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CLERODENDRUM COLEBROOKIANUM WALP: A PHYTOPHARMACOLOGICAL REVIEW

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ABSTRACT

Clerodendrum colebrookianum Walp. belongs to family lamiaceae is widely used for the treatment of hypertension. It is a perennial shrub which is native to South and Southeast Asia. Traditionally, the leaves of this plant are used by the indigenous people of Northeast India as a remedy for the treatment of intestinal tapeworm infections. It is traditionally used in the treatment of diabetes, hypertension, cough and rheumatism. The major chemical components reported from the genus are phenolics, steroids, di- and triterpenes, flavonoids, volatile oils, etc. The present review focuses on the traditional use, chemical constituents and pharmacological activity of this plant. Antihypertensive, anthelimintic, analgesic, antioxidant and antistress activities are reported by various extracts of *Clerodendrum colebrookianum* Walp.

KEYWORDS: *Clerodendrum Colebrookinum* Walp, Lamiaceae, Hypertension, Pharmacological activity, Ttraditional use, Chemical constituent.

INTRODUCTION

The genus *Clerodendrum L. (Family:* Lamiaceae*)* is very widely distributed in tropical and subtropical regions of the world. More than five hundred species of the genus are identified till now, which includes small trees, shrubs and herbs. The genus is used as medicines specifically in Indian, Chinese, Thai, Korean, Japanese countries for the treatment of various lifethreatening diseases such as rheumatism , syphilis, typhoid, cancer, jaundice and hypertension etc[1]. *Clerodendrum colebrookianum* walp locally known as "Nephaphu" in Assam is a flowering shrub characterized by a foetid smell. *Clerodendrum colebrookianum* walp is a perennial evergreen shrub and grows up to 4-8 ft height.It is native to South and

Southeast Asia[2] .The young branchlets of this plant are usually four angled .The leaves are simple, opposite or rarely whorled. Leaf base is wedge- shaped to heart-shaped, margin is entire to slightly wavy, tip long-pointed to pointed. Flowers are white and it has 4-6 branched corymbose cymes at the end of branches. Inflorescences are loosely cymose or capitate in terminal or rarely axillary paniculate thyrses. The Calyx of the flower is campanulate or cup-shaped, densely pubescent. Corolla with a slender tube has 5 spreading lobes .Four Stamens are present,ovary 4-locular; ovules are pendulous or laterally attached.The fruit is a drupe with 41-seeded pyrenes, sometimes separating into 2 2-loculed or 41-locular mericarps. It flowers during postmonsoon from August to December [3-4]. The leaves and leaf twigs of this plant are used as home remedy for high blood pressure by the people of North-Eastern regions of India. The roots of *Clerodendron colebrookianum* Walp have anthelmintic, antibacterial, anti-fungal properties and are reported to cure bronchial asthma, gastrointestinal tract disorders, syphilis and gonorrhea and several hematological disorders. It has been traditionally used in the treatment of infant anti- colics pain, cough, dysentery helminthic infections, stomach disorder and headache and for some skin diseases. It is known as sla jarem among the Khasi and Jaintia tribes in Meghalaya consuming the water after boiling the leaves is a traditional practice for the treatment of high blood pressure, malaria and liver troubles and in case of rheumatic pains. Application of the warmed leaf - paste on the affected area is a common traditional practice[5-9].

DESCRIPTION OF THE PLANT

Taxonomy of The Plant

Kingdom : Plantae

Phylum: Magnoliophyta

Class :Magnoliopsida

Order : Lamiales

Family : Verbanaceae

Genus : *Clerodendrum L*

Species : *Clerodendrum colebrookianum* Walp

Fig- 1. Flowers,Leaves Of *Clerodendrum Colebrookianum* Walp

Chemical Constituents

The chemical constituent of *Clerodendrum colebrookianum* Walp leaves shows the presence of phenols, alkaloids, flavonoids, polyphenols, steroids etc. The hexane extract showed the presence of twenty eight compounds. Five new steroids, colebrinn A-E were also isolated

from the aerial part of the plant.The presence of β-sitosterol, sterol compounds,flavonoids, alkaloids, saponins, tannin, terpenoid ,steroid were also found. The plant reported to contain triacontane, amyrin, clerodin, (24s) ethyl cholesta 5, 22,25 trien 3-ol, clerodolone, clerodendo side, B-sitosterol, clerosterol, daucosterol, colebrin A-E[4,10-11]. Another class of constituents are terpenes which include: monoterpenes, diterpenes, triterpenes, iridoids and sesquiterpenes are found in this plant. Terpenes such as α-amyrin, β-amyrin, caryoptin, 3-epicaryoptin, 16-hydroxy epicaryoptin, clerodendrin A, B and C, clerodin, clerodermic acid, cleroinermin, friedelin, gramisterol, iridoids (inerminoside A, B, C and D, melittaside, monomelittoside, sammangaoside, dehydroroyleanone, sesquiterpene (sammangaoside A, B) clerodendrin A, uncinatone, saponins-A, friedelanone, lupeol, betulinic acid, royleanone and dehydroroyleanone, and betulin have been isolated from various Clerodendron species such as *C. inerme, C. phlomidis, C. paniculatum, C. colebrookianum, C. wildii, C. uncinatum, C. mandarinorum, C. thomsonae, C. fragrans, C.ugandense, C. chinense*. Terpenes such as tri acetane, clerodin,clerodin A are isolated from the whole plant of clerodendrum colebrookianum [12-16].Colebroside A (1), a new diglucoside of fatty acid ester of glycerin, was isolated from the aerial parts of Clerodendrum colebrookianum Walp., along with nine known compounds [10].

Qualitative Analysis of *Clerodendrum Colebrookianum* Walp Leaves[8,17]

Constituents	Amount
Flavonoid content(mg/g)	**32.83±0.49**
Saponin content(mg/g)	**88±0.94**
Phenol content(g/L)	**2.52±0.04**
Carbohydrate content(µg/ml)	**131.33±1.96**
Protein content(µg/ml)	**297.66±13.46**

TRADITIONAL USES [1,6-9]

Leaf- The leaves and leaf twigs of this plant are used as home remedy for high blood pressure by the people of North-Eastern regions of India. The leaf extract is mixed with small amount of common salt and is taken thrice daily in the treatment of abdominal pain. The leaves part is also used traditionally as an anthelmintic, blood purifier and the leaf juice is used in the treatment of infant's cough, diarrhoea and dysentery by the tribe of Arunachal Pradesh .The raw leaves and its decoction is used in the treatment of diabetes in Assam. The leaf part is also traditionally used in gastric disorders.

Tender stem-The tender stem is used in the treatment of gastric disorders.

Root- The roots of *Clerodendron colebrookianum* Walp have anthelmintic, antibacterial, anti-fungal properties and are reported to cure bronchial asthma, gastrointestinal tract disorders, syphilis and gonorrhea and several hematological disorders. Roots with bark are helpful in cough.

Leaf and root part is used by the Monipuri tribes for the treatment of skin diseases, cough and dysentery. This plant is used by the Khasi and Jayantia tribe of Meghalaya in the treatment of rheumatoid pain.

PHARMACOLOGICAL USES

Antiinflammatory Property and Analgesic Property

It was reported that the methanolic extract of C.C leaves showed potent anti-inflammatory effect on carageenan induced paw edema of wister albino rats. It was found that the active anti-inflammatory effect of this plant due to the presence of terpenes,glycosides and sterols.The methanolic extract of the C.C whole plant was found to have potent analgesic effect acetic acid induced male swiss albino mice and by using hot tail flick test .In acetic acid induced experiment, it was found that methanolic extract of the plant was administered i.p.in the dose of 100mg/kg b.w. and 200 mg/kg b.w. and 200mg/kg b.w. showed significant effect on mice($p<0.001$) in a dose dependent manner. The analegesic effect of the plant extract was also investigated in two different doses (100mg/kg b.w. and 200 mg/kg b.w.) by following the hot tail flick method and it was found that the leaf extract showed significant analgesic effect[2].

It was reported that the aq. Extract of C.C leaves was also found to have anti-inflammatory effect in acute and chronic stages of inflammation by free radical scavevenging activity and by the inhibition of both the cox1 and cox 2 enzymes. It was considered that the strong anti-inflammatory and analgesic effect of the methanolic extract of the plant was due to the presence of terpenes, sterols, glycosides and other polar bioactive components[18-19].

Antihypertensive Activity

It was revealed that the organic (n-butanol,ethyl acetate,chloroform) extract of C.C leaves were found to have potential antihypertensive activity. It was evaluated by using fructose induced hypertension model in rats and in isolated frog heart. The test sample showed negative ionotropic and positive chronotropic effect on isolated frog heart and significant ($p<0.001$) reduction in systolic blood pressure and heart rate was found in hypertensive rats.[20]

Anthelmintic Activity

It was observed that the leaf extract of C.C possesses a dose dependent efficacy against larval, immature and adult ages of *Hymenolepis diminuta*(a zoonotic tapeworm) .It was evaluated in experimentally induced Hymenolepis diminuta infections in wister albino rats. The efficacy of the extract was found to be considerably high only against the adult stage of the parasite[21].

Antistress Activity

The antistress property of C.C leaves aq. Extract was studied against cold restraint stress in swiss albino mice. There was a significant reduction in the WBC count, eosinophil, basophil level and spleen weight while the level of ALT, neutrophills, blood glucose and plasma corticosterone along with the liver weight was found to be increase significantly on stress treatment. Administration of C.C leaf extract (100mg/kg) significantly prevented the cold restraint stress induced alterations in these parameters. In this study, it was reported that such cold restraint stress induced apoptotic cell death including alterations in the leukocyte numbers, blood glucose level, ALT activity, liver and spleen weight could be prevented by using this C.C plant extract[22].

Antioxidant Activity

It was reported that the methanolic leaf extract of C.C plant showed potent *in vitro* antioxidant activity. It was evaluated by DPPH radical scavenging assay, Hydroxy radical scavenging assay, Superoxide radical scavenging radical assay, nitric oxide radical scavenging assay, singlet oxygen radical scavenging assay, peroxynitrite radical scavenging assay[17].

CNS Depressant Action

The leaf extract of C.C was studied on behaviour, convulsion, analgesia and sedative hypnosis of mice. From this study, it was observed that a marginal reduction of awareness and motor activity was observed in low (20mg) and moderate (40 mg) dose level of extract. It was found that 80 mg dose cause marked inhibition of awareness and motor activity. The extract prolonged the effect of mepobamate, diazepam, chlorpromazine and pentobarbitone significantly in a dose dependent manner. It was reported that pretreatment of the extract caused significant protection of strychnine and leptazol induced convulsion and mortality. A mild (or dose dependent) CNS depressant action of leaf extract of C.C was found on mice[23].

Antiperoxidative and Lipid Lowering Activity

This study was performed on wister albino rats. It was found that after chronic administration of C.C leaf extract cause a significant reduction of lipid peroxidation(TBARS) in plasma and tissues. Lowering of TBARS is with concomitant lowering of cholesterol indicating that there was a reduction of oxidative stress after the administration of C.C leaf extract. It was concluded that the leaves of C.C may be a useful therapy for hypercholesteromia through reducing oxidative stress and cholesterol level[24].

Hypolipidemic activity-The hypolipidemic effect of ethyl acetate extract of C.C leaves was found on cholesterol fed rats. For this study, the crude polyphenol fraction from the leaves were evaluated and showed a potent hypolipidemic effect[25].

Table: 1. Some Species of *Clerodendrum* Genus And Their Pharmacological Uses And Distribution In The World.

SCIENTIFIC NAME	PHARMACOLOGICAL USES	DISTRIBUTION
C. inerme Gaertn.	Antiviral,Larvicidal activity,Analgesic and antipyretic,Hypotensive,Antinematocidal,Antihepatotoxic,Antimicrobial agent[25-29].	India,Srilanka,South East Asian countries, Australia, Pacific Island.
C. phlomidis Linn. f. (*C. multiforum* Burm. F)	Analgesic activity, Anti-amnesic activity, Anti-asthmatic activity, Antidiarrhoeal activity, Anti-inflammatory activity, Antimicrobial activity, Antiplasmodial activity, Antiviral ,Nematicidal activity tudies, Hypoglycemic activity, Immunomodulatory activity[30-33].	India
C. serratum Spreng.	Bronchodialatory activity,antiasthmatic,Antibacterial activity,Wound healing activity,Anticarcinogenic activity,Antiinflammatory and antiallergic activity,Antioxidant activity[34-37].	India
C. infortunatum Linn.	Antinicrobial activity,Antioxidant activity,Wound healing activity,Hepatoprotective,Anticonvulsant activity,Analgesic activity,Anthelmintic activity,Antidiabetic activity [38-44].	The philippines
C. siphonanthus R. Br. *(C. indicum* (Linn) Kuntze)	Antiinflammatory,Antiasthmatic,Antibacterial activity,Antioxidant activity,used in the treatment of rheumatism, cough,veneral infection,skin diseases and in the treatment of beriberi disease[1,45]	India
C. glabrum E. Mey	Antioxidant activity,Anticollagenase activity[1]	Southern Africa
C. trichotomum	Antioxidant activity,Antiinflammatory activity,Antidiabetic,Antihypertensive, Antiviral,Sedative agent[1,46-49]	China,Korea,Japan
C. bungei Stued	Antitumour activity,used in the treatment of headeache,dizziness,hysteroptosis[50-51].	China
C. calamitosum L	Cytotoxic agent,Antimalarial,Antihypertensive,Antidiabetic,Sedative agent,Antibacterial,Diuretic and used in the treatment of kidney disease[52-54].	Indonesia,Taiwan
C. cyrtophyllum Turez	Antimicrobial and used in the treatment of fever,jaundice,typhoid and	Taiwan

	syphilis[1,52].	
C. chinense (Osb.) Mabberley *C.fragans(Vent.)wild*	Antiasthmatic, Antiinflammatory and used in the treatment of rheumatism,fever,jaundice,typhoid and syphilis[1,6].	Tropical regions of Asia
C. colebrookianum	Antihypertensive, Antiinflammatory, Analgesic, Anthelmintic, Antioxidant, Antistress activity[2,18-25].	India,South Asian Countries
C. myricoides	Antimalarial,Antimicrobial,Antibacterial,Antioxidant activity[55-57].	South Africa
C. petasites S. Moore	Antiinflammatory,Antiasthamic,used in the treatment of rheumatism,Antipyretic,Antimalarial [1,58-59].	India,South Africa, Srilanka, Malaysia, Vietnam, Southern China
C. philippinum Schauer	Antibacterial,Antiasthamic,Antiinflammatory,used in the treatment of rheumatism,Antianxiety,Antidepressant, Antifungal activity[1,60-61].	Australia

CONCLUSION

In developing countries, traditional medicine is often the only accessible and affordable treatment available. In many Asian countries traditional medicine is widely used .The medicinal plants serve as important therapeutic agents as well as valuable raw materials for manufacturing of numerous traditional and modern medicines. *C. Colebrookianum* is a plant of great traditional medicinal importance. Traditionally it is used in the treatment of various diseases due to its immense therapeutic potential. Various pharmacological activities of this plant have been reported including antihypertensive, antioxidant, anthelmintic, anti-inflammatory etc. which provide scientific evidence for some traditional therapeutic claims. So, attempt must be taken to isolate the characteristic bioactive compounds from this plant and detail pharmacognostic studies should be conducted to establish its traditional use.

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