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"*Clerodendrum serratum*" A potential herb for positive inference- A review

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Abstract
Most of the attention now a day is being focused on traditional medicine as the evidences is very strong regarding the treatment of many ailments. In case of allopathic medicine, a strict commitment on medication adherence has to be followed and there may be a chance of many ADRs if faulty methodology was followed. This can create a fear in the minds of the one using allopathy and lead to a great turn in the field of natural medicine as many found it was safe and effective. Such interest leads to have focus on herbs to treat major disorders or diseases. The one fall under this category is dementia, a chronic or persistent disorder of the mental processes which may lead to Alzheimer's disease. An entity herb that comes under this is *Clerodendrum Serratum* which is having many potential values to cure many ailments. The chemical constituent hispidulin, a source of great anti-oxidant potential is effective in protecting the mitochondria of neurons. This review provides the knowledge on *Clerodendrum Serratum* and its therapeutic benefits in detail.

Keywords: *Clerodendrum Serratum*, dementia, hispidulin, alzheimer's disease

Introduction
Natural products have been a significant source of medicinal agents for the alleviation or cure of human diseases since the dawn of civilization and are the primary source for the production of various drugs in modern times, regardless of their easy availability and complexity of compound reservoir [1]. Many of the medications licensed by the FDA over the past decade have been derived from natural product resources in different disease categories such as infectious, respiratory, cardiovascular, oncological, etc. [2].

Clerodendrum serratum is a shrub and belonging to the genus of flowering plant in the family Lamiaceae (Verbenaceae) [3]. It is commonly known as Bharangi in Hindi, Gujarathi and Gantu Bharangi in telugu and Kannada [4]. It is native to tropical and warm temperate regions. It was found throughout india at an altitude of 1500mts height and the plant parts mostly used were root and leaves. Roots are acrid, carminative, thermogenic, febrifuge used in inflammation [5]. Leaves are used in the application of cephalagia and ophthalmia. Seeds bruised and boiled in buttermilk are used as aperient and in dropsy.

Fig 1: *Clerodendrum Serratum* Plant

Clerodendrum serratum Linn. (Family: Verbenaceae) has been used in traditional treatment of various life threating diseases like typhoid, cancer, jaundice, syphilis and hypertension, anti-rheumatic, anti-asthmatic, febrifuge, in cephalagia and ophthalmia. Although, A validated analytical method, standardization and optimization of extraction conditions with respect to biological activity have not been reported. The qualitative and quantitative analysis of active constituents in *Clerodendrum serratum* is presented by HPLC coupled with FTIR and UV detections. The major chief constituents that are found in the plant are D-mannitol, hispidulin, cleroflavone, apigenin, scutellarein, serratagenic acid, acteoside, verbascoside, oleanolic acid, clerodermic acid, γ-sitosterol, β-sitosterol, cholestanol, clerosterol, campesterol and 24-ethyl cholesterol. *Clerodendrum* genus have been very well studied for their chemical constituents and biological activities, and 283 compounds, including monoterpene and its derivatives [6], sesquiterpene [7], diterpenoids [8,9], triterpenoids [10,11], flavonoid and flavonoid glycosides [12], phenylethanoid glycosides [13], steroids [14] and steroid glycosides [15], cyclohexylethanoids [16], anthraquinones [17], cyanogenic glycosides [18], and others have been isolated and identified.

Taxonomy [19]
Kingdom: Plantae
Division: Angiosperms
Class: Magnoliopsida
Subclass: Lamiidae
Order: Lamiales
Family: Verbinaceae
Genus: Clerodendrum
Specie: Serratum

Geographical indication
The family Verbenaceae is primarily confined to tropical regions. Species diversity of Clerodendrum is rich in

Southeast Asia and in Malayan Archipelago. However, most of the species are occurring in tropical Africa and in Southern Asia. A few are occurring in the tropical America and in Northern Australasia extending north into the temperate zone in eastern Asia (Mabberley, 2008). In India either about 18 species (Santapau and Henry, 1973) or about 30 species (Shastri, 1950) reflect Clerodendrum. Clarke (1885) described 26 Indian subcontinent species and grouped them under two sub-generals, Euclerodendron and Siphonanthus, respectively. Of the 26 species described by Clarke (1885), 4 species are classified as dubious or removed, 2 species are classified as Siphonanthus sub-genus, and 20 are classified as Euclerodendron sub-genus.

Microscopic Characteristics

Riped root was found in have stratified cork holding numerous14-20 layers of thin-walled, tangentially separated stretched cells; each stretched cell consists of approximately 3-5 layers of cells appearing; secondary cortex long, external 2 or 3 layers radially formed and tangentially extended, while the innermost part of the cells is polyhedral or triangular to egg-shaped with intercellular spaces. Many of these cells are formed into strongly thickened stone cells with aligned striations and widening channels with narrow lumen; some of the cells are fused with acicular crystals of calcium oxalate and a very small amount of brown coloring matter; secondary phloem lasts to sieve elements and parenchyma fall largely into the outer region [20].

Macroscopic Characteristics

Fully mature root is hard, woody appearance, cylindrical shape, 5 cm thick, with the appearance of lenticels on the outside surface with light brown colour; bark appears very fragile and readily distinguishable from a wide wood display striking medular rays. In transversely cut sections, parallel growth rings are commonly observed; short fracture and acrid taste**.**

Chemical constituents

For various ailments, the root part of the plant is mainly claimed traditionally. In the roots of Clerodendrum serratum the phytoconstituents are mainly carbohydrates, phenolics, flavonoids, and terpenoids. In *Clerodendrum serratum* [21], Sachdeva et.al (1965) reported various types of metabolites, such as primary and secondary. Zhu et.al (2001) characterizes two novel triterpenoid glucosides in *Clerodendrum serratum* [22]. Vasavada et.al (1967) isolated γ-Sitosterol from *Clerodendrum serratum* [23].

The major groups present are carbohydrates, steroids, flavonoids, terpens, and glycosides. Roots has beenfound to report various chemical constituents as terpenoids like Ursolic acid, sterols like γ sitosterol, flavonoids like Apigenin-7-glucoside and carbohydrate like D-mannitol. In case of leaf, Catchin, α-spinosterol, Luteoline, Polyphonolics, Diterpin –clerodin, Ethycholesta –5, 24 25-trine 3 β-o hispidulin and 7-o-gluconoids of hispidulin and Cruteuarein were present.

Table 1: Phytoconstituents of different parts of plant [24-27]

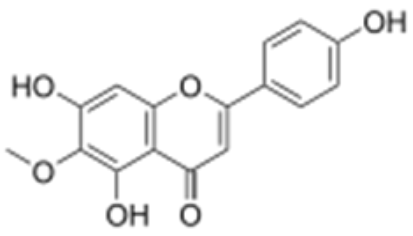
S. No	Part	Chemical Constituents
1	Root	Carbohydrates: D-mannitol Terpenoids: Serratagenic acid, Oleanolic acid, Queretaratic acid, Ursolic acid, Serratin Flavonoids: Aspigrnin-7-glucoside Steroids: γ-sitosterol Saponins
2	Leaves	Terpenoids: Serratin, Lupeol Flavonoids: Catchin, Hispidulin, Cleroflavone, Luteoline Steroids: α-spinosterols
3	Stem	Cabohydrates: sugar Terpenoids: Ursolic acid Steroids: β-sistosterol, Spinasterol Flavonoids: 5-hydroxy-7,4-dimethoxy flavone

Flavonoids

The isolated flavonoids like hispidulin and cleroflavone posess antioxidant, anti- microbial, anti- asthamatic, anti-tumour and CNS binding activity. Other flavonoids isolated from plants are apigenin, 7-hydroxy flavanone, scutellarein and pectolinarigenin (Shrivastava *et al*., 2007; Harbone, 1984; Mann *et al*., 1984).

Hispidulin

It is a naturally occurring monomethoxy flavone i.e scutellarein methylated at position 6. It is not only monomethoxy flavones but also a trihydroxy flavone. Hispidulin (4′, 5, 7-trihydroxy-6-methoxyflavone) is a flavones derivative found in plant such as *Grindelia argentina*, *Arrabidaea chica*, *Saussurea involucrate* (A rare traditional Chinese medicinal herb), *Crossostephium chinense*, Artemisia and Salvia species. Hispidulin is having Anti-oxidant, Anti-mutagenic, Anti-fungal, Anti-inflammatory and Anti-neoplastic activities. Recently It was found to be a potent benzodiazepine receptor ligand with positive allosteric properties [28] and also act as a partial modulator at γ-aminobutyric acid (GABA) receptors and posess Anti-convulsant activity in CNS [29,30]. This natural flavone is reported to be 100-fold more potent than theophylline in its property of inhibiting platelet aggregation.



Hispidulin

Pharmacological activities

Vazhayil *et al* (2017) reported flavonoid content apigenin (API) and luteolin [31] in *Clerodendrum serratum* (LUT)

significantly showed neuroprotective action for depressive-like behavioral symptoms in adult mice [32]. Narayanan, et.al (2011) reported anti-inflamatory and antipyretic activity animal model with ethanolic extract of *Clerodendrum serratum* root in hot plate method at dose of 50,100 and 150 mg/kg. Gupta, *et al* (1971) reported the presence of saponins having influence on mast cells of rat mesentery in animal model [33]. Gupta et.al (1968) reported antihistamine and anti-allergic activity with long term uses of saponins from *Clerodendrum serratum*. Gupta *et al* (1967) successfully evaluated inhibition of *Solanum xanthocarpum* and *Clerodendrum serratum* on histamine release from tissues. Vidya *et al* (2005) revealed hepatoprotective activity of *Clerodendrum serratum* 20 mg/kg orally of ethanol extract and 10 mg/kg orally of ursolic acid against carbon tetrachloride induced toxicity in male wistar strain rats. Moreover, further wound healing using 5% w/w ointment gel, from ethanolic extract of leaves and roots part was demonstrated in excision and incision model. Bhangare *et al* (2012) reported anti-inflamatory activity of aqueous extract from root of *Clerodendrum serratum* at low dose of (90 mg/kg) and highest dose at (180 mg/kg) in Rats granuloma pouch method. A delayed type hypersensitivity (DTH) reaction along with humoral antibody in mice was reported by Juvekar *et al* (2006) for phagocytic and proliferation assays for doses 100 and 200 mg/kg [34].

Pharmacological profile of plant

Bronchodilator Activity

Aqueous extracts of leaves of C.Serratum possess bronchodilator property. Icosahydropicenic acid (IHPA), a new pentacyclic triterpenoid saponin was first time isolated from the roots of C.serratum (L) Moon (Verbenaceae). IHPA, at the dose of 100mg/kg, showed significant protection of mast cell degeneration as compared to standard sodium cromoglycate. The compound also revealed significant inhibitory activity on histamine – induced gout tracheal chain preparation [35].

Anti-Bacterial activity

The ethanol extract of the roots of the plant have been screened for their antibacterial activity. The extract showed broad spectrum anti-bacterial activity against gram positive and gram-negative bacteria. The results were compared with the standard drug streptomycin and the zone inhibition was found to be increased with the increase in concentration of the extract and thus exhibiting concentration dependent activity [36].

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 [37].

Hepatoprotective activity

The ethanol extract of C. serratum roots and ursolic acid isolated from it were evaluated for hepatoprotective activity against carbon tetrachloride induced toxicity in male Wistar strain rats. The parameters studied were estimation of liver function serum markers such as serum total bilirubin, total protein, alanine transaminase, aspartate transaminase and alkaline phosphatase activities. The ursolic acid showed more significant hepatoprotective activity than crude extract. The histological profile of the liver tissue of the root extract and ursolic acid treated animal showed the presence of normal hepatic cords, absence of necrosis and fatty infiltration as similar to the controls. The results when compared with the standard drug silymarin, revealed that the hepatoprotective activity of the constituent ursolic acid is significant as similar to the standard drug [38].

Anti-oxidant activity

C. serratum aqueous extract has significant antioxidant activity against DPPH scavenging assay, superoxide scavenging assay, and FRAP assay. This radical scavenging activity could be attributed to the presence of flavonoids, alkaloids, glycosides, and phenolic compounds. Plant exhibits the antioxidant activity through the scavenging of free radicals, and FRAP showed significant reducing power activity with increased concentration of the sample [39].

Anti-cancer activity

The methanolic extract of leaves of *Clerodendrum serratum* were 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. The relative cell survival progressively decreased in dose dependant manner. Cytotoxicity studies by Tryphan Blue exclusion method also confirmed the anticancer activity of *Clerodendrum serratum* (200µg/ml showed 79% of Cytotoxicity inhibition) [40].

Anti-inflammatory and Anti allergic activity

Anti-inflammatory action in rats was assessed by Granuloma pouch method. The anti-allergic activity was evaluated by Milk induced Leucocytosis in mice and Bronchial Hyper-reactivity in Guinea Pigs sensitized with egg albumin (6 groups, n=6). This study shows that Low Dose (LD) of Bharangi root and High Dose (HD) of stem show anti-inflammatory (23%) and anti-allergic activity (21%) equivalent 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%) for LD of stem. This study indicates that Bharangi Root is more effective than Stem and its HD would be useful in anti-allergic and anti-inflammatory activity in diseases like asthma [41].

Antifertility

The testicular steroidogenesis and fertilities were lower in the MECS-treated rats, and anti-androgenic results were reported in hormonal study. Furthermore, histopathological findings confirmed the drug's male contraceptive function [42].

Conclusion

This paper describes the botany, phytochemistry and various pharmacological activities of *Bharangi (Clerodendrum serratum* Linn. Moon). Leaves contain glucuronide and flavones; bark has saponins, triterpenoids etc. Root reported presence of flavonoids, glycosides etc. Root bark contained D-mannitol. Further the research studies have proved hepatoprotective, antioxidant, anti-cancer, anti-inflammatory, antinociceptive, analgesic, anti-allergic,

anticholinesterase, anti-fungal activities and so on which has further scope for clinical trials to treat the diseases.

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