylla*, *Triclisia angustifolia*, *Triclisia loucoubensis*, *Triclisia patens* Oliv., *Triclisia macrocarpa*.

Ungulipetalum 1

Ungulipetalum filipendulum

Species in Kerala

Among the 72 genera and around 400 species reported, 20 species are found in Kerala. They are;

Table 2: Species reported from Kerala

Species	Common name
<i>Anamitra cocculus</i>	Garaphala, Kaipalathumka, Kollakkaya, Nanchuvalli, Pechuvalli, Pettumarunna
<i>Cissampelos pareira</i>	Karanakody, Malathangi, Pambuveru
<i>Cocculus hirsutus</i>	Pathalagarudakkodi
<i>Cocculus laurifolius</i>	Aadukolli, Marpinky
<i>Cocculus pendulus</i>	
<i>Coscinium fenestratum</i>	Maramanjil, Marathi, Manjavalli
<i>Cyclea peltata</i>	Padathali, Padavalli, Padakizhangu,
<i>Cyclea fissicalyx</i>	
<i>Cyclea barbata</i>	
<i>Diploclisia glaucescens</i>	Vattavalli, Vattoli
<i>Fibraurea darshanii</i>	
<i>Pachygone ovata</i>	Katukodyvally
<i>Stephania wightii</i>	Malathangi
<i>Stephania japonica</i> var. <i>discolor</i>	
<i>Stephania japonica</i> var. <i>japonica</i>	Patakilammu, Paasichedi Patavalli, Amrutavalli, Chitamruthu, Amrthu, Siddamirth
<i>Tinospora cordifolia</i>	Vallikanjiram
<i>Tiliacora acuminata</i>	Kaipamruth
<i>Tinospora crispa</i>	
<i>Tinospora formanii</i>	
<i>Tinospora sinensis</i>	Kattamruthu, Peiamruthu

All are reported as climbers and possess high medicinal values.

2.4 Brief description of some selected species

2.4.1 *Stephania*

Genus *Stephania* contains most number of plants; 43 varieties. Around 60 species are found in subtropical and tropical regions of Asia and Africa, 37 species including 30 endemics in China and few in Oceania. Tuberous roots of this genus are widely used in Chinese medicine. Most of *Stephania* genus are found as slender climbers and are conventionally used for the treatment of various sicknesses like dysentery, pyrexia, indigestion, urinary diseases, tuberculosis, dyspepsia, sore-breasts, abdominal ills, asthma, sleep disturbances, diarrhea, wounds, headache, leprosy, etc. Likewise, the other species of menispermaceae family, this genus is also famous for its alkaloid content, having more than 50 kinds of alkaloids such as morphines, hasubanans, berberines, hasubanalactams, and aporphines. *S. glabra* (Roxb.) Miers is one among the well-studied plants in this genus. Ethnobotanically, its rhizome decoction is used as antipyretic, antituberculosis, antidysenteric, etc. The aqueous extract of the dried rhizome along with the aerial root of *Trichosanthes multiloba* is used as an antianthelmintic agent against intestinal worms in Meghalaya. Properties like aphrodisiac, sedative, and analgesic effects were reported for the stems of *S. dinklagei* Diels, while the leaves of this plant is used to cure impotency in males and infertility in females. The roots of *S. hernandifolia* was used as a remedy for fever, dyspepsia, diarrhea, and urinary diseases. *S. rotunda* Lour is commonly used as an agent to treat dysmenorrhoea, abdominal ills, asthma, dysentery, wounds, fever, indigestion, head-ache, sore-breasts, etc. The roots of two *Stephania* genus; *S. tetrandra* and *S. Moore*, have been used in combination against hepato fibrogenic disease and also used as diuretic, antipyretic, anti-phlogistic, anti-rheumatic, and analgesic in China for centuries. *S. cepharantha*, another species, is known for its activity against various long-lasting diseases, and venomous snakebites in Japan. The Chakma and Tonchonga tribes of Bangladesh use vines of *S. japonica* for curing leucorrhoea, urinary problems like burning sensations during urination, presence of semen in urine, etc. Apart from this, these species also possess analgesic activity, anthelmintic activity, anti-viral activity, anti-inflammatory activity, antimicrobial

activity, antimalarial activity, antipsychotic activity, anti-proliferative activity etc.⁹

One of the most studied species of this genus is *S. japonica* Linn. In 2014, Uddin *et al.* reported the antioxidant activity of *S. japonica* Linn by DPPH assay and reducing power assay and reported that the IC₅₀ values (18.57 µg/mL) of the alcoholic extract seems to be moderate when compared to the standard ascorbic acid (1.97 µg/mL). The methanolic extract of leaves possesses anti-nociceptive activity, established in mice model¹⁰. It also exhibits anti-hyperglycemic effect, neuroprotective activity, insecticidal activity, anti-microbial and cytotoxic effect, anti-diarrheal activity etc.¹¹

Around 30 alkaloids such as asbenzylisoquinolines, protoberberines, and aporphines are also reported from the tuber of *S. glabra*. Earlier, this plant was included in genus *Cissampelos* and named as *Cissampelos glabra* due to its analogous taxonomical features with *Cissampelos* species. Later, it was moved to the genus *Stephania* grounded on dissimilar floral characteristics compared to *Cissampelos*. In some parts of India, *S. glabra* is considered as a threatened plant because of its overuse in traditional medicine. The aqueous decoction of the tuber is used against common fever, filariasis, pneumonia, malaria, typhoid etc.¹² Common names of plant includes *Stephania hernandifolia*, *Stephania japonica* etc.

2.4.2 *Cocculus*

About eight species are reported for this genus worldwide including Africa, South Asia, Europe, Central, and North America, Pacific Islands, and two species in China.⁴ They are mostly found as dioecious climbers, rarely trees, shrubs, or herbs. *Cocculus orbiculatus*, *Cocculus carolinus*, *Cocculus laurifolius*, *Cocculus orbiculatus* var. *orbiculatus*, *Cocculus diversifolius* are some of the species reported from this genus.

Cocculus hirsutus, commonly named as broom creeper, ink berry is an important flowering plant of this genus and has a threatened belonging. It is also well-studied. In Malayalam, it is renowned as pathalagarudakodi, pathalamuli, etc. In India, these are mainly found in Rajasthan.¹³ Tribals of Jhabua and Khargone and Dhar use the fruits of this plant to cure jaundice.¹⁴ The plant is also used as herbal medicines to treat numerous maladies including

inflammation, rheumatism, arthritis, muscle swelling, insect bites, pains, etc.¹⁵ It also has properties like diuretic, laxative. The root extract exhibited pain-relieving and anti-inflammatory effects. The leaves are useful against cough, neuralgia, gonorrhoea, ophthalmia, and used to treat skin infections. In Rajasthan, the cooked leaves are taken as a remedy for night blindness. Recent studies have shown the antidiabetic and spermatogenic activity of *C. hirsutus* in rats also.¹⁶

Cocculus pendulus also well-known as *Cocculus ellipticus*, *Menispermum ellipticum*, *Cocculus laevis*, is used in the traditional system for treating leprosy, syphilis, menstrual disorder, helminthic, inflammation, jaundice, malaria, fever, and rheumatic pain. The plant contains phytochemicals such as cocculine, sinococculine, pedulin, cocculidine, and cocsuline, while the root contains sangoline, pelosine, columbin, etc. Pharmacologically it possesses anti-inflammatory activity, wound healing activity, spermicidal activity, anti-oxidant activity, etc.¹³

Anamirta cocculus is a Southeast Asian and Indian climbing plant which is a source of picrotoxin, a poisonous compound with stimulant properties, often referred to as *C. indicus* or *Fructuscocculi* in pharmacology.¹⁷

2.4.3 Cissampelos

Cissampelos is a native of southern Africa. About 25 species are found, commonly in America, Africa, and few in Asia and one species in China. The name “*Cissampelos*” is emerged from Greek words “*kissos*” meaning “Ivy” and “*ampelos*” denotes “vine”. The name refers to the ivy-like growth of this plant with green rambling branches and the grape-like racemes of fruits.¹⁸ One of the well-studied species is *Cissampelos pareira*, which is a climbing herb, known as ambastha or lagupatha in India’s traditional system. In English, it is commonly referred to as velvet-leaf or Abuta and in Malayalam asmalathangi, vattavally, etc. Ethnobotanically, the plant, especially its roots, are used for treating several infirmities like dysentery, asthma, urinary difficulties like cystitis, etc. Two novel tropolisoquinoline alkaloids were isolated from the plant, Pareirubrines A and B having anti-leukemic properties. Deyamittin, pelosine, tertrandrine are also identified from the plant. The root of

the plant possesses *l*-curine, menisminine, pareirine, hayatine etc. It also has 0.2% essential oils.¹⁹

Cissampelos capensis, commonly known as “dawidjies” or “dawidjieswortel” in Africa, is one of the best known medicinal plant used by the Khoisan tribes of Maharashtra and rural natives of South Africa. Salutaridine, a morphinane alkaloid, aporphine alkaloids like Bulbocapnine, dicentrine were the main compounds reported from the leaves, though bulbocapnine, cissacapnine, cycleanine and insularine contained in the stem are the major compounds. The Khoisan of southern Africa gave a special significance for *C. capensis* in their ethnomedicine. The rhizomes are called as “dawidjies” or “dawidjiewortel” and are extensively used as a diuretic remedy and blood sterilizer. It also possesses several other pharmacological activities like antidiabetic activity, anticancer activity, antipyretic activity, etc. It is also taken for tuberculosis and helps in menstrual problems and pregnancy-related problems. Paste of leaves is used for wounds, syphilitic sores and snakebite.²⁰

2.4.4 Tinospora

Tinospora belongs to the tribe Tinosporeae which is characterized by weakly ruminant endosperm and foliaceous cotyledons. Over thirty species are reported from this genus that is widely distributed in tropical and subtropical Asia, Australia, Africa, the Pacific Islands, and Madagascar. Six species are present in China including three endemic. These deciduous species can grow from their detached stem, which helps them to escape deforestation.

It is reported that there are around 35 Tinospora species are present. These are generally climbing shrubs and mostly found in the subtropical and tropical areas of India. There are mainly three species: *T. crispa*, *T. cordifolia*, and *T. malabarica*. *T. cordifolia* is a deciduous climbing bush which are widely distributed in Asia, Africa, Australia, etc.

In Asia, it is found abundantly all through India, Sri Lanka, Bangladesh, and Nepal. It is also known as Guduchi, Giloy, or Amrita in Ayurveda. Guduchi is one among the most mentioned herbs of Ayurveda, used in various formulations like samshamaniya (maintain homeostasis), medhyarasayana etc.²¹

Preliminary investigation of aerial parts exhibited the existence of various phytochemicals like flavonoids, saponins, sterols, alkaloids, tannins, glucosides etc.²² In 2015, Sharma *et al.* reported the *in-vitro* and *in-vivo* anti-diabetic properties of various extracts.²³ The anti-proliferative ability of extracts was reported by Polu *et al.* and noticed that ethanol extract and dichloromethane extract exhibited noteworthy anti-proliferative activity in MCF-7 (breast carcinoma) and HCT-116 (human colorectal carcinoma) cells.²⁴

In the Indian medicinal system, the aqueous extract is used as a medication against diabetes, hepatitis, etc. Oral administration of alcoholic extract is a remedy for increased blood glucose levels.²⁵ In addition to Ayurveda, the plant finds a significant indication for its use in tribal or folk medicine. *Pramehaghna*, *Pramehahara*, *Mehaghna*, and *Mehahara* some of the antidiabetic agents containing *T.cordifolia* described in various Ayurvedic texts.

Ayurvedic Pharmacopoeia of India has also mentioned its antidiabetic efficacy. Maharashtra tribals, the Korkus, using this plant for treating fever, polyuria, and, diabetes.²³ *T. cordifolia* also rich in a wide variety of secondary metabolites. Furaniditerpenoids, clerodane diterpenoids, alkaloids, steroids, glycosides, lactones, phenolic compounds, and aliphatics are reported specifically from this plant. Protoberberines are the major class of alkaloids present, which include Berberine, jatrorhizine, choline, palmatine, magniflorine, isocolumbine, etc. Other major isolated compounds include the norditerpene furanditerpene glycosides such as cordifoliosides, palamatoside C and F and amritosides, sesquiterpenes tinocordifolioside and tinocordifolin. The clerodane diterpenoid cordioside, tinosporine and tinocordiside were also present in this plant.

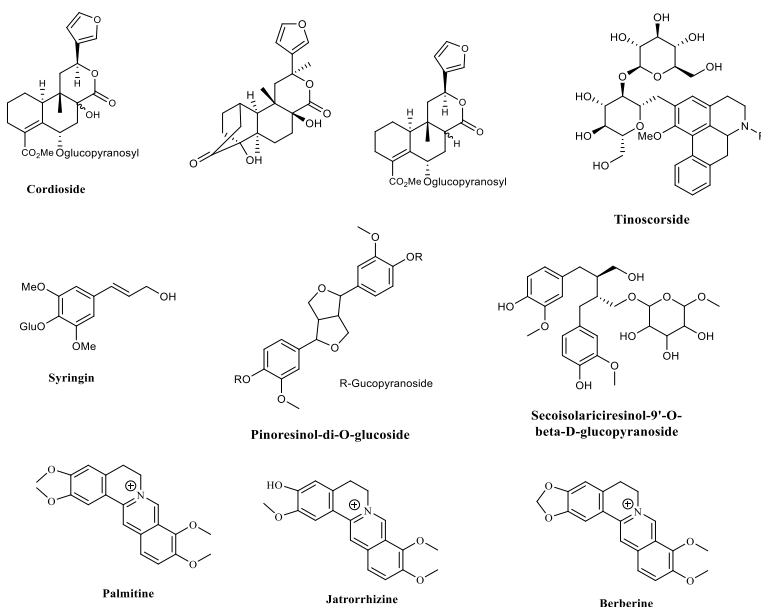


Figure 3: Compounds reported from *T. cordifolia*

The plant is mainly used in Ayurveda for its activity against diabetes. Alcoholic and aqueous extract of aerial part of *T. cordifolia* possesses high hypoglycaemic activity.²⁶ Immunomodulatory activity of different extracts like hexane, ethyl acetate, n-butanol, water, and isolated compounds were evaluated by Bala *et al.* Compounds 11-hydroxymustakone and N-formylannonain gave significant splenocyte proliferation, but more activity was found in extracts, suggesting that the activity is not concentrated on single compounds.²⁷

A clerodane diterpene glycoside, having sulfur, named as Cordifolide, also reported from the plant, was confirmed by single-crystal X-ray crystallographic analysis. It possesses immunomodulatory activity.²⁸

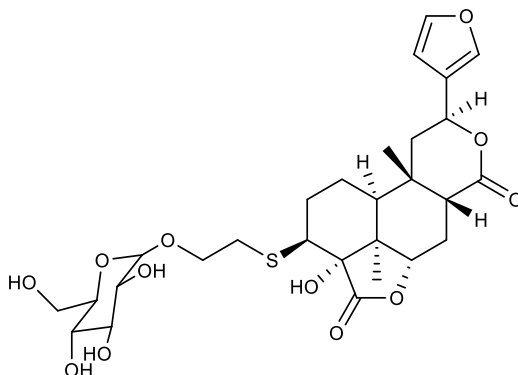


Figure 4: Structure of Cordifolide

Tinospora crispa (L.) Hook. f. & Thoms., another species of this genus, also famed as *Menispermum crispum* Linn., *Menispermum verrucosum*, *Cocculus villosus* DC., *Menispermum rimosum* Blanco, *Cocculus cordifolius* Walp., *Tinospora rumphii*, *Cocculuscrispum*, *Menispermum tuberculatum*, *Tinospora tuberculata*. These are climbers which inhabit subtropical and tropical areas of Asia and rainforests of the Philippines. They are also distributed in Indonesia, Thailand, Vietnam, etc. In these countries, it is also called bratawali, andawali in Indonesia, boraphet in Thai etc.²⁹ *T. crispa* is medicinally interchangeable with the related species *T. cordifolia* in India due to its similarity in appearance.

Medicinally these climbers are highly recommended for diabetes patients in traditional medicine. Decoctions of the stems have been used in Thai and Indonesian conventional medicine to cure many illnesses including hypertension, , diabetes, etc and is also used as a cardiotoxic.³⁰ It is also used in Malaysia as an agent against diabetes, hypertension, and as an insect repellent.³¹ Aqueous extracts effectively lessen the blood glucose level and its mechanism of action in the biological system remains unexplored. Bitter tonics of aerial part is also postulated to have an anti-oxidative effect since it is a rich source of polyphenolic compounds.³²

Various class of compounds such as furanoditerpenes, flavonoids, nucleosides, steroids, and alkaloids has been reported from *T.*

crispa. Clerodane furano diterpenes, commonly known as borapetosides, are the marker class of compounds present. These diterpenoids can also act as a toxic hepatitis drug. A patient developed toxic hepatitis due to the intake of aqueous stem extracts of *T. crispa*, as reported by Xavier *et al.*³³ Cycloeucaleanol and cycloeucalenone isolated from *T. crispa* exhibited cardiac contractility, which was well explained by Kongkathip *et al.* They analyzed that cycloeucaleanol amplified the right atrial force of contraction to some extent while cycloeucalenone displayed a minor variation from the control on the left and right atrial force.³⁴ Anticancer potentials of the plant were examined on head and neck squamous carcinoma cell lines (HNSCC) by Phienwej *et al.* *T. crispa* extract at a concentration of 100.0 mg/mL caused almost 50% reduction of cell survival.³⁵

The activity of different extracts on different cell lines like T47D Breast cancer cells (IC₅₀ of 13.15±0.45 µg/ml),³⁶ HeLa, MCF-7, MDA-MB-231, and 3T3 normal fibroblast cells were also studied.³⁷ Borapetoside E, another clerodane terpenoid, improves hyperlipidemia and hyperglycemia in High Fat Diet Induced Type 2 Diabetes Mice.³⁸ The Lam *et al.* study of the *in-vivo* hypoglycaemic actions of borapetosides A–C in normal and streptozotocin-induced type I diabetic mice, showed the lowering of plasma glucose levels.³⁹ Borapetoside C was one of the most potent α-glucosidase inhibitor reported from the plant with an IC₅₀ = 0.0527 ± 0.008 mg/ml, followed by 4-hydroxy benzaldehyde (IC₅₀ = 0.557mg/ml), and the alkaloids liriodenine and lysicamine (IC₅₀ = 0.562mg/ml). Borapetoside C also effectively suppressed α-amylase enzyme with an IC₅₀ of 0.775mg/ml.⁴⁰ Compounds tinosporols A–C and tinosporoside A also exhibit anti-hyperglycemic activity.⁴¹

List of compounds reported from *T. crispa* are:

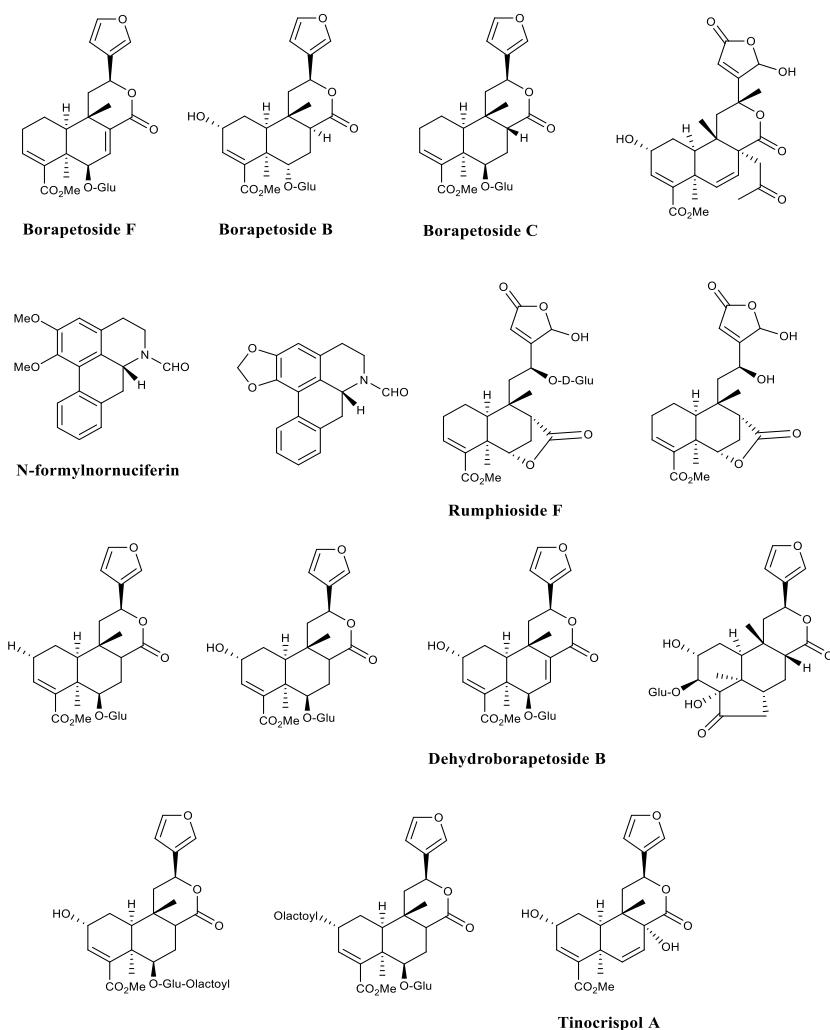


Figure 6: Compound reported from *T. crispata*

2.4.5 Coscinium

There are only two species reported from this genus; *Coscinium fenestratum* (Goetgh.) Colebr, *Coscinium blumeanum* Miers ex Hook.f. & Thomson. *Coscinium fenestratum* (Gaertn.) Colebr. is an unsympathetically endangered species and highly traded medicinal plant indigenous to South Asian regions and in some European parts. In Europe, it is known as False Columba or Tree turmeric. In India, it is restricted to the high rainfall wet evergreen, semi-deciduous and moist evergreen forests of Western Ghats.



Figure 7: Stem and leaves of *Coscinium fenestratum*

The plant is an important ingredient of Ayurvedic formulation Daruharidra and in Sri Lanka as a yellow dye. Industrially and medicinally, the plant is facing an overconsumption. The plant is chopped before it gets fit for its regeneration which makes it highly endangered. This overconsumption and difficulty in regeneration, has endangered it and the plant is now endemic to the Western Ghats. The plant is considered as critically endangered in Kerala, Maharashtra, Tamil Nadu, etc. due to 80% decline of wild population.⁴²

Coscinium fenestratum is a large woody climber, which grows with a cylindrical and yellowish stem. The plant is also renowned as *C. maingayi* Pierre, *Coscinium peltatum* Merr., *Menispermum fenestratum* Gaertn, *C. Wallichianum* Miers, etc. In Malayalam, it is well known as maramanjil, manjavalli, etc. and Sanskrit, it is known as darvi, daruharidra etc.

2.4.5.1 Medicinal importance

The plant is known for its medicinal potential. In the traditional system it is used in ophthalmopathy, ulcers, inflammation, skin disease, fever, abdominal disorders, as an antidote for snakebite, wounds to relieve pain etc.⁴³ Recently Karthika *et al.* reported that the methanolic extract possesses antioxidant activity, studied by spectrophotometric methods like DPPH assay, reducing power assay and ABTS scavenging assays, where the extract showed an IC₅₀ value 182.48 mg/mL.⁴⁴ The antibacterial effects of methanol extract also well studied by Nair *et al.* against different gram-positive and gram-negative bacteria in comparison with the major component of the plant, Berberine. Results showed that the activity

of aqueous and methanol extract was less when compared to the activity of berberine. Besides, berberine also found to be highly active against the various microorganisms tested. These results lead to the assumption that the berberine may be the main reason for the antibacterial activity of *C. fenestratum*, which is the major component present in the methanol extract.⁴⁵

The plant also possesses different medicinal properties like the potential for healing ulcers, dysentery, etc. The combination of honey and the tree bark is taken internally for curing jaundice. The bark is also used for curing gynecological issues and relieving body pain.⁴²

Protoberberine alkaloids are the major compounds present in the stem of *C. fenestratum*. Most of the biological activity reported for this plant are based on this class of compounds. Berberine, a yellow solid and the main component of the stem is responsible for the yellow color of the stem.

The other alkaloids reported from the plant include oxyberberine or berlambine, palmitine, deoxypalmitine, jatrorrhizine, berberrubine, thalifendine, tetrahydroberberine or canadine, oxotetrahydroberberine or 8-oxocanadine, etc. Aporphine alkaloid N,N-dimethylindocarpine was also reported from the plant.⁴⁶ Berberine and its derivative was also reported having a strong impact on the nervous system as well as an anti-amnesic effect against memory defect induced by scopolamine.⁴³

The compounds reported from the stem of *Coscinium fenestratum* includes;

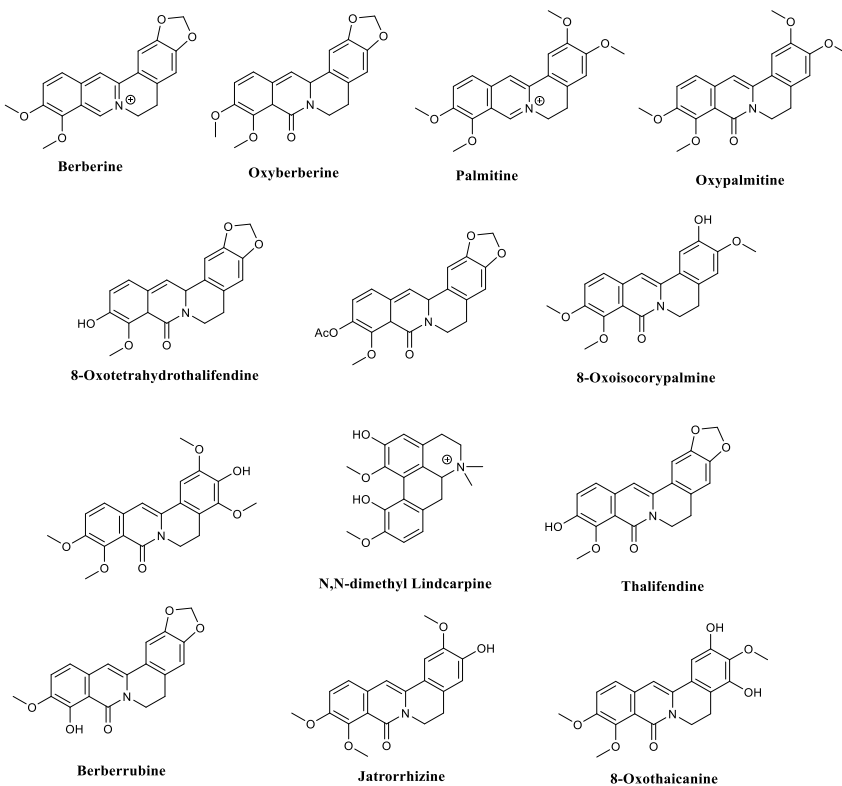


Figure 8: Compounds reported from *C. fenestratum*

Cosciniium blumeanum Miers ex Hook. f. & Thomson, a woody climber, mainly found in Indonesia and Malaysia. Vernacularly it is known as Mengkunyit, merkunit, sekunyit, kekunyit, akar kayu berduri, daun balik angin in Malaysia and Lubu alang in Indonesia. Palmatine and Jatrorrhizine were isolated from the plant by Yuenyongsawad *et al.* They tested the methanol and chloroform extract and isolated compounds for their antioxidant potential. The results showed that triacontanyl caffeate was primarily responsible for this property with an EC₅₀ value of 6.8 µg/ml. Jatrorrhizine and palmatine possessed moderate and lesser activity with an EC₅₀ values of 98.0 µg/ml and >100 µg/ml respectively.

2.4.6 Tiliacora

22 species are reported from genus *Tiliacora*, of which twenty species are scattered across Africa and two are found in Southeast Asia. These species are generally used to treat snakebites, as an

antimalarial drug, for menstrual problems, and to treat gastrointestinal. It is commonly known as the stem-fruit climber or elbow-leaf.⁴⁸

Here we are discussing mainly a large woody climber of this genus, *Tiliacora acuminata*. *T. acuminata* or *T. racemosa* is a large woody climber found throughout India, commonly called Tiliacoru, Kelelata, or Bhaglata, etc. Tribal communities like Santhals, Lodhas, Oraon, Mundas, Kherias, and Bhumijis of West Bengal use this plant for treating skin infections, filariasis, and snake and insect bites. In Ayurveda, it is called Krishnavetra which offers medication to so many diseases, specifically cancer.⁴⁹



Figure 9: Stem and leaves of *Tiliacora acuminata*



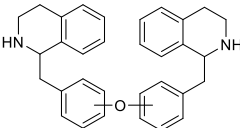
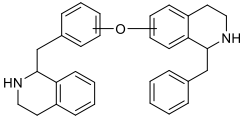
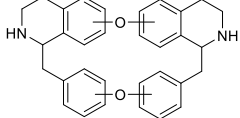
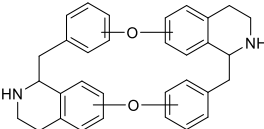
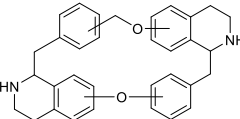
2.4.6.1 Medicinal importance

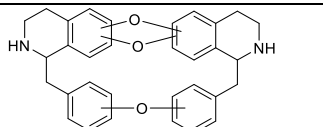
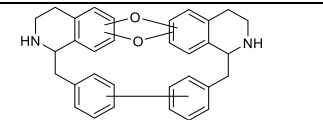
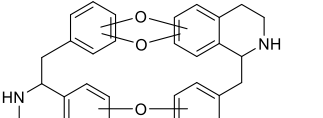
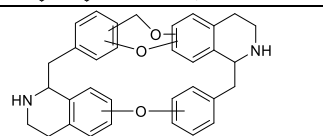
The roots possess an antimicrobial and anti-tumor activity and find extensive applications as an antidote to scorpion sting and snakebite. Externally, leaves and roots are applied for wounds and cuts. Leaves have anti-dandruff properties and kill lice and nits. The decoction of the leaf along with the paste of long peppers is preferred for strangury.⁵⁰ Alcoholic extract of the plant possess fungicidal activity,⁵¹ anti-microbial activity,⁵² water extract possess wound healing ability and hypoglycaemic activity,⁵³ etc. Acuminatide oil from the seed also reported.⁵⁴ Most of the biological activity of *T. acuminata* is due to the presence of dibenzylisoquinolinealkaloids(DBBI). Benzyloisoquinoline alkaloids (BIAs) are a group of plant secondary metabolites that comprise around 2,500 known structures.⁵⁵ Several well-known medicines are derived from BIAs, including narcotics like codeine and morphine, muscle relaxants papaverine, and (+)-tubocurarine, antimicrobials sanguinarine, and berberine, anticancer drug noscapine, etc. These compounds are also famous for their role in

making dart poison curare. BIAs are most common among the order Ranunculales, especially in families like Menispermaceae, Papaveraceae, Berberidaceae, and Ranunculaceae. BIAs owns a common biosynthetic pathway that starts from the condensation of two tyrosine derivatives; dopamine and 4-hydroxyphenylacetaldehyde lead the formation of a major intermediate S-norcoclaurine. Further, S-norcoclaurine is converted to S-reticuline, the vital intermediate in the biosynthetic pathway and the biosynthesis of many other structural types.⁵⁵

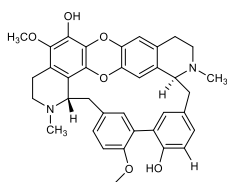
BIAs and DBBIs are of different types depending on the types of bridges present in its structural framework. Different classes of BIAs and DBBIs are:

Table 4: Different classes of BIAs AND DBBIs

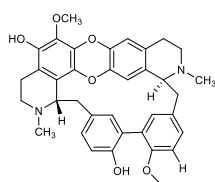
1-Benzylisoquinoline	
1-Benzyltetrahydroisoquinoline	
Bisbenzylisoquinoline alkaloids	
One bond Diphenyl ether (tail to tail)	
Diphenyl ether (head to tail)	
Two bonds Diphenyl ether (head to head) Diphenyl ether (tail to tail)	
Diphenyl ether (head to tail) Diphenyl ether (tail to head)	
Phenylbenzyl ether (head to tail) Diphenyl ether (tail to head)	

<p>Three bonds Diphenyl ether (head to head) Diphenyl ether (tail to tail)</p>	
<p>Diphenyl ether (head to head) Phenyl-piperonyl (tail to tail)</p>	
<p>Diphenyl ether (head to tail) Diphenyl ether (tail to head)</p>	
<p>Diphenyl ether (head to tail) Phenyl and benzylphenyl (tail to head)</p>	

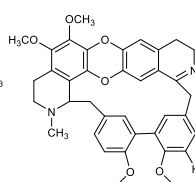
The major alkaloids reported from *T. acuminata* includes Tiliacorine, tiliarsin nortiliacorine, tiliamosine, tiliacorinine, tiliarine, tiliarsine, tiliacosine, N-methyltiliamosine, Nordinklacorine, N-methyltiliarine, tiliamine, N-methylferuloylamine.



Tiliarsine



N-methyltiliarine



Tiliamine

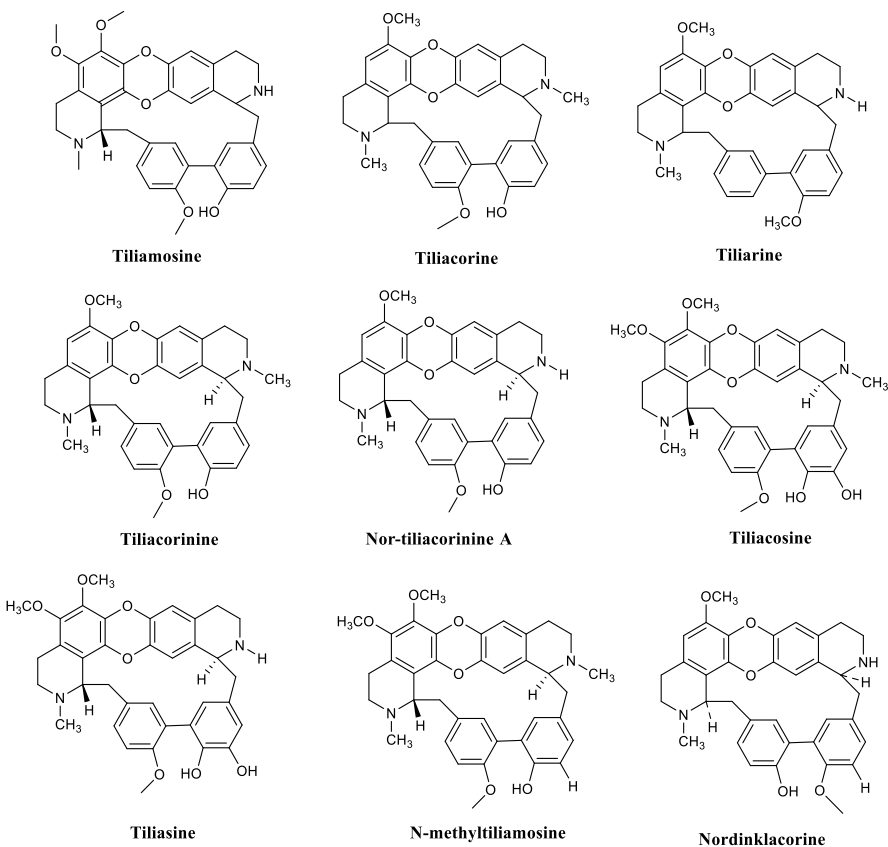


Figure 10: Compounds reported from *T. acuminata*

2.4.7 Cyclea

29 species in South and South East Asia, 13 species including five endemics, in China are reported from this genus. Major species include *Cyclea barbata*, *Cyclea sutchuenensis*, *Cyclea hypoglauca*, *Cyclea racemosa*, *Cyclea wattii*, *Cyclea longgangensis*, *Cyclea insularis*, *Cyclea ochiaiana*, *Cyclea meeboldii*, *Cyclea gracillima*, *Cyclea debiliflora*, *Cyclea polypetala*, *Cyclea tonkinensis*.⁴

Cyclea peltata Hook. f. & Thoms. is a succulent medicinal plant endemic to India. Vernacularly, it is known as padakizhangu or malaithangi in Malayalam and pata root in English. In Ayurveda, it commonly referred to as rajapatha. Medicinal properties of *C. peltata* is well documented in Ayurveda and is mentioned in most of the Ayurvedic texts like Charaka Samhita, Sushrutasamhita and

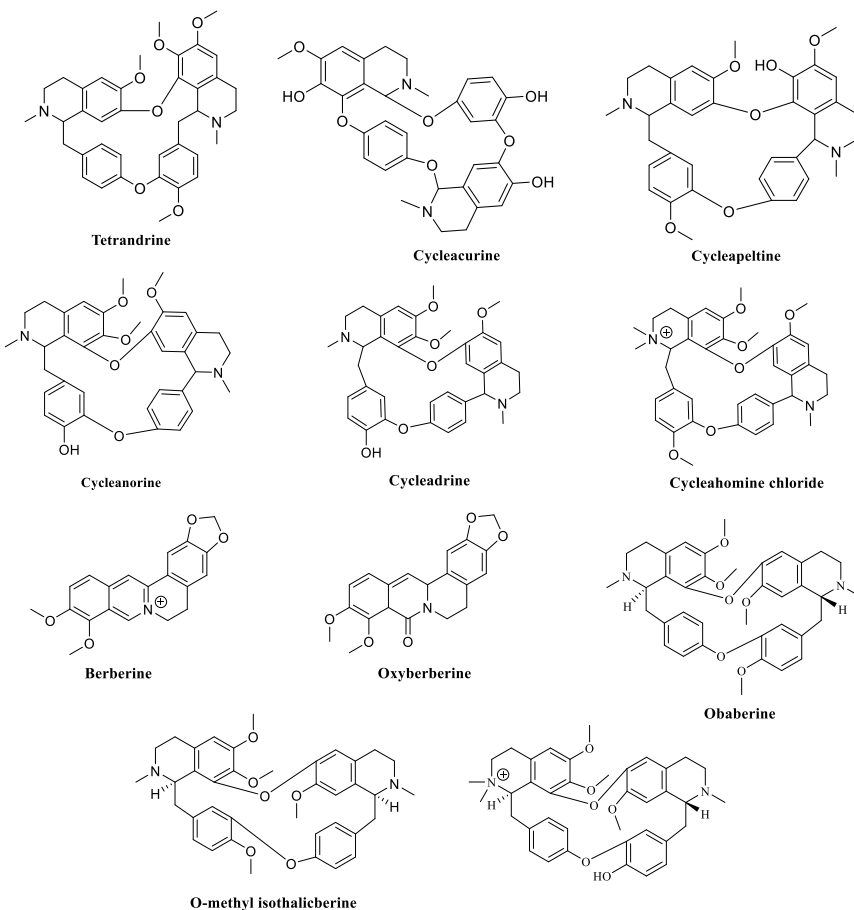
Ashtangahridya. The worldwide distribution of this species is recorded from India to Malaysia, including Sri Lanka and Andaman-Nicobar islands. Within India, it grows in areas having elevation up to 800-900m. Its habitat is mainly in Western Ghats of Karnataka, Maharashtra, Kerala, and Tamilnadu and other moist deciduous forests of Peninsular India.

2.4.7.1 Medicinal Importance

Leaves and rhizomes are edible. Dried powder of rhizome along with hot water is given to cattle to improve fertility. The roots possess many medicinal activities used for digestive disorders, bronchitis, cough, jaundice, diuretic, splenomegaly, as an anti-inflammatory etc. in the Indian traditional system. The plant is widely used in folk medicine as well as a remedy for cough, fever, kidney disorder, urinary disorder, and especially snake poisoning. In Kerala, the Kurichiya tribe uses the tuberous roots of *C. peltata* along with a little salt as a remedy for stomach pain. The Kani tribes in Aarukani Hills of Tamil Nadu use tuber and leaves to treat Chickenpox, diarrhea, wounds, and scabies. The leaves are used as coolant, antidandruff, antipyretic, diuretic, etc. In parts of coastal Karnataka, leaves are being conventionally used for the treatment of herpes.⁵⁶ 'Hinguvachadi Choornam' contains roots of *C. peltata* as one of its main ingredients, for treating gastric ulcer and allied stomach ailment. National Medicinal Plant Board of India acknowledged this shrub as "medicinal plant species in high trade sourced from tropical forests."⁵⁷

Different extract level studies also confirm the traditional knowledge. Leaves have anti-inflammatory and antibacterial activity.⁵⁸ Jyothi *et al.* studied the antibacterial properties of various extracts against gram-positive and gram-negative bacteria.⁵⁹ Literature reports suggest that the most potent part of the plant is roots, which possess different biological activities like antioxidant activity, antiulcer activity, where the antioxidant activity can be attributed to the presence of D-tetrandrine and DL-tetrandrine present in it. It is reported that the plant contains 0.9% of tetrandrine, which is bisbenzylisoquinoline alkaloid.⁶⁰

Other compounds reported from the plant include oxyberberine, berbamine, oxyacanthine, isotetrandrine, oblongamine, dauricine, cycleanorine, cycleaurine, cycleahomine chloride, cycleanine, etc



3. Role of Menispermaceae family in the treatment of infectious diseases

Menispermaceae family

3.1 Amrithotharam kashayam

The polyherbal Ayurvedic formulation Amrithotharam kashayam is prepared by mixing the plant parts of three medicinal plant; *Zingiber officinale* (Sundi), *Tinospora cordifolia* (Amrith, Guloochi), *Terminalia chebula* (Hareetaki). *Tinospora cordifolia* otherwise known as Amrith or Guloochi in Ayurveda is one of the main components.

It is reported to acts as a mild laxative, reduce symptoms of indigestion, and used against chronic fever.⁶¹ Sometimes the drug was prescribed for treating viral diseases like Chikungunya.⁶²

Likewise, *Tinospora cordifolia* and other plants of menispermaceae family is an ingredient of various Ayurvedic formulations. Some are given below;

3.2 Pachanamritham kashayam

Pachanamritham kashayam is reported to have a high antimicrobial potential and is normally recommended in Ayurveda for fever and indigestion. *Tinospora cordifolia* is one of the coreconstituents of this ayurvedic formulation. The other ingredients are *Vetiveria zizanooides* (Usheera), *Adathoda vasica* (Vasa), *Cyprus rotundus* (Mustha), *Zingiber officinale* (Sundi), *Androgrphis paniculata* (Kiratha tiktha), *Plectranthus veteveroides* (Hreebera), *Fumaria parviflora* (Parpata) *Coriandrum sativum* (Dhanyaka), *Tragia involucrate* (Yavasha).

3.3 Vyaghryadi kashaya

Vyaghryadi Kashaya is normally recommended for treating fever, asthma, cough, cold, and general body ache. It is a concentrated decoction of *Solanum xanthocarpum* (Vyaghri), *Tinospora cordifolia* (Amrith, Guloochi), *Zingiberofficinale* (Sundi), *Pipper longum* (Pippali).

3.4 Guloochyadi Kashaya

Gulochyadi Kashayam also renowned as Guduchyadi Kashayam is mainly used for fevers, nausea, vomiting, excessive thirst, infections associated with a burning sensation, loss of appetite, etc. It has antimicrobial action and anti-inflammatory properties. The ingredients if the formulation involves *Tinospora cordifolia* (Amrith, Guloochi), *Prunus cerasoids* (Padmaka), *Azadiracta indica* (Nimba), *Coriandrum sativum* (Dhanyaka), *Pterocarpus santalinus* (Raktha Chandana).

3.5 Elakanadi kashayam

Elakanadi kashayam is another ayurvedic formulation, which makes use of *Tinospora cordifolia*. The drug is used for the treatment of chronic asthma and achronic bronchitis in Ayurveda. The other ingredients include *Elattaria cardamomum* (Elam), *Pipper longum* (Pippali), *Glycorriza glabra* (Yashtimadhu), *Zingiber officinale* (Sundi),

Cyprus rotundus (Mustha), *Adathoda vasica* (Vasa), *Azadiracta indica* (Nimba), *Psuedarthria viscida* (Saliparnai), *Desnmodium gangeticum* (Prisniparni), *Solanum melongena* (Brihathi), *Solanum xanthocarpum* (Kantakari), *Tribulus terrestris* (Gokshura), *Aegle marmalos* (Vilwa), *Gmelinaarborea* (Kasmari), *Stereospermum colais* (Patala), *Oroxylum indicum* (Syonaka), *Plectranthus veteveroids* (Hreebreea).

3.6 Bhargyadi kashyam

Bhargyadi kashyam is effective in treating malaria otherwise called Vishamjwara. The medicine possesses pharmacological properties like anti-bacterial, anti-pyretic, digestive, hepatoprotective anti-emetic, and laxative properties.⁶³ Two species of menispermaceae family; *Cocsiniumfenestratum* or Daruharidra and *Tinospora cordifolia* are used for the preparation of this polyherbal formulation. The other constituents of this decoction include *Cleodendrum serratum* (Bhargi), *Piper longum* (Pippali), *Cassia occidentalis* (Kasamarda), *Curcuma longa* (Haridra), *Cocsinium fenestratum* (Daruharidra), *Adathoda vasica* (Vasa), *Tinospora cordifolia* (Amrith, Guloochi), *Zingiber officinale* (Sundi), *Coriandrum sativum* (Dhanyaka).

4. Conclusion

India is home to an immensely diverse catalogue of medicinal plants. They play a significant role in traditional medicines like Ayurveda, Siddha, Unani, etc. Dried powders of plant or their extracts are used for this purpose. Detailed phytochemical analysis of these medicinal plants became a necessity to understand the mode of action and to derive new therapeutical scaffolds. Menispermaceae is an important family that consists of around 400 species. Alkaloids are the major component, especially benzyloisoquinoline alkaloids, atropine alkaloids, protoberberine alkaloids, etc. These alkaloids possess various medicinal activities like anti-cancer, anti-diabetic, diuretic, immunomodulatory activity, anti-oxidant activity, etc. Here we discussed the phytochemistry and pharmacology of five selected plant species of menispermaceae family, and the detailed review of reported compounds, especially alkaloids present in it. Most of the remaining species are not phytochemically well explored. Hence, a detailed study of other species to understand the phytochemistry and the role of these phytochemicals in their medicinal activity is

recommended so that the traditional system of medicine can be scientifically validated. In addition, these plants are an integral part of the various ayurvedic formulations, which warrants the exploration of phytochemistry and pharmacology of these medicinal plants.

References

- [1] McMurry, J. E., Secondary Metabolites: An Introduction To Natural Product Chemistry, *Org. Chem. With Biol. Appl.* **2009**, 1016–1046.
- [2] Müller, H.; Brackhagen, O.; Brunne, R.; Henkel, T.; Reichel, F. Natural Products in Drug Discovery, *Ernst Schering Res. Found. Workshop*, **2000**, No. 32, 205–216.
- [3] Maria, J.; Filho, B., Alkaloids of the Menispermaceae, **2015**.
- [4] Gilbert, M. G., Menispermaceae, 1–31.
- [5] Shine, V. J.; Anuja, G. I.; Suja, S. R.; Raj, G.; Latha, P. G., J. Bioassay Guided Fractionation of *Cyclea Peltata* Using in Vitro RAW 264.7 Cell Culture, Antioxidant Assays and Isolation of Bioactive Compound Tetrandrine, *J. Ayurveda Integr. Med.* **2018**, 5–10.
- [6] Anubrata Paul, A. V. A. S. R.; SRM. *Int. J. of Pharma and Bio Sciences*, Preliminary phytochemical screening of six medicinal **2016**, 7 (1), 77–81.
- [7] Semwal, D. K.; Semwal, R. B. Efficacy and Safety of *Stephania Glabra*: An Alkaloid-Rich Traditional Medicinal Plant. *Nat. Prod. Res.* **2015**, 29 (5), 396–410.
- [8] Jahan, R.; Khatun, M. A.; Nahar, N.; Jahan, F. I.; Chowdhury, A. R.; Nahar, A.; Seraj, S.; Mahal, M. J.; Khatun, Z.; Rahmatullah, M. Use of Menispermaceae Family Plants in Folk Medicine of Bangladesh., *Adv. Nat. Appl. Sci.* **2010**, 4 (1), 1–9.
- [9] Kumar, D.; Badoni, R.; Semwal, R.; Kumar, S.; Jas, G.; Singh, P.; Rawat, U. The Genus *Stephania* (Menispermaceae): Chemical and Pharmacological Perspectives. *J. Ethnopharmacol.*, *J. Ethnopharmacol.* **2010**, 132 (2), 369–383.
- [10] Md. Moniruzzaman, Sarwar, Hossain.; Partha, Sharoti, Bhattacharjee. Author ' s Accepted Manuscript of *Stephania Japonica*.; *J. of Ethnopharmacology*, **2016**,
- [11] Das, A. K.; Molla, S.; Sykat, M. R.; Ali, A.; Haque, T.; Rahman, L.; Babu, I. M.; Islam, H.; Islam, M. T., Phytochemical and Pharmacological Review on *Stephania Japonica*. **2019**, 14(1), 10433–10436
- [12] Semwal, D. K., Natural Product Research : Formerly Natural Product

Letters Efficacy and Safety of *Stephania Glabra* : An Alkaloid-Rich Traditional Medicinal Plant, **2014**, 37–41.

- [13] Jangir, S.; Wing, P., A Review on *Cocculus Pendulus* (j. r. Forst. & g. Forst.) Diels: Traditional Uses, Phytochemistry and Pharmacological Properties, *Indian Journal of Drugs*, **2016**, 4 (2), 57–62
- [14] Rakkimuthu, R.; Kavithakrishnan, R.; Suganyadevi, P.; Aravinthan, K. O f Phytom Quantita Ative Phyt Tochemic Cal Analys Sis and Th Eir Antiox Xidant Act Tivity of *Cocculus Hirsutu Us* (1 .) Die Els Fruit. M.; *Int. J. of Phytomedicine*, **2012**, 4 (4) 447-455
- [15] Rishikesh, Meena.; Mukesh, Kumar, Meena.; Herbal & Alternative Medicine. **2017**, 1 (2).
- [16] Sharanabasappa, A, Patil.; Sujaya, M.; Saraswati, B, Patil.; A Phrodisiac and Phytochemical Studies of *Cocculus Hirsutus* Extracts in a Lbino Rats., *Asian Pacific Journal of Reproduction*, **2014**, 3 (1), 23–29.
- [17] Satya, V.; Paridhavi, M.; Isolation and Characterization of Compounds from Fruits of *Anamirta Cocculus* (Linn .), *Int. J. of Pharmacognosy and Phytochemical Research*, **2016**, 8 (4), 619–622.
- [18] Kshetrimayum, B. Medicinal Plants and Its Therapeutic Uses. *Omics ebooks group*, **2017**.
- [19] Manu, A.; Tanvi, S.; Anu, D.; Neeraj, B.; Ahmad, S. A A., An inside review of *cissampelos pareira* linn: a potential medicinal plant of india, *Int. Research Journal of Pharmacy* **2012**, 3 (12), 38–41.
- [20] De Wet, H.; Van Heerden, F. R.; Van Wyk, B. E., Alkaloidal Variation in *Cissampelos Capensis* (Menispermaceae), *Molecules* **2011**, 16 (4), 3001–3009.
- [21] Kundu, S.; Ahmed, K. M. M. M.; Mahavidyalaya, R. A., A Traditional Indian Herbs And Its Medicinal Importance-An Ayurvedic Approach with Contemporary View, *Int. J. of Ayurvedic and Herbal Medicine*, **2016**, 4, 2260–2267.
- [22] Singh, G.; Saxena, K.; research article phytochemical analysis of *tinospora cordifolia* by using different solvent extract, *Int. J. of Current Research*, **2017**, 9(11), 61213-61215,
- [23] Sharma, R.; Amin, H.; Galib; Prajapati, P. K. Antidiabetic Claims of *Tinospora Cordifolia* (Willd.) Miers: Critical Appraisal and Role in Therapy, *Asian Pac. J. Trop. Biomed.* **2015**, 5 (1), 68–78.
- [24] Polu, P. R.; Nayanabhirama, U.; Khan, Di Preliminary Evaluation of In Vitro Anti-Proliferative Activity of *Tinospora Cordifolia* (Willd) Miers and Estimation of Berberine Content by HPLC, *Der Pharmacia Lettre*, **2017**, 9 (6), 82-95
- [25] Sengupta, S.; Mukherjee, A.; Goswami, R.; Basu, S., S. Hypoglycemic Activity of the Antioxidant Saponarin, Characterized as α -Glucosidase Inhibitor Present in *Tinospora Cordifolia*. *J. Enzyme Inhib. Med. Chem.* **2009**, 24 (3), 684–690.

- [26] Patel, M. B.; Mishra, S. *Phyther. S.* Isoquinoline Alkaloids from *Tinospora Cordifolia* Inhibit Rat Lens Aldose Reductase. *Phyther. Res.* **2012**, 26 (9), 1342–1347.
- [27] Bala, M.; Pratap, K.; Verma, P. K.; Singh, B.; Padwad, Y., *J. of Ethnopharmacology*, **2015**, S0378-8741.
- [28] Pan, L.; Terrazas, C.; Lezama-davila, C. M.; Rege, N.; Gallucci, J. C.; Satoskar, A. R.; Kinghorn, A. D., a Sulfur-Containing Clerodane Diterpene Glycoside from *Tinospora Cordifolia*. *Org. letters*, **2012**, 14(8), 749–750.
- [29] Dweck, A. C.; Cavin J. P., Andawali (*Tinospora crispa*) - a review, *Pers. Care Mag.* **2006**, 33–39.
- [30] Praman, S.; Mulvany, M. J.; Williams, D. E.; Andersen, R. J.; Jansakul, C., *J. Crude Extract and Purified Components Isolated from the Stems of Tinospora Crispa Exhibit Positive Inotropic Effects on the Isolated Left Atrium of Rats. J.Ethnopharmacol*, **2013**, 149 (1), 123–132.
- [31] Parveen, A.; Huang, Y.; Fantoukh, O.; Alhusban, M.; Raman, V.; Wang, Y. H.; Wang, W.; Ali, Z.; Khan, I. A. Rearranged Clerodane Diterpenoid from *Tinospora Crispa*. *Nat. Prod. Res.* **2019**, 0 (0), 1–8.
- [32] Amom, Z.; Azman, K. F.; Ismail, N. A.; Shah, Z. M.; Arshad, M. S. M., An aqueous extract of *tinospora crispa* possesses antioxidative properties and reduces atherosclerosis in hypercholesterolemic-induced rabbits *J. Food Biochem.* **2011**, 35 (4), 1083–1098.
- [33] Cachet, X.; Langrand, J.; Riffault-Valois, L.; Bouzidi, C.; Colas, C.; Dugay, A.; Michel, S.; Boucaud-Maitre, D., Clerodane Furanoditerpenoids as the Probable Cause of Toxic Hepatitis Induced by *Tinospora Crispa*, *Sci. Rep.* **2018**, 8 (1), 1–11.
- [34] Kongkathip, N.; Dhumma-upakorn, P.; Kongkathip, B.; Chawanoraset, K.; Sangchomkaeo, P.; Hatthakitpanichakul, S., S, Study on Cardiac Contractility of Cycloeucalenol and Cycloeucalenone Isolated from *Tinospora Crispa*, *J. Ethnopharmacol.* **2002**, 83 (1–2), 95–99.
- [35] Phienwej, H.; Swasdichira, I. si; Amnuoyopol, S.; Pavasant, P.; Sumrejkanchanakij, P. P. *Tinospora Crispa* Extract Inhibits MMP-13 and Migration of Head and Neck Squamous Cell Carcinoma Cell Li, *Asian Pac. J. Trop. Biomed.* **2015**, 5 (9), 738–743.
- [36] Rollando, R., Combination of *Hedyotis Corymbosa* L. and *Tinospora Crispa* Ethanolic Extract Increase Cisplatin Cytotoxicity on T47D Breast Cancer Cells, *Asian J. Pharm. Clin. Res.* **2018**, 11 (7), 171–177.
- [37] Ibahim, M. J.; Wan-Nor, I. W. M. Z.; Narimah, A. H. H.; Nurul, A. Z.; Siti-Nur, S. S. A. R.; Froemming, G. A., Froemming, G. A, Anti-Proliferative and Antioxidant Effects of *Tinospora Crispa* (Batawali), *Biomed. Res.* **2011**, 22 (1), 57–62.
- [38] Xu, Y.; Niu, Y.; Gao, Y.; Wang, F.; Qin, W.; Lu, Y.; Hu, J.; Peng, L.; Liu,

- J.; Xiong, W., J Borapetoside E, a Clerodane Diterpenoid Extracted from *Tinospora Crispa*, Improves Hyperglycemia and Hyperlipidemia in High-Fat-Diet-Induced Type 2 Diabetes Mice, *Nat. Prod.***2017**, 80 (8), 2319-2327.
- [39] Lam, S. H.; Ruan, C. T.; Hsieh, P. H.; Su, M. J.; Lee, S, Hypoglycemic Diterpenoids from *Tinospora Crispa*, *J. Nat. Prod.***2012**, 75 (2), 153-159.
- [40] Hamid, H. A.; Yusoff, M. M.; Liu, M.; Karim, M. R., α -Glucosidase and α -Amylase Inhibitory Constituents of *Tinospora Crispa*: Isolation and Chemical Profile Confirmation by Ultra-High Performance Liquid Chromatography-Quadrupole Time-of-Flight/Mass Spectrometry, *J. Funct. Foods***2015**, 16, 74-80.
- [41] Gao, Y.; Niu, Y. F.; Wang, F.; Hai, P.; Wang, F.; Fang, Y. D.; Xiong, W. Y.; Liu, J. K. Clerodane Diterpenoids with Anti-Hyperglycemic Activity from *Tinospora Crispa*, *Nat. Products Bioprospect.***2016**, 6 (5), 247-255.
- [42] Tushar, K. V.; Satheesh, George; Remashree, A. *Coscinium Fenestratum* Review.Pdf. *J. of Plant Sciences*, **2008**, 3(2), 133-145.
- [43] B.K. Manjunatha, B. K. M.; Murthuza, S.; Sudharshan S,J, S. S.; Divakara R, D, R. Phytochemical Investigation and Hepatoprotective Activity of *Coscinium Fenestratum* Colebr., A Rare Endangered Spp., from Western Ghats of India *Paripex - Indian J. Res.***2012**, 2 (2), 14-16.
- [44] Karthika, K.; Gargi, G.; Jamuna, S.; Paulsamy, S.; Ajmal Ali, M.; Al-Hemaid, F.; Soliman Elshikh, M.; Lee, The Potential of Antioxidant Activity of Methanolic Extract of *Coscinium Fenestratum* (Goetgh.) Colebr (Menispermaceae), *J. Saudi J. Biol. Sci.***2019**, 26 (5), 1037-1042.
- [45] Nair, G. M.; Narasimhan, S.; Shiburaj, S.; Abraham T,K Antibacterial Effects of *Coscinium Fenestratum*. *Fitoterapia***2005**, 76 (6), 585-587.
- [46] Pinho, P. M. M.; Pinto, M. M. M.; Kijjoa, A.; Pharadai, K.; Díaz, J. G.; Herz, Protoberberine Alkaloids from *Coscinium Fenestratum*. *W; Phytochemistry***1992**, 31 (4), 1403-1407.
- [47] Keawpradub, N.; Dej-adisai, S. Songklanakarin J. S., Antioxidant and Cytotoxic Activities of Thai Medicinal Plants Named *Khaminkhruea* : *Arcangelisia Flava*, *Coscinium Blumeinum* and *Fibraurea Tinctoria*, *Sci. Technol.***2005**, 2 (27), 455-467.
- [48] De Wet, H.; Struwig, M.; Van Wyk, B. E. Taxonomic Notes on the Genera *Tiliacora* and *Tinospora* (Menispermaceae) in Southern Africa, *South African J. Bot.***2016**, 103, 283-294.
- [49] Vivek Kumar, T.; Vishalakshi, M.; Gangaraju, M.; Das, P.; Roy, P.; Banerjee, A.; Dutta Gupta,S., Evaluation of Antibacterial, Antioxidant and Nootropic Activities of *Tiliacora Racemosa* Colebr. Leaves: In Vitro and in Vivo Approach, *Biomed. Pharmacother.***2017**, 86, 662-668.
- [50] Yogeshwari, C.; Kumudha, P., Phytochemical Evaluation of *Tiliacora Racemosa* Colebr. Using Gas Chromatography-Mass Spectrometry,

- Asian J. Pharm. Clin. Res.* **2018**, 11 (2), 350–353.
- [51] Tripathi, Y. C.; Antifungal Activity of Alkaloids of *Tiliacora Racemosa*, *National Academy Science Letters*, **1989**, 12(3).
- [52] Kamyra, C. J.; Rau, A. R.; Subin, M. P., Phytochemical Analysis and Antibacterial Activity of *Euphorbia Hirta* Linn. and *Tiliacora Acuminata* Miers, *Nat. Environ. Pollut. Technol.* **2012**, 11 (1), 95–98.
- [53] Manda, R.; Seru, G.; Evaluation of Hypoglycaemic and Wound Healing Activities of *Tiliacora Acuminata*, *J. of Chemical and Pharmaceutical Research*, **2016**, 8 (5), 494–497.
- [54] Selvaraj, S. J.; Alphonse, I.; A New Lactone from Aerial Parts of *Tiliacora Acuminata*. Britto, S. J.; *Indian J. Chem. - Sect. B Org. Med. Chem.* **2008**, 47 (6), 942–944.
- [55] Hagel, J. M.; Facchini, P. J.; Benzylisoquinoline Alkaloid Metabolism: A Century of Discovery and a Brave New World, *Plant Cell Physiol.* **2013**, 54 (5), 647–672.
- [56] S., J. C.; S., M. M.; Ramesh, R. Evaluation of the Wound Healing Activity of *Caesalpinia Bonducella* and *Cyclea Peltata* Extracts in Experimentally Induced Diabetic Rats, *Int. J. Pharm. Pharm. Sci.* **2017**, 9 (10), 211.
- [57] Meena, J.; Santhy, K. S., Evaluation of the Antioxidant Potential of Methanol Extract of *Cyclea Peltata* in DAL Model, *The Pharma Innovation Journal*, **2015**, 4 (1), 71–75.
- [58] Sridhar, S. An in-vitro study on anti-inflammatory and anti-bacterial activities of ethyl acetate extract from the leaves of *Cyclea peltata*, *Indo American J. of Pharmaceutical Sciences* **2017**, 4 (12), 4334–4342.
- [59] Abraham, J.; Thomas, T. D., Antibacterial Activity of Medicinal Plant *Cyclea Peltata* (Lam) Hook & Thoms., *Asian Pacific J. Trop. Dis.* **2012**, 2, S280–S284.
- [60] Shine, V. J.; Latha, P. G.; Shyamal, S.; Suja, S. R.; Anuja, G. I.; Sini, S.; Pradeep, S.; Rajasekharan, S., Gastric Antisecretory and Antiulcer Activities of *Cyclea Peltata* (Lam.) Hook. f. & Thoms. in Rats, *J. Ethnopharmacol.* **2009**, 125 (2), 350–355.
- [61] Sulaiman, C. T.; Balachandran, I., Chemical Profiling of an Indian Herbal Formula Using Liquid Chromatography Coupled with Electro Spray Ionization Mass Spectrometry, *Spectrosc. Lett.* **2014**, 48 (3), 222–226.
- [62] Dilip, C.; Saraswathi, R.; Krishnan, P. N.; Azeem, A. K.; Raseena; Azeez, A.; Ramya; Jose, J., Comparative Evaluation of Different Systems of Medicines and the Present Scenario of Chikungunya in Kerala. *Asian Pac. J. Trop. Med.* **2010**, 3 (6), 443–447.
- [63] Satyadev, K.; Jinesh, Kumar, Jain; Swapnil, Singhai, role of bharangyadi kwath in the cases of visham jwara (malaria), *Int. J. of Development Research*, **2017**, 07, 13650–13654.