Review Article

Phytochemical and Pharmacological Properties of *Clerodendrum serratum* Linn.: A Comprehensive Review

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ABSTRACT

Bharangi is one of ayurvedic herbal remedies, mainly used for respiratory diseases. *Clerodendrum serratum* Linn. (Lamiaceae) are widespread in tropical and subtropical regions of the world. The ethnomedical importance of the plant has been reported in various indigenous medical systems such as Ayurveda, Siddha and Unani. In Ayurveda it is used to treat various conditions such as shwasa (difficulty in breathing), kasa (cough), vrana (wound), shotha (swelling) and many vataja conditions (disorders of the nervous system). Some of the main components found in plants are D-mannitol, hispidulin, cleroflavone, apigenin, scutellarein, serratagenic acid, acteoside, verbascoside, oleanolic acid, clerodermic acid, γ-sitosterol, β -sitosterol, cholestenol, clerosterol, campesterol and 24-ethyl cholesterol etc. Traditionally it has also been used to combat rheumatism, relieve asthma, headaches and ophthalmia with fever. C serratum is used as an antioxidant, antibacterial, anticancer, hepatoprotective, wound healing, antiallergic, anti-asthmatic, anti-inflammatory, etc.

Keywords: Bharangi, *Clerodendrum serratum*, Phytochemistry, Traditional use Pharmacological activity, Acute toxicity study.

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INTRODUCTION

Bharangi botanically identified as *Clerodendrum serratum* Linn. belongs to the family Verbenaceae, which is now included in the Lamiaceae family. Therapeutic effects of roots of *C. serratum* have been indicated in traditional systems of medicine like Ayurveda and Unani. In ancient and later ayurvedic literature, Bharangi is widely mentioned in the treatment of Swasa and Kapha (respiratory diseases) as an ingredient in various groups of medicines. *C. serratum* has a long been considered a traditional medicine to treat asthma, inflammation and infectious diseases.[1]

The Sanskrit word Bharangi literally means that which is glorious. Another name for the same plant, Bhrguja, implying that is a relation of the plant with the great sage Bhrgu. In Samhita kala this medicine is widely used for many diseases mainly for Swasa (breathlessness), kasa (cough), vrana (wound), shotha (swelling) and many vataja disorders (neurological disorders). Different synonyms of Bharangi denote external morphological characteristics and pharmacological activities such Padma (flowers look like that of lotus), Kharashakha (the leaves have a rough texture), Bharangi (it destroys the diseases or it is having the power equivalent to sun), Vatari (enemy of vata dosa), Kasaghni (relieves cough). [2,3]

A

B

Figure 1: *Clerodendrum serratum*, A: dried roots, B: whole plant

Vernacular Names [4]

Bengali: Bamunhatee, Bamanhatee, Bhuijam

English: Blue glory, Beetle killer

Gujarati: Bharangee

Hindi: Bharangi

Kannada: Gantubarangee

Malayalam: Cheruthekku

Marathi: Bharangee, Bharang

Punjabi: Bhadangee

Sanskrit: Angaravalli, Padma, Brahmanayashtika, Barbura

Tamil: Cheruteku

Telugu: Ganttubrarangee

Urdu: Bharangi, Baharangi.

Taxonomical Identification [4,5]

Family: Lamiaceae/ Verbenaceae

Subfamily: Ajugoideae

Genus: Clerodendrum

Species: serratum

Habitat

Clerodendrum serratum Linn. is found more or less throughout India, especially common in assam, Bengal and in forests up to 1500m altitude. It is reported to be rare and endangered in Gujarat.[2,6]

Globally in Africa, south Asia, America and northern Australia, Ceylon, Malay, Penninsula.[7]

Phytochemistry

Group of major chemical constituents found in the *Clerodendrum serratum* Linn. are carbohydrates, phenols, flavonoids, terpenoids and steroids.[1]

In root: Saponins, D - mannitol, Stigmasterol, oleanolic acid, Queretaroic acid, Serratagenic acid, β -Sitosterol, γ-sitosterol Clerosterol identified as 5, 25- stimastadien-3β o, Clerodone as 3β- hydroxyl- lupan 12- one, B- sitosterol, Lupeol, A steroidal glycoside, Phytosterols, Ferulic acid, Arabinose, Scutellarcin, Baicalein, Serratin and Ursolic acid.

In leaf: Catchin, α-spinosterol, Luteoline, Polyphonolics, Diterpin – clerodin, Ethycholesta – 5, 24,25- trine 3β- o hispidulin and 7-o- gluconoids of hispidulin and Cruteuarein.[2,4,5,8,6,9,10]

The minerals reported in the plant were: Na, Mg, Al, K, Ca, V, Cr, Mn, Fe, Co, Ni.[25]

Table 1: The group of chemical constituents, compounds and pharmacological activity

Group of chemical constituents	Compounds	Pharmacological activity
Carbohydrates	D - mannitol	-
Flavonoids	Catechins leucoanthocyanidins, flavanones, flavanonols, flavones, anthocyanidins, flavanols, chalcones, aurones, isoflavones • Hispidulin • Cleroflavone • Apigenin • 7 – hydroxy flavanone Scutellareinand pectolinarigenin	Anti – oxidant Anti – microbial Anti – asthmatic Anti – tumor CNS – binding
Phenolics	Serratagenic acid, acteoside, indolizino, verbascoside	Anti – oxidant, Anti – microbial, Anti – proliferative, Antihypertensive, anti-cancer.
Terpenes	betulin, oleanolic acid, clerodermic acid, betulinic acid, friedelin and monomelittoside	Weak CNS activity, Strong molluscicidal, Fungitoxic.
steroids	γ-sitosterol, β-sitosterol, cholestanol, clerosterol, campesterol and 24-ethyl cholesterol	-

Table 2: Phytoconstituents screening of *Clerodendrum serratum* leaves extracts [31]

Phytochemical Constituents	Petroleum Ether	Chloroform	Alcohol	Aqueous
Alkaloids	-	-	+	-
Flavonoids	+	-	+	+
Carbohydrate	+	+	-	+
Saponins	+	-	+	-
Terpenoids	+	-	+	+
Steroids	+	+	+	+
Tannins	-	-	+	-
Glycosides	-	-	-	-

Key: Present phytochemicals are represented by (+) sign, absent phytochemicals are represented by (-) sign

Ethnomedicinal/ Traditional Uses

C. serratum (Bharangi) is widely used in indigenous systems of medicine for the treatment of respiratory disease, especially asthma, and several other diseases in a crude combination with several other drugs such as Sati (Hedychium spicatum Sm. Zingiberaceae) and Pushkarmoola (Inula racemosa Hook.f. Asteraceae) and also present in capsule or tablet form of various strengths.[1]

According to Aryabhishek it is useful in cough, swelling, breathlessness, wound, fever, rheumatism, tuberculosis etc.[3]

The Ayurvedic Pharmacopoeia of India indicated the use of the dried roots for cough, bronchitis, dyspnea, chest diseases and sinusitis.[4]

PHARMACOLOGICAL ACTIVITIES

1. Anti- inflammatory activity

Anti-inflammatory effect in rats were assessed by the Granuloma pouch method. The anti-allergic activity was assessed by Milk induced Leucocytosis in mice and Bronchial Hyper-reactivity in ovalbumin – sensitized Guinea Pigs. (6 groups, n=6). This study showed that Low Dose (LD) of Bharangi root and High Dose (HD) of stem show anti-inflammatory (23%) and anti-allergic activity (21%) comparable to Dexamethasone (21%) But the high dose of Bharangi root has promising anti-inflammatory (44%) and anti-allergic activity (35%). Anti-allergic activity is minimal (8.6%) in stem LD. This study points out that Bharangi Root is more effective than Stem and its HD is useful in anti-allergic and anti-inflammatory activity in conditions such as asthama; which needs to be further confirmed.[11]

The ethanolic root extract of C. serratum showed significant anti-inflammatory activity in Carrageenan - induced oedema in rats, and also in the cotton pellet model in experimental mice, rats and rabbits at concentrations of 50, 100 and 200 mg/kg.[12]

In another study, the methanol extracts of the aerial and root parts of *Clerodendrum serratum* Linn. was conducted to examine its anti-rheumatic properties based on the effects on carrageenan paw oedema in rats. The results showed that the roots possess significant while the aerial parts exhibited moderate anti –inflammatory activity. Thus, from the study it is evident that the roots of *Clerodendrum serratum* L. possesses potent anti-rheumatic properties.[13]

2. Anti – asthmatic activity

The ethanolic extract of roots of *Clerodendrum serratum* attenuates production of inflammatory mediators in oval albumin-induced asthma in rats, rats at low dose and high dose.[14]

Evaluate the anti-asthmatic activity of alcoholic extract of *Clerodendrum serratum* induced by oval albumin in Swiss albino mice (18-25g) at concentration100mg/kg and 200mg/kg significantly reduced the total number of cells ($p < 0.001$) eosinophils (** $p < 0.001$) in BAL compared with the untreated group of OVA sensitized mice. treatment *with Clerodendrum serratum* during the challenges significantly reduced the number of total cells in the BAL. Similar results peripheral blood count and eosinophil count were obtained.[15]

In another study, a hydroalcoholic extract was prepared from the samples of a polyherbal drug –Bharangyadi which contained *Clerodendrum serratum*, Hedychium spicatum and Inula racemosa. In this study the graph clearly presented significant increase in lung volume and compliance and decrease in airways resistance which is can be seen as the decrease in the settling time in respect to normal patient response justifying the use of the drug in asthama.[16]

3. Antioxidant

In the DPPH radical scavenging assay, different concentrations (50, 100, 150, 200, 250µg/ml) of *Clerodendrum serratum* roots and ascorbic acid (50, 100, 150, 200, 250 µg/ml) significantly showed the inhibitory activity with IC50 value were 175 and 137 respectively. In the reducing power assay, a linear increase in reducing power was observed over a concentration range 20- 120

µg/ml sample, equivalent to 20 -120 µg/ml ascorbic acid. In hydrogen peroxide scavenging assay, the inhibitive effect of CSR extract was found to be moderate when compared to other assays. The inhibition of 73.32 ± 0.002%, and 64.49 ± 0.242% were observed with ascorbic acid (standard) and ethanolic root extract at highest concentrations, respectively.[17]

Determination of antioxidant activity by Free radical scavenging activity (FRSA) assay. The ability of the test samples to scavenge DPPH was assessed on the basis of the effective concentrations 50% (EC50) values, defined as concentration of antioxidant (test samples) required to reduce the absorbance at 517 nm of DPPH*solution concentration to half of the initial value. The extracts of C. serratum were measured for antioxidant activity, using 1,1-diphenyl-2- picrylhydrazyl (DPPH*) radicals scavenging assay, and compared with those of the well-known antioxidants such as BHT, ascorbic acid and quercetin. Amongst the four extracts, ME-CS, was found to contain the highest polyphenolic contents, demonstrated highest free radical scavenging activity.[18]

4. Anticancer activity

Aqueous and methanolic extracts *Clerodendrum serratum* root used to study anti-cancer activity in Swiss albino mice. Mice were treated with the extracts (100 and 200 mg/kg/day per orally) respectively for 14 days. The parameters studied were mean survival time, percentage increase in life span, body weight, hematological parameters such as RBC, WBC and Hb, biochemical investigations viz. ALAT, ASAT, total protein. The study confirmed that the methanolic extract of the roots of *Clerodendrum serratum* exhibits anticancer activity at the doses of 100 and 200 mg/kg body weight.[19]

Methanol extract of leaves of *Clerodendrum serratum* are screened for their anticancer activity by in vivo the various parameters such as hematological studies and protein estimation, solid tumor volume, median survival time (MST), life span (%LS) and in vitro studies was carried out by Tetrazolium salt assay and Tryphan blue dye exclusion method in adult Swiss albino mice (25-30g). Two concertation 200mg/kg and 400mg/kg. The relative cell survival progressively decreased in dose dependent manner. Cytotoxicity studies anticancer activity confirmed by Tryphan Blue exclusion method *Clerodendrum serratum* (200µg/ml showed 79% of Cytotoxicity inhibition).[20]

5. Antinociceptive activity

Albino mice were used to assess antinociceptive activity with alcoholic extract of *Clerodendrum serratum* roots at the dosage of 50, 100, 200 mg/kg per orally by acetic acid induced writhing and hot plate methods. Morphine sulphate (5 mg/kg, subcutaneously) was used for comparison. The result showed a significant reduction in acetic acid induced writhing, which demonstrates and persists potent antinociceptive effect and further has been supported by hot plate method where a significant increase in AUC (area under the time response curve) was observed. The response was much lower than that to morphine sulphate.[12]

6. Hepatoprotective activity

The ethanol extract of *Clerodendrum serratum* roots and ursolic acid isolated from it were evaluated for hepatoprotective activity against carbon tetrachloride induced toxicity in male Wistar strain rats. Rat was orally administered 20 mg/kg/day ethanol extract and 10 mg/kg/day per orally of ursolic acid concomitantly for 14 days. It revealed that the hepatoprotective activity of constituent ursolic acid extracted from roots of *Clerodendrum serratum* is significant as similar to the standard drug and showed more significant hepatoprotective activity than crude extract.[21]

Another study was carried out with the aqueous and alcoholic extract of the leaves of *Clerodendrum serratum* at the dose of 200 mg/kg per orally in Swiss albino mice. The results showed significant decrease in liver weight and biochemical parameters like ASAT, ALAT, SGOT, SGPT, ALP, Bilirubin, Total protein compared to control group. Thus, the research provides the pharmacological evidence of ethno medicinal property of *Clerodendrum serratum* in the treatment of hepatotoxicity.[22]

7. Wound healing activity

Ethanolic extracts of roots and leaves of *Clerodendrum serratum* were obtained and their wound healing potency was evaluated on Albino rats. The results show higher wound healing potency of root extract as compared to leaf extract. [5,23]

8. Antibacterial activity

The ethanol extract of roots of the plant have been screened for their antibacterial activity. The extract (7.5 mg/disc) showed broad-spectrum antibacterial activity against gram positive and gram-negative bacteria. The results were compared with the standard drug streptomycin (10 µg/disc). The zone inhibition was found to be increased with the increase in concentration of the extract and thus exhibiting concentration dependent activity.[5, 24]

9. Anti- pyretic activity

Rabbits were treated with an alcoholic extract of roots of *Clerodendrum serratum* (50, 100, 200 mg/kg per orally). Paracetamol 100 mg/kg per orally was used for comparison. The reduction in pyrexia after *Clerodendrum serratum* administration indicated the antipyretic activity of this plant. The response at higher doses was almost comparable to that of paracetamol.[11,25]

10. Analgesic activity

In this study analgesic effect of the ethanolic extract of leaves of *Clerodendrum serratum*. Linn was evaluated at the dose of 200 and 500 mg/kg by tail flick method and acetic acid induced writhing test in Wistar rats for seven days orally and standard group rats were administered

diclofenac sodium (10mg/kg per orally) one hour before study on seventh day. The drug showed significant analgesic activity when compared to standard drug.[24,26]

11. Antifertility

In a preliminary screening, the 50 percent ethanolic extract of the plant (excluding root) showed a spermicidal activity in rats which was confirmed in the fractionated extract. The extract at two percent showed in vitro spermicidal activity in both rat and human semen. In another study, the n-butanol soluble fraction of the fifty percent ethanolic extract of the plant (excluding root) also exhibited in vitro spermicidal activity in human semen at two percent concentration. The acetone and methanolic extracts of the root did not exhibit anti - implantation activity in rats at 150 mg/kg p.o[26]

The plant treatment results in affecting both Spermatogenesis and cauda epididymal spermatozoa and the epididymal sperm motility and sperm count found decreased may be due to the decreased supply of testosterone level in rats. It may be concluded from the study that the plant caused infertility in male rats.[27]

12. **Antihistaminic activity**

It was of interest that both the alcoholic extract and the saponin isolated from the root bark of an indigenous plant, Clerodendrum serratum, which has been used for the treatment of bronchial asthma, caused release of histamine from lung tissue. Long term administration of the saponin in 20 mg/kg doses caused significant depletion of the amines from the lungs of rats treated with the drug. The saponin fraction like other histamine releasing substance, was not found to manifest any antihistamine activity or to give protection against anaphylactic shock in sensitized guinea-pigs exposed to egg albumin (antigen) micro-aerosols. However, the continued daily administration of the drug, 20 mg/kg (1/15 of the LD50 dose 307.7 mg/kg), intramuscularly for 20 days to sensitized guinea-pigs have been found to gradually develop a defense against it anaphylaxis.[28]

13. **Antifungal**

Aqueous extract of leaves had no significant effect on the mycelia growth (8 to 38.2 percent inhibition) of the keratinophilic fungi, viz., Nannizia gypsea (strain -), N. gypsea (strain +), N. incurvata (strain +), N. fulva (strain -) and N. fulva (strain +). However, it exhibited antifungal activity against Curvularia tuberculata, the causative fungus of die-back disease and Pestalotiopsis mangiferae, the causative organism of leaf spot disease.[29]

14. **Anti-allergic activity**

The present study was screened by milk induced Leucocytosis in Albino mice with aqueous extract of *Clerodendrum serratum* root and stem in low (130 mg/kg, p.o) and high dose (260 mg/kg, p.o) respectively for fourteen days. Both root and stem have shown anti - allergic effect, but at high dose of *Clerodendrum serratum* root showed significant activity when compared with dexamethasone.[10]

15. **Anti- microbial**

Aqueous extract of *Clerodendrum serratum* stem bark, when screened against 13 pathogenic strains, exhibited a broad – spectrum activity by inhibiting seven strain s with inhibition zone ranging from 15 to 20 mm.[30]

TOXICOLOGICAL DATA OF *CLERODENDRUM SERRATUM* L.

- The acute oral toxicity study of whole plant extract *of Clerodendrum serratum L.* were performed on three female rats, were treated with methanol extract of the arial parts and roots of the *Clerodendrum serratum* L. by oral administration at a dose of 2000mg/kg body weight. The animals that survived throughout the experiment increased their body weight by day 14 as compared to day 0. No abnormalities were detected in animals during necropsy.[12]
- Acute oral toxicity of alcoholic and aqueous extract was determined using nulliparous, non-pregnant female mice. The LD50 determination was done in mice(20-25g) according to OECD guidelines by using Up and Down procedure. LD50 of alcoholic and aqueous extracts of *Clerodendrum serratum* was found to be above 2000mg/kg for each.[21]
- According to the records of Ayurvedic Pharmacopoeia of India (2001), the daily clinical dose recommended for adult, ranges from 3–6 g of root powder and about 10–20 g of kwatha churna.[4]

DISCUSION

The medicinal plants such as *clerodendrum serratum* L. has been evaluated for various pharmacological activity. Thus, the goal of this article to review the phytochemistry, pharmacological activity and toxicological data of *clerodendrum serratum* L. The chemical compounds such as saponin, Catchin, olionalic acid, carbohydrates, flavonoids, phenols, steroids, terpenes etc. have been reported in *Clerodendrum serratum*. Further the research studies have proved hepatoprotective, antioxidant, anti-cancer, anti-inflammatory, antinociceptive, analgesic, anti-allergic, anti-asthmatic antifertility activities.

CONCLUSION

Bharangi (*Clerodendrum serratum* Linn.) is a drug of choice, especially for curing various disease Shwasa (breathlessness), Kasa (cough), Vrana (wound), Shotha (swelling) and many Vataja disorders (neurological disorders) etc. Various chemical compound such as saponin, Catchin, olionalic acid, carbohydrates, flavonoids, phenols, steroids, terpenes etc. have been reported in *Clerodendrum serratum*. It has various pharmacological activities and so on which has further scope in field of medicine and therapeutic significance.

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