



Review Article

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**PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF
CLERODENDRUM COLEBROOKIANUM WALP: A REVIEW**

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ABSTRACT

Clerodendrum colebrookianum Walp is a perennial shrub which is native to South and Southeast Asia. Traditionally, it is used in the treatment of various diseases due to its immense therapeutic potential. It is widely used by the indigenous people of Northeast India as a remedy for treatment of various diseases like diabetes, hypertension, stomachache, jaundice, cough and rheumatism. The plant possesses different biologically active components like Colebrin A, Colebrin B, Colebrin D, Colebrin E, β -Sitosterol etc. This review reported various pharmacological activities of the plant such as antihypertensive, anti-inflammatory, analgesic, hepatoprotective, antioxidant, anthelmintic and some other activities which provide scientific evidence for some traditional therapeutic claims.

Keywords: *Clerodendrum colebrookianum*, Ethnomedicine, Phytochemistry, Pharmacology

INTRODUCTION

Medicinal plants are the excellent source of natural products and phytochemicals which serve as important therapeutic agents as well as valuable raw materials for manufacturing of numerous traditional and modern medicines. In developing countries, traditional medicine is often the only accessible and affordable treatment available. In many Asian countries, traditional medicine is widely used. *Clerodendrum colebrookianum* is a plant of great traditional medicinal importance. 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. The genus is used as medicines specifically in Indian, Chinese, Thai, Korean and Japanese countries for the treatment of various life-threatening diseases such as rheumatism, syphilis, typhoid, cancer, jaundice and hypertension etc¹. *Clerodendrum colebrookianum* Walp is a flowering shrub characterized by a foetid smell. 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 *Clerodendrum colebrookianum* Walp have anthelmintic, antibacterial, anti-fungal properties and are reported to cure bronchial asthma, gastrointestinal tract disorders, syphilis and gonorrhoea and several hematological disorders. It has been traditionally used in the treatment of infant anti-colic pain, cough, dysentery, helminthic infections, stomach disorder and headache and for some skin diseases²⁻⁶. Based on the traditional widely use of this plant as therapeutic agent, the present review highlights extensive studies of pharmacological properties of this plant which had been carried out in an experimental animal model and in vitro to substantiate the folklore claim.

Botanical Description

Clerodendrum colebrookianum Walp is a perennial evergreen flowering shrub or small tree and grows up to 1.5-3 m in height. It is native to South and Southeast Asia⁷. The plant grows generally in moist and waste places. 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 borne in 4-6-branched corymbose cymes, at the end of branches. Calyx is campanulate or cup-shaped, densely pubescent, corolla with a slender tube. 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 post-monsoon from August to December⁸.

Table 1: Taxonomy Hierarchy

Kingdom	Plantae
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Lamiales
Family	Verbenaceae
Genus	<i>Clerodendrum</i> L.
Species	<i>Clerodendrum colebrookianum</i>
Binomial name	<i>Clerodendrum colebrookianum</i> Walp

Phytochemistry

The chemical constituent of *Clerodendrum colebrookianum* showed the presence of phenols, alkaloids, flavonoids, polyphenols, steroids etc⁹. GCMS analysis of *Clerodendrum colebrookianum* hexane extract showed the presence of 28

compounds¹⁰. Five new steroids, colebrin A-E were also isolated from the aerial parts of the species¹¹. Moreover, presence of β -sitosterol and sterol compounds in the leaves of *Clerodendrum colebrookianum* has already been reported¹². β -sitosterol, a bioactive phytoconstituent that decrease the serum cholesterol and also have cardio protective potentiality which is a valid scientific basis for consuming it for better health in North east region of India¹³.

Pharmacological Studies

Hypolipidemic activity

Crude polyphenol fraction obtained from the ethyl acetate extract of *Clerodendrum colebrookianum* leaves administered in graded oral doses (0.25 g, 0.5 g and 1 g/kg b.w. /day) for a period of 28 days in cholesterol fed rats showed Significant rise in plasma total cholesterol (TC), triglycerides (TG), phospholipids (PL), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C) and decrease in high-density lipoprotein cholesterol (HDL-C) Increased lipid profile has been depleted and high-density lipoprotein cholesterol (HDL-C) has been increased after chronic feeding of Crude polyphenol *Clerodendrum colebrookianum* (CPCC). In addition, CPCC leave extract enhanced the excretion of fecal cholesterol (FC) but could not arrest the 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase activities in cholesterol fed rats. Histopathological observations showed loss of normal liver architecture in cholesterol fed rats which were retained in CPCC treated groups. The findings of the study suggested that CPCC had a strong hypolipidemic function and could be used as a supplement in healthcare foods and drugs. Ethyl acetate extract of *Clerodendrum colebrookianum* leaves showed potent hypolipidemic effect in cholesterol fed rats¹⁴.

Antioxidant activity

Aqueous and acetone extract of *Clerodendrum colebrookianum* leaves showed the highest total phenolic content (2.348 mg/ml), when compared to methanol, ethanol and chloroform extracts, which was 0.549 mg/ml, 0.408 mg/ml and 0.407 mg/ml, respectively. The antioxidant activity was more significant for aqueous extract, when compared to other extracts in vitro antioxidant (DPPH) studies¹⁵. Different concentrations of the water, alcoholic, petroleum ether and ethyl acetate extracts of the dried leaves of *Clerodendrum colebrookianum* showed a significant inhibition of lipid peroxidation in in vitro lipid peroxidation induced by FeSO₄-ascorbate in rat liver homogenate. Water extracts at concentrations (w/v) of 1:30, 1:50, 1:200 and 1:1000 showed the strongest inhibitory activity over the other organic extracts, suggesting maximum antioxidant effect. Chronic feeding of the water extract to Wistar albino rats (both sexes, 150–200g) in 1 or 2g /kg/day doses for 14 days significantly increased the ferric reducing ability of plasma by 19% and 40% on the seventh day, and by 45% and 57% on the fourteenth day of treatment, respectively. Thiobarbituric acid reactive substances (TBARS), as a marker of lipid peroxidation, and some cellular antioxidants (superoxide dismutase, catalase and reduced glutathione) were estimated in heart, liver and kidney showed significant reduction in hepatic and renal TBARS with both the doses, without any change in myocardial TBARS. There was no change in the level of antioxidants in heart, liver and kidney, except for the hepatic superoxide dismutase. Leaves extract of *Clerodendrum colebrookianum* showed increased antioxidant capacity of blood and had an inhibitory effect on the basal level of lipid peroxidation of liver and kidney¹⁶. Methanolic leaves extract of *Clerodendrum colebrookianum* showed potent in vitro antioxidant activity by DPPH radical scavenging assay, Hydroxy radical scavenging assay, Superoxide radical scavenging radical assay, nitric oxide radical scavenging assay,

singlet oxygen radical scavenging assay and peroxynitrite radical scavenging assay¹⁷.

Anti-inflammatory activity

Aqueous extracts and its aqueous, n-butanol, ethyl-acetate, and chloroform fractions of *Clerodendrum colebrookianum* leaves at the dose of 200mg/kg/p.o. showed significant inhibition of carrageenan and histamine-induced inflammation and cotton pallet-induced granuloma formation on acute and chronic inflammation in rats. The test samples, except n-butanol fraction, exhibited inhibitory effect for both COX-1 and COX-2, in in vitro assay but their percentage of inhibition values differs from each other. The test samples (aqueous extracts, aqueous, n-butanol, ethyl-acetate, and chloroform fractions) at 100 μ g concentration exhibits 54.37%, 33.88%, 62.85%, 56.28%, and 57.48% DPPH radical-scavenging effect respectively in in vitro antioxidant study¹⁸. Methanolic extract of *Clerodendrum colebrookianum* leaves showed potent anti-inflammatory effect on carrageenan induced paw edema in Wistar albino rats. It was found that the active anti-inflammatory effect of this plant due to the presence of terpenes, glycosides and sterols¹⁹. Aqueous extract of *Clerodendrum colebrookianum* leaves showed anti-inflammatory effect in acute and chronic stages of inflammation by free radical scavenging activity and by the inhibition of both the COX-1 and COX-2 enzymes²⁰.

Antipyretic activity

Hexane extract (HECC) and methanol extract (MECC) of the whole plant of *Clerodendrum colebrookianum* at doses of 100mg, 300mg and 500mg/kg b.w. showed significant anti-pyretic effect in yeast (10ml/kg b.w.)-induced pyrexia in albino rats and the effect also extended up to 5 hours after the drug administration. The anti-pyretic effect of HECC and MECC was comparable to that of a standard antipyretic agent paracetamol (150 mg /kg, b.w., p.o)²¹.

Analgesic activity

The methanolic extract of the *Clerodendrum colebrookianum* whole plant administered intraperitoneally in the dose of 100mg/kg b.w. and 200 mg/kg b.w. and 200mg/kg b.w. showed potent analgesic effect in acetic acid induced male Swiss albino mice in a dose dependent manner by using hot tail flick test. The leaf extract showed significant analgesic effect in two different doses (100mg/kg b.w. and 200 mg/kg b.w.) by following the hot tail flick method²².

Antimicrobial activity

Acetone extract of *Clerodendrum colebrookianum* leaves showed significant antimicrobial activity and exhibited significant zone of inhibition (mm) of 14 \pm 0.3, 13 \pm 0.3 and 15 \pm 0.2 for *Escherichia coli*, *Serratia marcescens* and *Staphylococcus aureus*, respectively²³.

Antihypertensive activity

100 μ g/mL of aqueous extract (AECc), its aqueous, n-butanol (nBFc), Ethyl-acetate (EtFc) and Chloroform fractions of *Clerodendrum colebrookianum* leaves showed calcium antagonism in rat ileum and at 50 μ g/mL and 75 μ g/mL doses exhibited Rho-associated coiled-coil protein kinase (ROCK-II), phosphodiesterase-5 (PDE-5) inhibition respectively where, EtFc was caused maximum 68.62% (ROCK-II) and 52.28% (PDE-5) inhibition, but none of the test sample was exhibit effect in angiotension converting enzyme (ACE) at 100 μ g/mL. The test samples also showed negative inotropic and chronotropic effect on isolated frog heart and significant ($P < 0.001$) reduction in systolic blood pressure and heart rate in hypertensive rats compared to control²⁴. Docking studies showed that three chemical constituents (acteoside, martiniside, and osmanthuside

β6) out of 21 reported from the *Clerodendrum colebrookianum* to interact with the anti-hypertensive drug targets with good glide score. In addition, they formed H-bond interactions with the key residues Met156/Met157 of ROCK I/ROCK II and Gln817 of PDE5. Further, molecular dynamics (MD) simulation of protein–ligand complexes suggest that H-bond interactions between acteoside/osmanthuside β6 and Met156/Met157 (ROCK I/ROCK II), acteoside and Gln817 (PDE5) were stable. The present investigation suggests that the anti-hypertensive activity of the plant is due to the interaction of acteoside and osmanthuside β6 with ROCK and PDE5 drug targets. The identified molecular mode of binding of the plant constituents could help to design new drugs to treat hypertension²⁵.

Hepatoprotective and oxidative stress activity

Post oral administration of different doses of *Clerodendrum colebrookianum* leaves extract (50,100 and 200 mg/kg b.w.) showed significant decrease in different biochemical oxidation and collagen content in Iron overload induced liver injury by intraperitoneal administration of iron dextran into mice. The extract effectively enhanced the antioxidant enzyme levels and also exhibited the potential activity of the reductive release of ferritin iron. The protective effect of the plant extract on injured liver was furthermore supported by the histopathological studies that showed improvement histologically. The study revealed that the plant extract has hepatoprotective efficiency for iron overload diseases in mice and possess potential in vitro iron chelation effect and protection of Fenton reaction induced DNA damage²⁶.

CNS depressant activity

Clerodendrum colebrookianum leaves extract at the dose of 20mg/kg and 40 mg/kg showed marginal reduction of awareness and motor activity whereas at the dose of 80 mg/kg, the extract showed marked inhibition of awareness and motor activity in mice. The extract prolonged the effect of meprobamate, diazepam, chlorpromazine and pentobarbitone significantly in a dose dependent manner. Pretreatment of the extract caused significant protection of strychnine and leptazol induced convulsion and mortality²⁷.

Anti-stress activity

Administration of aqueous leaves extract of *Clerodendrum colebrookianum* at the dose of 100mg/kg prevented the cold restraint stress and showed anti-stress property in induced cold restraint stress in Swiss albino mice by significant reduction in the WBC count, eosinophil, basophil level and spleen weight while the level of ALT, neutrophils, blood glucose and plasma corticosterone along with the liver weight was found to be increase significantly on stress treatment. The studies 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 plant extract²⁸.

Anthelmintic activity

Leaves extract of *Clerodendrum colebrookianum* at three different doses, i.e. 200, 400 and 800 mg/kg b.w. given singly for 5 days in experimentally induced *Hymenolepis diminuta* (a zoonotic tapeworm) infections in Wistar rats showed that the leaves extract possesses a dose-dependent efficacy against the larval, immature and adult stages of *Hymenolepis diminuta*. However, the efficacy of the extract was found to be considerably high only against the adult stages of the parasite. A single 800 mg/kg dose of extract, given for 5 days, resulted into 68.42% reduction in the eggs per gram of feces (EPG) counts and 62.50% reduction in the worm counts. The study suggested that leaves of this plant possess significant anthelmintic properties and supports

their use against intestinal tapeworm infections in traditional medicine²⁹.

CONCLUSION

Keeping in view the above literature, *Clerodendrum colebrookianum* has excellent therapeutic effect for treatment of a wide spectrum of health disorders in traditional and folk medicine. Further, it needs to biochemical studies, isolation, characterize the active component of toxicities and elucidate more insight on the mechanism of action of different active compound and their bioavailability which may lead to discover the potential lead compounds or molecules against life threatening diseases of human life such as hypertension, diabetes. Development of database, proper harvesting and cultivation techniques and also awareness programs in the state as well as region level for the conservation and management of potential species are utmost important.

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