Review Article
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# A PHYTOPHARMACOLOGICAL REVIEW OF *ALSTONIA SCHOLARIS*: A PANORAMIC HERBAL MEDICINE

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**ABSTRACT**
Nature has bestowed our planet with an enormous wealth of medicinal plants which are highly esteemed all over the world as a rich source of therapeutic agents for the prevention and cure of diseases and ailments. There are many herbs on earth which lies unexplored in the field of medicine or science. One such herb is *Alstonia scholaris* which is an ornamental plant, commonly known as Devil's tree, Dita bark, Saptaparna. *Alstonia scholaris* has a promising place in the Ayurvedic system of medicine due to its various medicinal values like antidiabetic, antibacterial, antianxiety, anticancer, hepatoprotective, anti-inflammatory, analgesic effects. The plant is rich in alkaloids, flavonoids, saponins, steroids, reducing sugars and phenolic compounds which witness the ample amount of medicinal potential of the herb. In the present review, the complete update on the plant has been enlightened to evaluate the medicinal values of the plant, also aiming to draw necessary attention of the researchers as a frontier one.
**Keywords:** *Alstonia scholaris*, Apocynaceae, Phytochemical constituents, Pharmacological activities

## INTRODUCTION

Finding healing powers in plant is an ancient idea. The increasing interests on traditional ethno medicine may lead to discovery of novel therapeutic agents. Many of the plant species have been documented pharmacologically and clinically in the world, which are endowed phytochemicals with marked activity on different pathological condition of different diseases[1]. Herbal medicine has become an integral part of standard healthcare, based on a combination of time-honored traditional usage and ongoing scientific research. Rising interest in medicinal herbs has increased scientific scrutiny of their therapeutic potentials and safety[2]. The Apocynaceae family consists of about 250 genera and 2000 species of tropical trees, shrubs and vines. This family is known for plants that have a very high biological activity and medicinal properties. Some of the well known of this family such as *Rauwolfia serpentina*, *Alstonia scholaris* and *Alstonia venenata* are known for the ample amount of medicinal potential[3]. *Alstonia scholaris* Linn, which is popularly known as "Saptaparni" or the "Devil tree" is one of the most versatile medicinal plants having a wide spectrum of biological activity[4]. It is a common tree, growing up to 3.0 meter in height, distributed throughout the sub-Himalayan belt, West Bengal, Bihar, peninsular India and Southeast Asia[5]. It is a beautiful foliage tree with a large canopy, and because of this, it has become a popular ornamental tree in the landscapes and gardens in the warm and temperate regions of Florida, Texas, and California in the United States[6]. Historically, the plant was scientifically named by Linnaeus as *Echites scholaris*. However, to commemorate the great botanist Professor C. Alston, the generic name was changed to *Alstonia*, whereas the species name *scholaris* was retained to signify its use in schools in South East Asia, where the wood is traditionally used to make blackboards and wooden slates[7]. *Alstonia scholaris*, known to be a powerful medicinal plant has been studied well for the bio active principles present in the leaf, stem and the root barks[3].

**Table 1: Vernacular name of *Alstonia scholaris*[8]**

| Language | Name |
|---|---|
| English | Dita bark, White cheese wood |
| Hindi | Chatian, Satvin |
| Sanskrit | Saptaparna |
| Bengali | Chattin |
| Tamil | Pala |
| Gujarati | Saptaparni |

**Table 2: Systematic position of *Alstonia scholaris*[8]**

| | |
|---|---|
| Kingdom | Plantae |
| Order | Gentianales |
| Family | Apocynaceae |
| Tribe | Plumeriae |
| Subtribe | Alstoniinae |
| Genus | *Alstonia* |
| Species | *Alstonia scholaris* |

### Morphological Characteristics

#### Leaves

Leaves are 4-7 in a whorl, coriaceous, bluntly acuminate, dark green above and pale beneath. Leaf stalk is 1-1.5 cm long, the lamina is elliptical or elliptical-lanceolate, glabrous or sparsely hairy, tapering towards the base, 11.5-23 x 4-7.5cm is the size. Upper surface is dark green; the lower surface is green-white. The tip of the leaf is rounded or shortly pointed, tapering towards the base[9].

#### Bark

Bark is rough, tessellated corky grey to grey white and contains whorled branches. The outer blaze is cream to yellowish in color with abundant, milky latex that flows rapidly when cut[4].

#### Flowers

Greenish white flowers in umbrellately branched manner. They are 7-10 mm long, white, cream or green. The tube is hairy lobes sparsely or densely pubescent; 1.5-4 mm long, the left margins overlapping, strongly perfumed[4].

**Fruits**

Fruit a pendulous, two lobed, dehiscent follicles, brown or green, dry or wood, spindle shaped, 15-32 cm long, 4-6mm in diameter, containing numerous flat, oblong, brown seeds[9].

**Figure 1 Leaves of *Alstonia scholaris***

**Figure 2 Bark of *Alstonia scholaris***

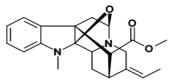
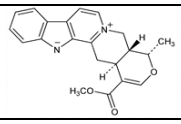
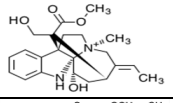
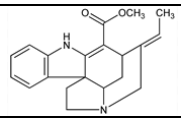
**Figure 3 Flowers of *Alstonia scholaris***

**Figure 4 Fruits of *Alstonia scholaris***

**Biochemical Constituents**

The phytochemical constituents of *Alstonia scholaris* have been extensively investigated; nearly four hundred compounds have been isolated and characterized. Alkaloids, iridoids, coumarins, flavonoids, leucoanthocyanines, reducing sugars, simple phenolics, steroids, saponins and tannins were documented as the chief chemical constituents[1]. *A.scholaris* contains some of the important alkaloids such as echitamine, tubotaiwine (stem and root bark), akuammicine (root bark), echitamidine (stem bark), pseudthe chief o-akuammidine (leaves, root bark), picrinine (stem bark, leaves, flowers), picralinal, nareline (leaves), strictamine (flowers), (leaves), ditamine (stem bark), echitenine (stem bark), an indole alkaloid (flowers)[10]. The new indole alkaloid, alstonamine and a sitsirikine type indole alkaloid, rhazmanine, have been isolated from the leaves[1]. Non alkaloid constituents of the flowers are n-hexacosane, lupeolt Beta-amyrin, ursolic and palmitic acids. On steam distillation, flowers yield an essential oil[10]. *Alstonia scholaris* flowers were found to contain alkaloids, carbohydrates, amino acids, phenols, tannins, cardiac glycosides, saponins, flavonoids, terpinoids, steroids, fixed oils and fats[3]. Among other constituents, isookanine-7-o-alpha-lrhamnpyranoside, a new flavanone glycoside and Alstonoside, a secoiridoid glycoside has been recorded. Presence of agr-amyrin, bgr-amyrin, lupeol acetate, venenative, rhazine and yohimbine have been noted. Linalool, cis and trans linalool oxides, alpha-terpineol, 2-phenylethyl acetate and terpinen-4-ol and steroids are among the other phytoconstituents of the plant[8].

**Table 3: Chemical constituents of *Alstonia scholaris***

| Chemical constituent | Structure |
|---|---|
| Picrinine |  |
| Alstonine |  |
| Echitamine |  |
| Akuamicine |  |

**Traditional Uses**

**Bark**

The bark of *Alstonia scholaris* is useful in malarial fevers, abdominal disorders, dyspepsia and in skin diseases[11]. The bark is bitter, astringent, digestive, laxative, anthelmintic, antipyretic, stomachic, cardiotonic and tonic[12]. The bark extract has been reported to possess antiplasmodial, immunostimulant, anticancer effect and is also hepatoprotective[13]. In Ayurveda it is reported that the bark of the plant when soaked in water overnight, can reduce the blood glucose level after oral administration[14]. Bark is also used as febrifuge, depurative and galactogogue[15]. It is effective in leprosy, skin diseases, pruritis, chronic and foul ulcers, asthma, bronchitis, agalactia and debility[12]. In folklore medicine, milky juice is applied on wounds, ulcers and rheumatic pains; mixed with oil and dropped into ear, it relieves ear ache[15].

**Leaves**

The leaves have been used traditionally as folk remedies for the treatment of many diseases including diarrhea, dysentery, and malaria and snake bites[16]. Juice of the leaves acts in certain cases as a powerful galactogogue[15]. Leaves used in beriberi, dropsy and congested liver. Latex applied to sores, ulcers, tumors and rheumatic swellings[10].

**Fruits**

The ripe fruits of the plant are used in syphilis and epilepsy. It is also used as a tonic, antiperiodic, and anthelmintic[7].

**Miscellaneous uses and as herbal formulations**

*Alstonia scholaris* is an antimalarial drug used in many marketed Ayurveda preparations. The methanolic extract of this plant was found to exhibit pronounced antiplasmodial activity[17]. The plant is reported to have anti-mutagenic effect[18]. The drug is reported to cause paralyzing effect on the motor nerves and consequent fall in blood pressure. The plant has hepatoprotective activity on liver injury[15]. Saptaparna has been reported to be used in the management of hypertension by tribal people of Sikkim[19]. It is used in various Ayurvedic preparations like Saptaparnasatvadi vati, Saptachadadi vati, Saptacchadadi vati, Saptacchadadi taila, Saptacchadadi kvatha and saptaparna ghanasara[10].

**Pharmacological Activities**

**Antidiabetic and antihyperlipidemic activity**

The aqueous extract of *Alstonia scholaris* significantly reduced elevated blood glucose level in streptozotocin (STZ) diabetic rats without showing any hypoglycemic effect in normal rats. The antidiabetic effect of the extract could be due to increased utilization of glucose by peripheral tissues, improved sensitivity of target tissues for insulin or it may be due to improved metabolic regulation of glucose. *Alstonia schoalris* bark significantly reduced serum triglyceride levels in STZ diabetic rats support its long term use not only for better control of blood glucose but also for normalization of disturbances in lipid metabolism which may prevent further predisposition of the patients to cardiovascular complications. Thus bark of *Alstonia scholaris* L possesses antidiabetic and antihyperlipidemic effects in STZ diabetic rats. The antiatherogenic potential of the bark extract indicates its usefulness not only in diabetes mellitus but also in long term complications associated with diabetes mellitus[14].

**Antibacterial activity**

*In-vitro* antibacterial activity of methanolic, aqueous and total alkaloid extracts from the trunk bark was evaluated against two gram-positive bacteria including bacillus subtilis and streptococcus pyrogens and four gram negative bacteria, *Escherichia coli*, pneumonia, Pseudomonous aerugenosa and proteus mirabilis using disk diffusion method. All extracts showed varying degrees of inhibitory activity against all bacteria. Aqueous extract was found very active against both gram-positive and gram-negative bacteria in comparison to other extracts. Total alkaloid extract was found only active against gram-negative bacteria[21]. Demonstration of antibacterial activity of *A. scholaris* against test bacteria is an indication that the possibility of sourcing alternative antibiotic substances in this plant for the development of newer antibacterial agents. Bacteria used in this study are associated with different type of infections including wounds, burns, typhoid fever, cough, urinary infection and skin infections[20].

**Antioxidant activity**

The antioxidant potential of different extracts of *Alstonia scholaris* were evaluated using various in vitro tests including 1, 1-diphenyl-2-picryl-hydrazil (DPPH), free radical scavenging, metal ion chelating, hydrogen peroxide scavenging, superoxide anion radical scavenging, and ferric thiocyanate reducing ability. Dichloromethane (DCM) and ethyl acetate (EA) fractions were found to have significant ($p<0.01$) free radical scavenging and metal ion chelating properties, whereas the petroleum ether and n-butanol fractions lack the in vitro antioxidant property. These various antioxidant activities were compared to standard antioxidants such as butylated hydroxyanisole (BHA) and l- ascorbic acid. These results indicate that DCM and EA possess powerful in vitro antioxidant activity. The encouraging results of DCM and EA with the various *in vitro* antioxidant tests proved the plant as a reducing agent, metal chelator, its hydrogen donating ability and effectiveness as scavengers of hydrogen peroxide, superoxide, and free radicals[15].

**Anticancer activity**

The anticancer properties of this medicinal plant was evaluated on two-stage process of skin carcinogenesis induced by a single application of 7, 12-dimethyabenz(a)anthrecene (100 lg/100 ll acetone), and two weeks later, promoted by repeated application of croton oil (1% in acetone/thrice a week) till the end of the experiment (16 weeks) in Swiss albino mice. The tumor incidence, tumor yield, tumor burden and cumulative number of papillomas were found to be higher in the carcinogen treated control compared to animals treated with Alstonia scholaris extract. Furthermore, a significant increase in reduced glutathione, superoxide dismutase and catalase but decrease in lipid peroxidation was measured in ASE administered experimental groups than the carcinogen treated control. This study demonstrated the chemopreventive potential of Alstonia scholaris bark extract in DMBA-induced skin tumor genesis in Swiss albino mice[21].

**Antiinflammtory and analgesic activity**

The analgesic activities of plant were investigated using acetic acid-induced writhing, hot-plate and formalin tests in mice. The anti-inflammatory activities were carried out *in vivo* and *in vitro*, including xylene-induced ear edema and carrageenan-induced air pouch formation in mice, and COX-1, -2 and 5-LOX inhibition. It has been exhibited that the alkaloid fractions reduced acetic acid-induced writhing response in mice, significantly. In the hot-plate test, alkaloids did not increase the latency period of mice obviously. In the formalin test, alkaloids did not inhibit the licking time in first phase, but significantly inhibited the licking time in second phase of mice. The alkaloid fractions remarkably inhibited xylene-induced ear edema and increased significantly SOD activity and decreased levels of NO, PGE2 and MDA significantly, in air pouch mice model. Moreover, some alkaloids exhibited inhibition of COX-1, COX-2 and 5-LOX *in vitro* anti-inflammatory assay, which supported alkaloids as the bioactive fraction. Thus it was concluded that the alkaloids fraction of *Alstonia scholaris* leaf which includes three main alkaloids, picrinine, vallesamine and scholaricine, may produce the anti-inflammatory and analgesic effect peripherally. In *in vitro* tests, alkaloids exhibited inhibition of inflammatory mediators (COX-1, COX-2 and 5-LOX), which is accordant with results on animal models[22].

**Immunostimulating effect**

The immunostimulating effect of *Alstonia scholaris* bark extracts was studied in BALB/c mouse. The aqueous extract at 50 mg/kg b.w. enhanced phagocytic activity of immunosuppressed mice significantly ($P<0.01$). At 50 and 100 mg/kg b.w. the extract prevents the decrease of immune system induced by prednisone. The aqueous extract at 100 mg/kg b.w. increased lytic activity of peritoneal exudate cells against Escherichia coli significantly ($P<0.05$). The aqueous extract at 50 mg/kg b.w. induced the cellular immune response while at 100 mg/kg b.w. inhibited the delayed type of hypersensitivity reaction[23].

**Antitussive, antiasthmatic and expectorant activity**

The anti-tussive activity of plant was evaluated using three different models including ammonia or sulfur dioxide induced mice coughing, and citric acid induced

guinea pigs coughing. The anti-asthmatic activity was investigated on guinea pigs bronchoconstraction induced by histamine. The expectorant activity was evaluated by volume of phenol red in mice's tracheas. The alkaloids fraction significantly inhibited mice's frequency of cough induced by ammonia, increased mice's latent period of cough induced by sulfur dioxide, and increased guinea pigs' latent period of cough and inhibited frequency of cough. Besides, the alkaloids fraction increased delitescence of convulsion, and tumbles of guinea pigs in anti-asthmatic test, and enhanced tracheal phenol red output in expectorant evaluation. Moreover, the main alkaloid, picrinine exhibited anti-tussive and anti-asthmatic activities *in vivo*[24].

**Hepatoprotective activity**

The hepatoprotective effect of *Alstonia scholaris* on liver injuries induced by carbon tetrachloride ($CCl_4$), beta-D-galactosamine, acetaminophen and ethanol were investigated by means of serum-biochemical and histopathological examinations. Post treatment of *A. scholaris* reduced dose-dependently the elevation of serum transaminases level and histopathological changes such as cell necrosis, inflammatory cell infiltration, which were caused by the single administration of 32 microliters/kg $CCl_4$ or 600 mg/kg acetaminophen in mice. *A. scholaris* significantly lowered 288 mg/kg beta-D-galactosamine induced serum transaminases elevation in the serum-biochemical analysis in rats. A tendency was also shown to inhibit cell necrosis and inflammatory cell infiltration caused by beta-D-galactosamine in histopathological examination[13].

**Antianxiety and antidepressant activity**

Ethyl acetate (EA) fraction from ethanolic extract of *Alstonia scholaris* leaves was assessed against various antianxiety models like elevated plus maze, open field, hole board, light dark box, mirror chamber and foot shock induced aggression models. The change in brain monoamines was estimated. The possible serotonergic effect was tested by 5-Hydroxy Tryptophan induced wet dog shake, tail suspension and modified forced swim test. EA was found to be significantly active in open field test, foot shock induced aggression and mirror chamber models of anxiety. However lack of activity in elevated plus maze, light-dark box, hole board test models, decrease in spontaneous motor activity, potentiation of 5-HTP, increase in 5-hydroxy tryptamine in brain indicate EA to have serotonergic effects. Decrease in immobility time in tail suspension test which was inhibited by reserpine and increase in swimming behavior in forced swim test were conclusive evidence of selective serotonin reuptake inhibition. Thus it was suggested that EA from *Alsonia scholaris* leaves possesses antianxiety and antidepressant activities. The apparent mechanism of action is selective serotonin reuptake inhibition[25].

**Antidiarrhoeal and spasmolytic activity**

In the *in vivo* study, the crude extract of *Alstonia scholaris*, which tested positive for the presence of alkaloids, provided 31-84% protection against castor oil-induced diarrhea in mice at 100-1000 mg/kg doses, similar to loperamide. In isolated rabbit jejunum preparation, the *Alstonia scholaris* caused inhibition of spontaneous and high K (+) induced contractions, with respective EC (50) values of 1.04 (0.73-1.48) and 1.02 mg/mL (0.56-1.84; 95% CI), thus showing spasmolytic activity mediated possibly through calcium channel blockade (CCB). The CCB activity was further confirmed when pretreatment of the tissue with the plant extract (0.3-1 mg/mL) caused a rightward shift in the Ca (++) concentration-response curves similar to verapamil, a standard calcium channel blocker. These results indicate that the crude extract of *Alstonia scholaris* possesses antidiarrhoeal and spasmolytic effects, mediated possibly through the presence of CCB-like constituent(s) and this study provides a mechanistic base for its medicinal use in diarrhea and colic[26].

## CONCLUSION

The present study shows the pharmacognostic and phytochemical properties of various bioactive compounds present in *Alstonia scholaris*. Some of the meticulous studies on this plant have proved its medicinal value beyond any doubt as mentioned in the article which can form the basis for motivating the scientist community in exploring more information about this plant. Therefore, our efforts should be directed towards the review of medicinal plant, screening of activity, isolation and characterization of the active principles and elucidation of the relationship between structure and activity that can aim towards clinical relevance. The global scenario has shown a great increase in phytomedicine research. So, the drug development from this plant has tremendous scope in the future.

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