



PHYTOCHEMICAL & PHARMACOLOGICAL ACTIVITY OF AGNIMANTHA (*CLERODENDRUM PHLOMIDIS* LINN.F) – A REVIEW

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Abstract : The World Health Organisation (WHO) estimated that 80% of the population of developing countries rely on traditional medicines, mostly plant drugs, for their primary health care needs. *Agnimantha* [*Clerodendrum phlomidis* Linn.f. Syn. *C. multiflorum* (Burm.f.) O.kuntze, *Clerodendrum phlomoides* Linn.f.], family verbenaceae, is one of the ingredient of *Dashamoola*¹. In traditional systems of medicine, leaves, stem, aerial parts and root of the plant are used in *Shotha* (inflammation), *Prameha* (glycosuria), *Jwara* (coryza), *Upadamsha* (gonorrhoea), *Sthaulya* (obesity) etc. Various research has been carried out for isolation of chemical constituents and therapeutic potential of *Clerodendrum phlomidis*. This review is an attempt to compile the phytochemical and pharmacological activity Of *Clerodendrum phlomidis*.

Key words : *Agnimantha*, *Clerodendrum phlomidis*, chemical constituents, pharmacological activity.

VERNACULAR NAMES² :

- Sanskrit : Agnimantha, Gandhapushpa, Nadeyi, Jayanti, Tarkari, etc.
 Marathi : Arani , Arni, Airanamula, Takalimula, Tekar.
 Hindi : Arni, Piran, Pirun, Urni.
 Tamil : Takkari, Thalangi, Thalludhalai, Sayandi, Taludalai, Tirugdulai, Vadamadakki.
 Telugu : Nelli, Taluki, Takko-lamu, Tekkali.
 Malayalam : Munja, Peruvelum, Tirutalai.
 Bengali : Arni, Ganiyari, Goniari.
 Conarese : Taggi.
 Gujarati : Aranimula, Arni, Irun.
 Kannada : Taggi, Taggi-Beru.
 Oriya : Hontari, Ganiary.
 Santali : Panjot.
 Sind : Gharyat.
 Las Bela : Tankar

BOTANICAL DESCRIPTION² :

Clerodendrum phlomidis Linn.f. [Syn. *C. multiflorum* (Burm.f.) O.kuntze, *Clerodendrum phlomoides* Linn.f., *Clerodendron phlomoides* Willd.]

A large bush or small tree, reaching 9 m. high, with more or less pubescent branching branches.

leaves : 3.8-6.3 by 3.2-3.8 cm., ovate or subrhomboid, obtuse or acute, coarsely crenate-dentate or subentire, undulate, glabrous above, more or less puberulous beneath, base truncate or subcordate; petioles 6-20 mm. long.

Flowers : moderate sized, fragrant, in small dichotomous axillary cymes arranged so as to form a rounded terminal panical; bracts obovate or lanceolate acute leafy. Calyx 1cm. long or more, divided about half way down, glabrous, not enlarged in fruit, segments ovate, acutely acuminate, veined. corolla white or pinkish; tube 2-2.5cm long, slightly pubescent outside, glabrous inside; lobes nearly equal, exceeding 6 mm long, elliptic, obtuse, veined. Filament slightly pubescent below. Ovary & style glabrous.

Drupe: 6mm. long, broadly obovoid, depressed, the top about level with the points of the persistent calyx-lobes, normally 4-lobed with 1 pyrene in each lobe (1-3 sometimes suppressed).

PHARMACOGNOSY :

Root³ : It shows exfoliating cork, consisting of 10-15, occasionally more, rows of tangentially elongated, thin-walled cells; secondary cortex consists of round to oval parenchymatous cells, a few containing rhomboidal crystals of calcium oxalate; secondary phloem consists of isodiametric, thin-walled, parenchymatous cells, a few of them containing rhomboidal crystals of calcium oxalate; phloem rays distinct, consisting of radially elongated cells; secondary xylem shows a wide zone, consisting of usual elements, all being lignified; vessels found in single as well as in groups of 2-3, scattered throughout xylem region; xylem parenchyma simple pitted, squarish wide lumen; xylem rays 1-5 seriate, consisting of radially elongated cells; rhomboidal crystal of calcium oxalate packed in xylem parenchyma and xylem rays; abundant simple, round starch grains measuring 6-17 μ in dia., found scattered throughout.

Powder - Dull yellow; shows fragments of cork cells, small, pointed, aseptate, lignified fibres, simple, pitted vessels, lignified cells packed with rhomboidal crystals of calcium oxalate and numerous simple, round to oval starch grains having narrow hilum, measuring 6-11 μ in diameter.

Leaf⁴ : Leaf is dorsiventral with 1 to 2 or 3 layers of palisade cells, both glandular and non-glandular hairs are present. Stomata are cruciferous. Palisade ratio is 2.4, stomatal index 8.26 (upper), 10.29 (lower), vein islet no.11 and veinlet termination number 17.

DISTRIBUTION⁴:

They are distributed throughout the drier parts of India, in sub-himalayan tracts of Rohilkhand, N. Oudh, Orrisa, Chota Nagpur, Bihar, Bangal, Punjab, Gujarat, Konkan, Deccan, N. Circars and Karnataka.

PROPOGATION AND CULTIVATION⁴ :

It can be propagated by seeds and root suckers and grow well on a variety of soil. In nature it is found generally on waste lands, along rivers, railway tracks etc.

SUBSTITUTES⁵ :

In Ayurvedic formulary of India, *Clerodendrum phlomidis* Linn.f has been accepted as Agnimantha, whereas *Premna integrifolia* Linn. and *Premna mucronata* Roxb. are considered as substitutes.

USES :

The decoction of the root is aromatic, astringent and used as a demulcent in gonorrhoea. The juice of leaves is used as an alternative and bitter tonic. It is also given to children during convalescence from measles⁶. In southern India, the juice of leaves is given in neglected syphilitic complaints in doses of half an ounce or more twice daily. The Santals rub the plant over their bodies in dropsy³. The plant is reported to be useful in inflammation, glycosuria, pox, coryza, scrotal enlargement and postnatal complaints⁴.

CHEMICAL COMPOSITION :

Root : β -sitosterol, γ -sitosterol, ceryl alcohol, clerodin (C₂₄H₃₄O₇), clerosterol (C₂₉H₄₈O) and clerodendrin-A(C₂₇H₂₆O₁₇)⁷. α -L-rhamnopyranosyl-(1 \rightarrow 2)- α -D-glucopyranosyl-7-O-naringin-4'-O- α -D-glucopyranoside-5-methyl ether (C₃₄ H₄₄ O₁₉)⁸.

Stem : D-mannitol, β -D-glucoside of β -sitosterol, β -sitosterol and ceryl alcohol⁹.

Aerial parts: Lup-20(29)-en-3-triacontanoate(C₆₀H₁₀₈O₂), tetratriacontanol and 24 β -ethylcholesta-5, 22E,25-triene-3 β -ol were reported isolated from aerial parts¹⁰.

Leaves: A crystalline non-glucoside bitter principle (C₁₇H₁₆O₆), ceryl alcohol, β -sitosterol, γ -sitosterol, palmitic acid, cerotic acid and an unidentified sterol (C₂₈H₄₈O)¹¹. Scutellarein (5,6,7,4'-tetrahydroxy flavones), pectolinarigenin (6,4'-dimethoxy scutellarein) and a flavanone¹². A chemotaxonomic marker of the genus, (24S)-ethylcholesta-5,22,25-triene-3 β -ol (C₂₉H₄₆O) was isolated from the leaf¹³. Chalcone glycoside (4,2',4'-trihydroxy-6'-methoxychalcone-4,4' α -D-diglucoside, m.p. 186— 188 °C, C₂₈H₃₄O₁₅), pectolinarigenin, 7-hydroxy flavone and 7-hydroxy flavanone 7-O-glucoside¹⁴.

Flowers: 6,4'-dimethyl-7-acetoxyscutellarein, pectolinarigenin, hispidulin, apigenin and luteolin¹⁵. Chalcone glycoside (4,2',4'-trihydroxy-6'-methoxychalcone-4,4' α -D-diglucoside, C₂₈H₃₄O₁₅), pectolinarigenin, 7-hydroxy flavone and 7-hydroxy flavanone 7-O-glucoside¹⁴.

The stem, leaf and flower parts were reported positive for alkaloids, saponins and tannins¹⁶.

Leaf oil : terpinen-4-ol (25.92%); caryophyllene (26.71%) and beta-bisabolene (18.10%) as the major and phytol (5.08%) as the minor constituent¹⁷.

PHARMACOLOGICAL ACTIONS :

Anti-inflammatory activity :

Aerial parts¹⁸:

In carrageenin-induced paw edema model, *Clerodendrum phlomidis* aerial part at doses of 200 and 400 mg/kg caused significant inhibition of paw edema by 34.02 % and 26.80% respectively, 4 hours after carrageenin administration. The study shows that an chloroform extract of *Clerodendrum phlomidis* exhibit significant anti-inflammatory effect in albino rats. Results of two doses are also comparable with standard drug (phenylbutazone).

Root bark¹⁹:

Anti-inflammatory activity of aqueous extract of root bark of *Clerodendrum phlomidis* (CP) was evaluated in models of acute inflammation viz. carrageenan induced rat paw oedema and acetic acid induced peritonitis in mice and against chronic inflammation was assessed in model of cotton pellet granuloma in rats. The activity of CP was compared with aspirin and Dashamoolarishta (a multi-ingredient plant formulation containing *Clerodendrum phlomidis*) which served as positive controls. CP in the dose of 21.6 ml/kg showed significant anti-inflammatory activity 15.85 % inhibition in the carrageenan model and 50.38% inhibition in the model of chronic inflammation). In the peritonitis model, the maximum anti-inflammatory activity (27.32% inhibition) was seen with the corresponding dose in mice.

Analgesic activity²⁰ :

Intraperitoneal administration of *Clerodendrum phlomidis* aerial parts Methanolic and Ethyl acetate extracts in the Hot plate test (200 mg/kg), and acetic acid induced abdominal constriction test (200 mg/kg) showed significant analgesic activity. *Clerodendrum phlomidis* revealed the presence of high sterols, saponin glycosides and flavonoids. The flavonoids are known to possess Anti- inflammatory activity by inhibiting the cyclooxygenase responsible for synthesis of inflammatory prostaglandins.

Antiarthritic activity²¹ :

The anti-arthritic effect of oral administration of ethanolic extract of *Clerodendrum phlomidis* on Freund's adjuvant induced arthritis has been studied in Wistar albino rats. The loss of body weight during the arthritic condition was corrected on treatment with ethanolic extract of *Clerodendrum phlomidis* at 250 and 500 mg/kg body weights. The swelling of the paws during the secondary lesions was also markedly reduced on treatment with ethanolic extract of *Clerodendrum phlomidis* and this result was confirmed using radiographic analysis and the changes in the density of Hind Limb Bone Mass (HLBM) was measured using photodensitometer and aluminium step wedge. The HLBM was significantly reduced on treatment with ethanolic extract (250 and 500 mg/kg body weight) of *Clerodendrum phlomidis* and standard drug Indomethacin (10 mg/kg).

Antimicrobial studies :

Root²²:

Ethanol extract at 106.66µg/ml showed a significant result against *Escherichia coli* was observed as the most sensitive (15.33mm). Chloroform extract also showed good antimicrobial activity against *Staphylococcus aureus* with a zone of inhibition of 14.67mm. Among the isolated compounds, Ethyl- 2- hydroxy -4- methyl benzoate shows good antimicrobial activity than 3,6,7-trihydroxy-2-(3-methoxyphenyl)-4H-chromen-4-one and Phenyl acetic acid against *Staphylococcus pyogenes*, and *Candida albicans* with a zone of inhibition of 9mm respectively at 60µg/ml.

Stem and leaves²³:

Methanolic and acetone extracts of stems and leaves (combined) were screened for five Gram-positive bacteria, seven Gram-negative bacteria and three fungi species by an agar diffusion method, respectively. Acetone extract was not active while the methanolic extract showed inhibition against *Citrobacter freundii* and *staphylococcus epidermidis*. Ethyl acetate and hexane extracts of leaves and stems at concentration of 1 mg/ml were screened for human pathogens and plant pathogens by poison plate technique, respectively. The leaf extract (particularly hexane extract) was more active than stem extract on both pathogens.

Aerial parts²⁴ :

Aerial parts of the plant were extracted successively by using petroleum ether, chloroform, ethyl acetate and methanol as solvents according to their increasing polarity. Dried

extracts were tested for anthelmintic activity using *Pheretima posthuma* as a species of earth worm and compare the paralysis time and death time with standard drug albendazole. Ethyl acetate and methanol extracts shows comparable anthelmintic activity with standard drug albendazole.

Antiobesity activity²⁵ :

Anti-obesity activity of alcoholic and methanolic extracts of roots of *Clerodendrum phlomidis* was evaluated against obesity induced by feeding high fat diet for 13 weeks to C57BL/6J female mice and one group was kept on normal chow diet in order to evaluate the effect of *Clerodendrum phlomidis* on food intake, body weight changes, digestive enzyme activity, lipid metabolism, thromogenesis, adiposities diameter and histology of fat pad. Methanolic extract showed strong anti-obesity effect compare to alcoholic extract of *Clerodendrum phlomidis*.

Antihepatotoxic activity²⁶ :

Antihepatotoxic activity of the chloroform, petroleum ether, methanol fractions of *Clerodendrum phlomidis* whole plant assessed by performing biochemical parameters and histopathological studies against toxicity caused by the carbon tetrachloride. The histopathological studies of the liver showed swelling and necrosis in hepatocytes in CCl₄ treated rats, treatment with different fractions have reduced significantly the necrosis and swelling of the hepatocytes. The biochemical parameters also showed the significant antihepatotoxic activity.

Antifertility²⁷:

The post-coital antifertility activity of the dichloromethane root extract at dose levels (100, 200, 400 and 600mg/kg, orally) was evaluated in mature female rats by observing no. of implants and estrus cycle. The root extract showed 25.89, 41.97, 93.30 and 100 percent inhibition of implantation at doses of 100, 200, 400 and 600 mg/kg body weight

respectively. Among the four doses of extract, dose of 200, 400 and 600 mg/kg were found to be significant when compared with control.

Anti-amnesic activity²⁸ :

The aqueous extract of the *C. phlomidis*, 100 and 200 mg/kg, per oral (p.o.) was administered for 6 successive days to both young and aged mice. Exteroceptive behavioral models such as elevated plus maze and passive avoidance paradigm were employed to evaluate short term and long term memory respectively. Scopolamine [0.4 mg/kg, intra peritoneal(i.p.)], diazepam (1 mg/kg, i.p.) were employed to induce amnesia in mice. To delineate the mechanism by which *C. phlomidis* exerts nootropic action, its effect on brain acetyl cholinesterase levels were determined. Piracetam (200 mg/kg, i.p.) was used as a standard nootropic agent. Pretreatment with *C. phlomidis* (100 and 200 mg/ kg, p.o.) for 6 successive days significantly improved learning and memory in mice. It reversed the amnesia induced by scopolamine, diazepam and natural ageing. It also decreased the acetyl cholinesterase levels in the whole brain.

Anti-asthmatic activity²⁹ :

Ethanol extract of *Clerodendrum phlomidis* leaves exhibited significant percent decreased contraction at 100mg/ml in isolated guinea pig ileum preparation, histamine induced bronchoconstriction in Guinea pigs. It significantly prolonged the latent period of convulsions followed by exposure to histamine aerosol at the dose of 400mg/kg, (per oral) and showed maximum protection of 59.04 % at 4th hour as compared to Chlorpheniramine maleate (Standard) 1mg/kg, (per oral) . This offered maximum protection of 65.04 % at 4th hour.

Antioxidant activity³⁰ :

The free radical scavenging activity of root of *Clerodendrum phlomidis* extracts, obtained by sequential extraction with various polarities of solvents (Petroleum ether, chloroform, ethyl acetate and ethanol) was evaluated by three different in vitro methods: DPPH radical scavenging, superoxide anion radical scavenging and total antioxidant activity. The ethanolic extract showed best free radical scavenging activity than that of other three extracts. The super oxide radical scavenging activity of ethanolic extract (IC₅₀ = 60 µg/ml) was better than that of standard Quercetin (IC₅₀ = 130 µg/ml).

Antidiarrhoeal activity³¹ :

The methanolic extract at doses of 200, 400, 600 and 800 mg/kg was evaluated for castor oil-induced diarrhoea, gastrointestinal motility and prostaglandin E₂-induced enteropooling in albino rats (Wistar strain, 180 to 200 g, either sex). The methanolic extract at 600 and 800 mg/kg showed significant inhibition of defecation frequency and decrease in propulsion of the charcoal meal through gastrointestinal tract. The extract also significantly inhibited prostaglandin E₂-induced enteropooling in almost all the dose levels.

Hypoglycemic activity³²:

Methanolic and ethyl acetate extracts of *Clerodendrum multiflorum* stems are investigated for alpha amylase in-vitro inhibitory activity and hypoglycemic effect by oral administration at different doses in rats. It showed good in-vitro alpha amylase inhibitory activity as compare to standard acarbose. Also the oral administration of methanolic and ethyl acetate extract at dose of 200mg/kg body weight exhibited a significant hypoglycaemic activity in normal rats and antihyperglycemic activity in alloxan induced diabetic rats.

Immunomodulatory activity³³ :

Oral administration of methanol extracts of *Clerodendrum phlomidis* Linn. and *Premna integrifolia* Linn. roots (300 mg/kg x 7 days) in mice prior to immunization with Sheep Red Blood Cells (SRBC) resulted in a significant increase in haemagglutinating antibody titre, plaque forming cell assay and delayed type hypersensitivity to SRBC. *C. phlomidis* showed higher specific immune activity as compared to *P. integrifolia*. *C. phlomidis* and *P. integrifolia* enhanced the non specific immune response in carbon clearance test and showed significant immunoprophylactic effect, when tested on E. coli induced abdominal sepsis. In the present study *C. phlomidis* showed higher response to specific immune activity as compared to *P. integrifolia*, whereas in case of non specific immune activity both the roots showed almost equal response.

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