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Review Article

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Biological evaluation of *Alangium salviifolium* (L. F.) Wangerin

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ABSTRACT

Alangium salviifolium (L.f.) Wangerin (Akoul) is a deciduous, rambling shrub or a tree, up to 10m in height with a maximum girth of 1.2m, which grows in the wild throughout the hotter parts of India. In Ayurveda the roots and the fruits are used for treatment of rheumatism, and hemorrhoid. In traditional system of medicine, it is used as laxative, astringent, pungent, purgative, alleviates spasms, anthelmintic, emetic, antiprotozoa, hypoglycemic. The present review is therefore an effect to give a detailed survey of the literature on its pharmacognosy, phytochemistry, traditional and pharmacological uses.

Keywords: *Alangium salviifolium* (L.f.) Wangerin, Pharmacognosy, hypoglycemic.

INTRODUCTION

Herbalism is a traditional medicinal or folk medicine practice based on the use of plants and plant extracts. Herbalism is also known as botanical medicine, medical herbalism, herbal medicine, herbology, and phytotherapy. India has a rich flora that is widely distributed throughout the country. Herbal medicines have been the basis of treatment and cure for various diseases and physiological conditions in traditional methods practiced such as Ayurveda, Unani and Siddha.

Alangium salviifolium has been used by traditional healers in the treatment of skin cancers by means of local application of the root. In recent years ethno medicinal studies received much attention on natural resources to light the numerous medicines, especially of plant origin which needs evaluation on modern scientific lines such as phytochemical analysis, pharmacological and clinical trials. The reported phytochemical and pharmacological studies on this plant support its traditional uses and may prove to be useful for clinical evaluation and development of drugs.

TAXONOMY

Table 1 Classification of *Alangium salviifolium* according to Bentham and Hooker's

Kingdom	Plantea
Class	Dicotyledons
Order	Cornales
Family	Alangiaceae
Genus	*Alangium*
Species	*Alangium salviifolium*

Table 2 Synonym / Vernacular names of *Alangium salviifolium* [1, 2]

Sanskrit	Ankola, Ankota, Nikochaka, Deerghakeela
Kannada	Ankolimara, Ansaroli, Ankol
Malyalam	Ankolam, Velittanti
Tamil	Alangi, Ankolum
Telgu	Ankolamu, Udagu
Bengali	Akarkanta, Baghankura
Gujrati	Ankol, Onkla
Marathi	Ankola
Hindi	Angol, Ankora, Dhera
English	Sage leaved alangium

BOTANICAL DESCRIPTION

Figure 1 *Alangium salviifolium* Linn A. Mature plant B-C Floral bud Leaves D. Fruit E. Spine of stem

It is deciduous shrub or small to medium-sized thorny tree up to 18 m tall; bark surface rough and pale brown; twigs grey or purple-brown, glabrous or pubescent, often with spines up to 12 mm long. Leaves alternate, simple, without stipules; petiole up to 1.5 cm long, hairy; blade elliptical to obovate, oblong or lanceolate, 3–23 cm × 1.5–9 cm, base cuneate or rounded, apex rounded to obtuse or acute, 3–9 veined from base. Inflorescence an axillary cyme, sessile or nearly so golden-brown pubescent. Flowers bisexual, regular, 5–10-merous, white, cream with a slight orange tinge, fragrant; buds cylindrical; pedicel 2–8 mm long; calyx tube urn-shaped, 1–2.5 mm long, lobes triangular, up to 1.5 mm long; petals strap-shaped, 12–28.5 mm × 1–2.5 mm, densely pubescent outside, glabrous or pubescent inside; stamens 10–32, 5–14 mm long; ovary inferior, 1–2-celled, style 8.5–27.5 mm long, glabrous, stigma conical or head-shaped, slightly lobed. The berries are ovoid, ellipsoid or nearly globose, glabrous, smooth and violet to purple. Seeds are albuminous. It can be propagated by seed and is reported to have a fairly good natural regeneration.

DISTRIBUTION

Alangium salviifolium is found in lowland rainforest and riverine forest up to 750m altitude. In tropical Africa *Alangium salviifolium* occurs in eastern Kenya, eastern Tanzania and Comoros. It is widespread in tropical Asia, from India to China, Thailand, the Philippines, Indonesia and Papua New Guinea. It is found in India especially in

Western Ghats. It is native to Western Africa, Madagascar, Southern and Eastern Asia (China, Malaysia, Indonesia, India, and Philippines), tropical Australia, the western Pacific Ocean islands and New Caledonia. In India, it is found throughout the Hyderabad forests and Sitamata wildlife sanctuary, Rajasthan [3].

USES

The stems are used for spears in Kenya. In India the wood is valued for musical instruments and furniture. It is used in building as beams, for flooring, furniture, cabinet work, inlaying, carving, bobbins, spindles, shuttles, rice pestles, tool handles, walking sticks, gunstocks and handicraft articles in Asia. The twigs are used for brushing the teeth in India.

MEDICINAL AND TOXIC ASPECTS

Alangium salviifolium has been used by traditional healers in the treatment of skin cancers by means of local application of the root. It reduces blood pressure when taken orally due to its vasodilator activity [4]. In Comoros a decoction of the whole plant together with the fruit of coconut palm is used externally for the treatment of boils. Various parts of the plants are used as traditional medicines in India. The stem is used to cure diarrhoea and vomiting. The leaves are used to cure asthma and as cataplasm to reduce rheumatic pains. The fruit is used as purgative, expectorant, carminative and as an antidote for poisoning, and fruit juice is applied to cure eye diseases. The roots are used as a purgative, to expel worms, and to cure piles, hypertension, diarrhoea, fever, back pain, blood disorders.

In India a mixture of mature fruits of *A. salviifolium* with honey and rootstocks of sweet flag (*Acorus calamus* L.) are used to manage pests on agricultural crops. It also has various medicinal properties and used as laxative, antiepileptic activity [5], astringent, antiulcer [6], pungent, purgative, alleviates spasms, anthelmintic, emetic, antiprotozoa, hypoglycemic [7, 8]. It has been reported that it used to cure skin diseases leprosy, scabies [9, 10] and as contraceptives for pigs and cattle rearing by the tribes in the Malayalies [11, 12, 13]. Stem and root barks of *A. salviifolium* were screened for their helicobactericidal activity by Austin *et al* [14] in 2002. It is endemic and endangered species used for timber, fuel and fodder for its good nutritional value in summer season some of West Himalayan areas in India [15, 16]. In Ayurveda the roots and the fruits are used for treatment of rheumatism, burning sensation and haemorrhages. Root barks of *A. salviifolium* externally used for as an antidote against snake/ scorpion [17], rabbits, rats, bite and dogs. Phytochemical and antiinflammatory evaluation of *A. salviifolium* root extract has been done by Yesupadam [18] *et al* in 2011. In Ayurveda the roots and the fruits are used for treatment of rheumatism, and hemorrhoid externally.

PRELIMINARY PHYTOCHEMICAL STUDIES

Various parts of the plant was subjected to extraction in different organic solvents for their extractive value and preliminary phytochemical investigation, which revealed the presences of various primary metabolites viz. soluble sugars, starch, proteins, lipids, ascorbic acid, phenols etc. and secondary metabolites like flavonoids, steroids, alkaloids, terpenoids, glycosides, tannins etc. all the metabolites had showed various degree of color intensities with different color reactions with their amount in the samples [6, 11, 18-24].

COMPOUNDS EXTRACTED FROM *ALANGIUM SALVIIFOLIUM*

The compounds 1-methyl-1H-pyrimidine-2, 4-dione and 3–0-β-D-glucopyranosyl-(24β)-ethylcholesta-5, 22, 25-triene have been extracted from the flowers.

Recent phytochemical studies of this plant resulted in the isolation of several flavonoid, phenolic compound, irridoid glycosides and oxyoglucoside of some alcohol. Some alkaloids, 1', 2'-dehydrotubulosine, alangine, markine, venoterpine, ankorine, alangine A and B, alangicine, markindine, lamarckinine, emetine [25, 26], tubulosine, isotubulosine, deoxytubulosine, cephaeline, isocephaeline, psychotrine, neocephaeline, 10-O-demethylcephaeline, 2'-N-(1"-deoxy-1"-beta-D-fructopyranosyl) cephaeline, protoemetine, protoemetinol, salsoline, and alangiside were isolated from the dried fruits of *Alangium lamarckii* by Itoh *et al* [27] in 2000. a- and b- Alangine, Alangicin, Marckindine, Tubulosin and emetine were obtained from this plant [28].

PHYTOCONSTITUENTS IN DIFFERENT PLANT PARTS [29]

Root- Alkaloids cephaeline, tobulosine, isotobulosine, psychotrine and alangiside.

Root Bark- Alkaloids A & B, Alangicine,d-methylpsychotrine, marckine, marckidine, lamarckinine.

Leaves- Alkaloids Alangimarkine, Ankorine, Deoxytobulosine alengiside, Sterols and three triterpenoids.

Fruits: Alkaloids Cephaeline, N-methylcephaeline, deoxytobulosine and Alangiside.

Seed- Alkaloids Alangimarine, Alamanine, Alangimaridine, Emetine, cephaeline, Psychotrine.

PHARMACOLOGY

Antimicrobial activity

Stem bark of *Alangium salviifolium* showed significant antimicrobial activity against all the selected strains of bacteria, fungi and yeast [30-32].

The methanol extracts of *Alangium salviifolium* flowers showed a wide spectrum of antibacterial activity against both Gram-Positive and Gram-Negative bacteria [33-34]. Leaf extracts of *Alangium salviifolium* has been evaluated for antibacterial activity against pathogenic strains of *Escherichia coli*, *Proteus vulgaris*, *Bacillus subtilis*, *Enterobacter faecalis*, *Serratia marcescens* and *Klebsiella pneumoniae*35-40. Stem and root barks of *Alangium salvifolium* were screened for their helicobactericidal activity by Austin *et al* [14] in 2002.

The ethanolic extract of root of *A. salviifolium* and 8 week old callus showed maximum antibacterial activity against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Klebsella pnemoniea* and *Salmonella typhirium* as the test bacteria and against selected fungi *Aspergillus niger, A. fumigatus, A. flavus, Fusarium oxysporum, Penicillum sps* and *Rizopus sps* [41].

Antioxidant activity

The antioxidant activity of callus and other plant parts of *Alangium salviifolium* was measured using 2, 2`-diphenyl-1-picryhydrazyl (DPPH) free radical and superoxide radical scavenging assays. The results showed that all the parts exhibited antioxidative activity. The highest DPPH radical scavenging activity (90.76±1.14%) and superoxide radical scavenging activity (73.6±1.45%) were recorded in 8week old callus. The different plant parts as well as callus had showed superoxide radical scavenging activity [42].

In Nitric oxide method, alcohol extract of ASW roots presented more antioxidant activity than aqueous extract., Alcoholic extracts, Aqueous extract and Ascorbic acid exhibits 74.9%, 59.7% and 83.5%, inhibition and the EC50 (µg)-308.80, 450.8 and 201.32 µg/ml respectively [39].

Molluscicidal activity

Molluscicidal activity was done using the method of Singh and Agarwal [43]. For each test group, adult *L. acuminata* (2.60 ± 0.30cm long) were maintained in each of five glass aquaria containing three liters of dechlorinated tap water at 25°C. The test organisms were exposed to different concentrations of crude powder of root, stem, leaf and ethanolic extract by adding the test materials to aquariums. Snail mortality, established by the contraction of body within the cell and a failure of response to a needle probe, was recorded every 24 hrs for 72hrs

The molluscicidal activity of *Alangium salvifolium Linn.* crude powder of root, stem, leaf and ethanolic extract was time and dose dependent. After 72 hrs the toxicity of root (LC50= 240.15mg/L) was higher than leaf (LC50= 256.50 mg/L) and stem (LC50= 263.12mg/L). The ethanolic extract was exceptionally toxic to *Lymnaea acuminate* (LC50= 17.45mg/L at 72 hrs) [44].

Acute-toxicity studies

Healthy adult albino rats of either sex, starved overnight, were divided into groups (n=6) and were orally fed with increased dose of ethanol extract. Total ethanol extract administered orally in doses of up to 2g/Kg, did not produce any sign of toxicity and mortality in rats when observed for 14 days after administration [5, 6, 24].

Anti-inflammatory activity

The percent inhibition in paw volume of rats at 0, 1, 2, 3 and 4 h was calculated.

The ethanolic extract (500 mg/kg) was found to be more effective than all other treatments ($p < 0.05$) and showed 36.84, 56.88, 55.11 and 65.53% inhibition in paw volume at 1, 2, 3 and 4 h, respectively.

In acetic acid-induced writhing in mice, ethanolic extract (41.07%) and water extract (27.43%) showed significant analgesic activity, whereas the chloroform extract (17.79%) was ineffective. All three extracts showed analgesic activity but out of these extracts for the ethanol extract it was the most significant. Ibuprofen, the reference drug, inhibited 46.12% of the number of writhing elicited by acetic acid.

Ethanolic extract of *Alangium salvifolium* Linn. inhibit the paw edema as time and dose dependent manner. After 180 minutes at 300mg/ gdw concentration the extract inhibits 76.11% paw volume than the standard diclofenec sodium which inhibits 71.64% paw volume [18, 20, 44].

Analgesic activity
The methanol extract of *Alangium salviifolium* plant roots has been studied for analgesic and anti-inflammatory activities in animal models [45].

The analgesic activity of *Alangium salvifolium* Linn. ethanolic extract was dose dependent. The writhe movements were reduced 63.0±0.70 in control to 47.5±0.48 at 100 mg/gdw of crude ethanolic extract and 18.5 ± 1.7 at 300 mg/gdw concentration. The analgesic activity of 300mg/gdw is comparable to diclofenec sodium drug [44].

Wound healing activity
In studies using excision wound model, animals treated with ethanol extract of *Alangium salviifolium* showed a significant decrease in epithelization period as evidenced by shorter period for fall of escher as compared to control. The drug extract also facilitated the rate of wound contraction significantly at both the dose levels. Granulation, collagenation, collagen maturation and scar maturation are some of many phases of wound healing which run concurrently, but independent of each other. Use of single model is inadequate and there is no reference standard which can collectively represent the various components of wound healing as drugs which, influence one phase may not necessarily influence another. Hence in our study we have used three models to assess the effect of leaf extract on various phases of wound healing.

The result of present study showed that ethanolic extract of *Alangium salviifolium* possesses a definite prohealing action. This is demonstrated by a significant increase in the rate of wound contraction and by enhanced epithelization. Significant increase was also observed in skin breaking strength and hydroxyproline content which was a reflection of increased collagen levels that was further supported by histopathological evidence and gain in granuloma breaking strength. This indicated improved collagen maturation by increased cross-linking while an increase in dry granuloma weight indicated higher protein content [21].

Anti-arthritic activity [24]
The experimental protocol was for 21days and on the day one, Fruends adjuant 0.1ml (1ml contains 1mg mycobacterium Tuberculosis (H37Ra, ATCC25177) heat killed and dried, 0.25 ml mineral oil and 0.15ml mannide mono oleate was administered into the sub plantar region of right hind paw. The individual extracts were administered to respective groups at a dose of 100mg/kg for 21 days. The paw volume and paw thickness was measured at day 4, day 8, day 14 and day 21. All the extracts of *Alangium salviifolium* wang showed potent anti-arthritic activity by Fruends adjuvant arthritis model and the potency of the activity follows the order standard > chloroform > ethyl acetate > aqueous > petroleum ether > methanol. Steroids are reported to possess anti-inflammatory property; since these phytoconstituents are found in our extracts may have contributed for exhibited anti-arthritic activity by inhibiting the inflammation due to the Fruends adjuant (inflammogen)

Anticonvulsant activity (Maximal electroshock (MES)-induced seizures)
The ethanolic extract of *Alangium salviifolium* at a dosage of 250 and 500 mg/kg showed 67.77% and 80.70% inhibition of convulsions produced by MES. The ethanolic extract at the dose of 500 mg/kg showed activity comparable to that of standard drug diazepam (83.01% inhibition). The effect of MES was dose-dependent. It increased the time to the onset of seizures from 36.53±4.1 min to 47.32±8.0 min at the dose of 250 mg/kg *i.p.* and from 37.54±4.5 min to 61.23±10.24 min at the dose of 500 mg/kg *i.p.* At this dose MES was nearly as efficacious as diazepam, 10 mg/kg. [7]

Antiepileptic activity [46]
In the case of maximal electroshock induced seizures (MES), it was observed that the pentylenetetrazole induced seizures (EEAS) 250 and 500 mg/kg were showed 67.75% and 81.56% inhibition of convulsion, respectively. AEAS

at the doses of 250 mg/kg and 500 mg/kg were exhibited the 46.59% and 64.61% inhibition of convulsion produced by MES, respectively. The Diazepam inhibited 91.25% of convulsion. In the model of PTZ induced seizures, it was observed that EEAS showed 11.22% and 26.53% protection from seizures at the dose of 250 and 500 mg/kg, respectively while the AEAS showed 29.59% and 62.24% protection from seizures at the doses of 250 and 500 mg/kg, respectively. The Diazepam showed 85% protection from seizures5.

Antidiabetic activity

The extracts of *Alangium salvifolium* seed extracts have shown a significant ($p < 0.01$) increase in glucose tolerance. The chloroform, ethanol and aqueous extracts reduced the glucose levels to normal. Maximum effect was observed for ethanol extract. These results indicate that the extracts which show significant activity, may have the capacity to block glucose absorption through the GIT, similar to acarbose and other molecules. Treatment of alloxan induced diabetic animals with standard drug (metformin), chloroform, ethanol and water extracts of seeds of plant *Alangium salvifolium* Linn. showed significant reduction in blood glucose level, increased body weight and impaired serum biochemical parameters as compared to disease control group.

Alangium salvifolium seed extracts significantly inhibited diabetes induced by alloxan. For ethanolic extract and metformin, the antidiabetic activity was significant ($p < 0.01$) in all respects as compared to chloroform and aqueous extracts. Alloxan treatment caused permanent destruction of β-cells. It can therefore be said conclusively that the responses shown by various extracts exert their effect by extra pancreatic mechanism to normalize alloxan-induced hyperglycemia. The ethanolic extract as well as the chloroform and aqueous extracts showed significant ($p < 0.01$) restoration of the body weight in diseased animals to normal level.

Hypercholestrolemia, hypertriglyceridemia and hyperuricemia have been reported to occur in alloxan diabetic rats and a significant increase observed in our experiment was in accordance to these studies. Repeated administration of *Alangium salvifolium* extracts had decreased the blood glucose, urea, total cholesterol and triglycerides significantly, whereas increased the HDL-cholesterol level.

Treatment of alloxan induced diabetic animals with standard drug (metformin), chloroform, ethanol and water extracts of seeds of plant *Alangium salvifolium* Linn. showed significant reduction in blood glucose level, increased body weight and impaired serum biochemical parameters as compared to disease control group.

Antifertility effect

Daily administration of petroleum ether, ethyl acetate, chloroform, methanol or aqueous extracts of *A. salvifolium* at a dose of 100mg/kg body weight for eight days starting from the first day of pregnancy showed significant abortifacient activity in comparison to vehicle treated group.

These results indicate the *A. salviifolium* (Linn.f) Wang produced mainly abortifacient activity and less antiimplantation activity. It indicates that the herbal drugs may have anti-progesterone effects. Mifepristone is a competitive inhibitor that acts both at progesterone and glucocorticoid receptors. It is a weak partial agonist with predominantly antagonistic activity to progesterone. The available data in the present study indicate that the ethyl acetate, chloroform and aqueous extracts may possess antiprogesterogenic activity [11].

Larvicidal Activity

Among the four solvents of leaves of *Alangium salvifolium* tested for its larvicidal activity against *Artemia salina* Chloroform and Methanol extract showed 100 % mortality at the lowest level of concentration, i.e., 0.25ml/10ml v/v. Hexane extract has showed 100 % larvicidal potency at the concentration of 0.5ml/10ml volume. However, very poor activity was recorded for aqueous extract of the leaves of *Alangium* salvifolium [19].

Pesticidal Activity

Among the four solvents of leaves of *Alangium salvifolium* tested for its pesticidal activity against the storage pest, *Sitophilus oryzae* Hexane extract showed mortality rate of 80 % and 100 % of mortality at the interval of 24 hours and 48 hours respectively. Aqueous and Chloroform extract showed more than 50 % of mortality after 48 hours of exposure. However, Methanol extract has showed only lower level of mortality rate [19].

Anti Ulcer Activity

By performing anti ulcer activity on male wistar rats, it can be concluded that the ethanolic extract of *Alangium salvifolium* has a significant anti ulcer activity at 400mg/kg and 800mg/kg dose that is in a dose dependent manner. The results were comparable with that of standard and control groups. The phytoconstituents present in ethanolic extract like flavonoids and phenolic compounds may be responsible for the said activity [6].

DISCUSSION

The reliance of such a large portion of the population on traditional medicine can be attributed to a number of factors, relatively good accessibility to the plants, affordability and extensive local knowledge and expertise amongst the local communities [47]. Because of this strong dependence on plants as medicine, it is important to study their safety and efficacy [48]. Medicinal herbs and their preparations (hot and cold infusions, decoction, and tinctures) are widely used by human beings all over the world [49].

The present review study showed the medicinal and toxic aspects, preliminary phytochemical, pharmacological (antioxidant, antimicrobial, analgesic, anti-inflammatory, antidiabetic, mollucicidal, pesticidal, antifertility, larvacidal, antiulcer, antiepileptic, wound healing, anti arthritic, anticonvulsant activity) studies.

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