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## Medicinal Properties and Phytoconstituents of *Alstonia scholaris*: A Review

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### ABSTRACT

*Alstoniascholaris* is a traditionally medicinal plant native to India and South Asia. It is reported that this plant is used as anticancer, antimicrobial, antimutagenic, antifertility, anti-inflammatory, antioxidant, hepatoprotective agent. *A. scholaris* is also rich in various phytochemicals like alkaloid, flavonoid, steroids, triterpenoids and phenols which is responsible for its pharmacological activity. Therefore, the aim of this review is compilation of phytochemistry, ethnobotanical and pharmacological use of *A. scholaris* so as to provide better scope for the use of this plant in pharmacological related studies.

**KEYWORDS** - *Alstoniascholaris*, Phytochemicals, Medicinal properties.

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### 1. INTRODUCTION

*Alstoniascholaris* is an evergreen tree grows in tropical region of Asia. It can grow to hundred meters height with white coloured flowers. 'Scholaris' name has given to this species because its wood has been used for making boards in school. India and china have been known for their traditional methods of medication like Ayurveda, Unani and Siddha. This plant belongs to *Alstonia* genus (Figure 1.1). This genus is reported to be useful in various diseases like malaria, fever, insomnia, chronic diarrhoea, and rheumatic pain (Akhtar and Bano, 2002)

*A. scholaris* is used in various Ayurvedic preparations like Saptaparnasatvadivati, Saptachadadivati, Saptacchadadikvatha and Saptaparnaghanasara for uses in treating asthma, malaria, cough, jaundice, stomach issues, headache and fever.

### 2. CLASSIFICATION

Kingdom: Plantae

Order: Gentianales

Family: Apocynaceae

Subtribe: Alstoniinae

Genus: *Alstonia*

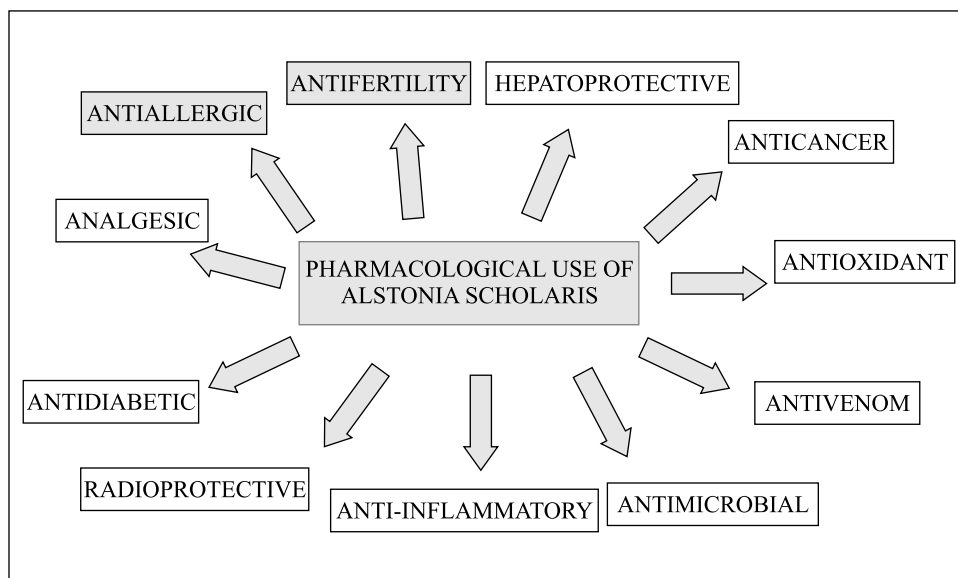
Species: *Alstoniascholaris*



**Figure1:** (a) Tree and (b) Flower of *Alstoniascholaris*

### 3. ETHANOBOTANICAL USES

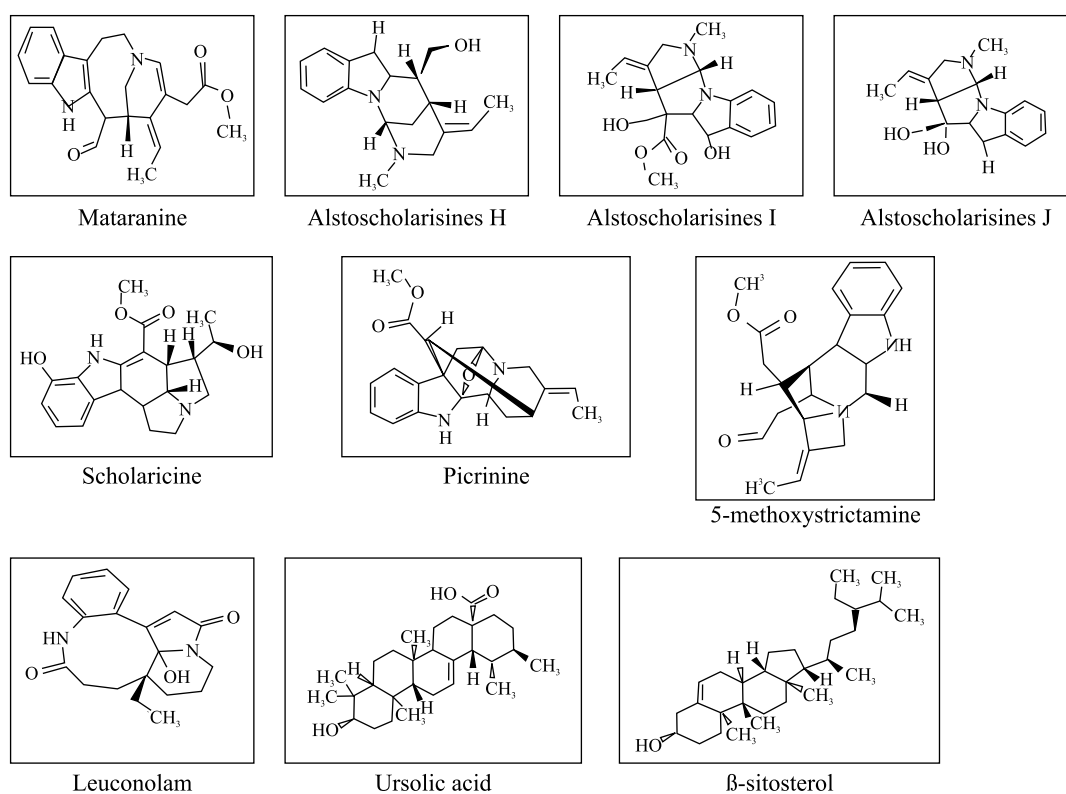
This plant is used as tonic for stomach-ache, reoccurrence of various diseases, stimulant etc. It is also used to treat fever (Rajakumar and Shivanna, 2010) , arthritis (Yusuf et al., 2006) , impotence, leucorrhoea (Bhandary, 1995), animal bite (Prusti and Behera, 2007) , antidote to poison, malaria, skin diseases (Molliket al., 2010) , leprosy, toe cracks, cellulites (Saikia, 2006) , hypertension (Chhetri, 2005) , swelling (Deb et al., 2009) , delivery related pain (Sharma and Kumar, 2011). The bark of this plant is used for the treatment for gastro-intestinal problems like diarrhoea, fever, dysentery, jaundice, hepatitis, ulcer. Traditionally, it is used to treat heart related disorders (Singh and Sangwan, 2011). The Medicinal properties of *A. scholaris* summarised in the Figure 1.2.



**Figure 2:** Medicinal Properties of *A. scholaris*

### 3. PHYTOCHEMICAL CONSTITUENTS

Chromatographic studies of *A. scholaris* showed various types of phytochemical like alkaloid, monoterpenoids, flavonoids, tannins, triterpenes, sterol, esters etc (Singh *et al.*, 2017). HPLC study of methanolic extract revealed that *A. scholaris* contains variety of phenolic acid like gallic acid, ellagic acid catechin and kaempferol (Shang *et al.*, 2010). Ethanoic acid and 10% aqueous ammonia with acidic solution adjusted to pH 9–10 was extracted to give TA fraction (10g). Scholaricine (6%), 19-episolaricine (2%), picrinine (10%) and vallesamine (6%) (Zhao *et al.*, 2017) were isolated and showed airways antiallergic effect and down-regulation of inflammatory cells, cytokines, and the balance of antioxidants (Zhao *et al.*, 2017, Zhao *et al.*, 2018, Hadiet *et al.*, 2009). Some Phytochemicals have been reported in *Alstonia Scholaris*'s (Figure 1.3).



**Figure 3:** Phytochemicals in *A. scholaris*

### 4. MEDICINAL PROPERTIES

#### 4.1 Analgesic and Anti-Inflammatory Activities

*In vivo* studies reported that administration of *A. scholaris* at 200mg/kg significantly reduced pain, mechanical hyperalgesia, heat hyperalgesia, cold by reverting the biochemical changes caused by chronic constriction injury as compared to pregabalin (Singh *et al.*, 2017). Shang *et al.* also found the anti-inflammatory and analgesic properties in *A. scholaris* extract. His team also isolated and fractionised

the alkaloidal extract of *A. scholaris* and found phytochemicals such as Picrinine, Vallesamine and Scholaricine. *In vitro* and *in vivo* studies of this alkaloidal extract reduced nitric oxide, PGE2 and malondialdehyde levels and increased antioxidant level against acetic acid and xylene induced inflammation in mice (Shang *et al.*, 2010). Zhao *et al.* carried out the airway anti-inflammatory effect of alkaloidal extract from *A. scholaris* in rats. It was found that alkaloids decreased the levels of anti-inflammatory parameters like WBCs, Lactate dehydrogenase, Superoxide dismutase, albumin, alkaline phosphatase in lipopolysaccharide-induced airway inflammation rat model (Zhao *et al.*, 2017, Zhao *et al.*, 2018). Alkaloids also restrained the cytokines production in lung of rat. *A. scholaris* also reduced the allergen specific airway inflammation in rats. It was further claimed that decrease in allergic inflammation was due to intra-nasal route rather than intra-peritoneal route. *A. scholaris* extract at dose of 400mg/kg was given to acetic induced pain in mice and it was found out that 79% pain was reduced and at the dose of 200mg/kg 73% pain was reduced. Also, Carrageenan induced paw oedema was decreased at 200 and 400 mg/kg dose (Arulmozhi *et al.*, 2007).

#### 4.2 Anti-allergic effect

Alkaloids like scholaricine and vallesamine present in *A. scholaris* could be responsible for the treatment of allergic asthma. It was also noted that *A. scholaris* extract administered for 3 times a day had significant effect than for single dose daily which could be due to prolonged retention time and the perpetuated plasma concentration. The reduction in interleukin 4, serum immunoglobulin type E was observed, as these molecules are proinflammatory molecule in asthma (Zhao *et al.*, 2017).

#### 4.3 Anti-fertility activity

The benzene extract of *A. scholaris* bark was given orally for 60 days in wistar rats. With extract given in rats, they observed the decrease in size of prostate gland, epididymites and seminal vesicle. The decrease in the production of spermatids and spermatocytes was observed. There was significant decrease in protein and other biochemical parameters related to testes and seminal vesicle (Gupta *et al.*, 2002).

#### 4.4 Radioprotective or Anti-Mutagenic Effect

The hydroethanolic extract of *Alstoniascholaris* has radioprotective efficacy in radiation induced biochemical and hematological changes (Gupta *et al.*, 2008). Animals with pretreatment of *A. scholaris* extract had significantly higher red blood cells count, hemoglobin values than the irradiated controls. *A. scholaris* also prevented total chromatid breaks at G<sub>2</sub> and G<sub>0</sub> phase in against Bleomycin induced chromosomal damage in cultured human lymphocytes (Mistry *et al.*, 2018).

#### 4.5 Anticancer activity

Jagetia and Baliga has studied the anticancer activity of *A. scholaris* and they found that alkaloid fraction of this plant was cytotoxic to different cancerous cell line like cervical (HeLa), liver (HepG2), leukemic (HL60), epidermal (KB) and breast (MCF-7). Plant alkaloidal fraction was treated to HeLa cells resulted in antineoplastic activity. 240mg/kg dose of this plant was found to be effective against cancer in mice. Alkaloidal extract of this plant caused disease free survival for the longer period of time in animals. They found out that *A. scholaris* has tumoricidal properties (Jagetia and Baliga, 2005). *A. scholaris* bark ethanolic extract had also showed antitumor activity against a mouse transplantable tumor (Jagetia and Baliga, 2004). Methanolic extract of *A. scholaris* was found to effective against two types of human lung cancer cell lines i.e., MOR-P [adenocarcinoma] and CORL23 [large cell carcinoma]. They extracted different phytoconstituents and performed their potential anticancer activity in which phytochemical

villalstonine had more significant effect than pleiocarpamine, O-methylmacralstonine and macralstonine (Keawpradub *et al.*, 1997). Cyclophosphamide is a reported drug used in chemotherapy to treat cancer when this cyclophosphamide was given with *A. scholaris*; it showed the enhanced and modulated anticancerous activity of cyclophosphamide in Ehrlich ascites carcinoma-bearing mice (Jagetia and Baliga, 2003). Hydroethanolic extract of *A. scholaris* at dose 4mg/ml was found to be most effective than lesser dose in benzo [a] pyrene induced forestomach carcinoma in female mice. Pre and post treatment of *A. scholaris* did not show any signs of tumor growth (Jagetia *et al.*, 2003).

#### 4.6 Antidiabetic activity-

Aqueous extract of *A. boonei* demonstrated significant antidiabetic and hyperglycaemic activities in dexamethasone-induced hyperglycaemic rats (Nkono *et al.*, 2014). Arulmozhi *et al.* evaluated the antidiabetic and hyperlipidaemic activity of ethanolic extract of *A. scholaris* against streptozotocin induced animal model for diabetes and they found out that *A. scholaris* significantly reduced the glucose level in blood and reduced lipid peroxidation. Antidiabetic effect of extract was there for 1 week onwards till the end of the study. However, *A. scholaris* did not reverse the streptozotocin induced damage in pancreatic beta cells (Arulmozhi *et al.*, 2010). Aqueous extract of *A. scholaris* bark also showed the antidiabetic effect in streptozotocin induced diabetes in rat. The four-week study was performed in which *A. scholaris* bark extract with dose of 150mg/kg and 300mg/kg significantly decreased blood glucose serum triglycerides, serum cholesterol, glycosylated haemoglobin and liver glycogen in diabetic rat (Bandawane *et al.*, 2011). *A. scholaris* extract was also given to alloxan induced diabetic rat and it was found that the extract was remarkably decreased the diabetes symptoms. (Sonawane and Lohar, 2011).

#### 4.7 Free Radical scavenging activity

Antioxidant activity of any medicinal plant is depicted by the 1,1-diphenyl-2-picryl-hydrazil (DPPH) free radical scavenging, hydrogen peroxide scavenging, superoxide anion radical scavenging, ferric thiocyanate reducing ability and metal ion chelating. Arulmozhi performed all of the above tests on the various extracts of *A. scholaris* in which Dichloromethane and ethyl acetate fractions possessed significant free radical scavenging activity compared with standard antioxidants like ascorbic acid and butylated hydroxyanisole (BHA) (Arulmozhi *et al.*, 2007). *A. scholaris* was found to be the most effective antioxidant among 17 medicinal plants like *Cynodondactylon*, *Morindacitrifolia*, *Tylophora*, *Ocimum sanctum*, *Tinosporacordifolia* etc. *A. scholaris* bark extract showed 81% nitric oxide scavenging activity (Ravishankar *et al.*, 2008). Kumar also suggested that *A. scholaris* extract possesses the antioxidant potential. Even its flower also exhibited the free radical like DPPH scavenging activity (Verma *et al.*, 2015).

#### 4.8 Hepatoprotective Activity

Hepatoprotective activity is majorly evaluated on the basis of biochemical, antioxidant (SOD, GSH, MDA, Hydrogen peroxide GPx, GST etc.) and hepatic parameters like AST, ALT ALP, LDH etc. Verma *et al.* also performed these biochemical parameters in acetaminophen induced hepatotoxicity. They suggested that ethanolic extract of *A. scholaris* had higher hepatoprotective effect as compared to aqueous extract. Oral administration of APAP caused disturbances in normal values of various enzymes in blood and liver but after extract treatment these values were found to be normal (Verma *et al.*, 2015). Lin also evaluated the *A. scholaris* hepatoprotective effect against CCL4, galactosamine, acetaminophen and ethanol induced liver toxicity, post treatment with *A. scholaris* prevented and reversed the damage caused by various toxicants (Lin *et al.*, 1996).

#### 4.9 Antimicrobial activity

Antimicrobial activity of *A. scholaris* was studied with different parts of the plant like stem bark leaves and root bark against gram positive and gram-negative bacteria (Khyade and Vaikos, 2009, Goyal and Varshney, 1995). It has been reported that phytochemical present in *A. scholaris* provides the antimicrobial activity. Various extract with different solvents like butanol, methanol, distilled water, chloroform showed the broad-spectrum antimicrobial activity against test organism like *Escherichiacoli*, *Candida* and *Pseudomonas aeruginosa*, *Mycobacterium tuberculosis* (Antony et al., 2012, Khan et al., 2003). Different phytochemicals of *A. scholaris* have shown different antimicrobial activity against *Bacillus subtilis*, *Escherchia coli*, *Shigella aureus*, *Staphylococcus albus*, *Proteus vulgaris* and *Pseudomonas pyocyanea*, *Klebsiella* and *Shigella dysentriaelike sterols were more active than hydrocarbon chains against gram-negative bacteria extracted from A. scholaris and hydrocarbon were more active against gram-positive and gram-negative bacteria.  $\alpha$ -amyrin and lupeol were not active against Bacillus subtilis, Escherchia coli but active against Shigella aureus. Staphylococcus albus, Proteus vulgaris and Pseudomonas pyocyanea, Klebsiella and Shigella dysentriae (Antony et al., 2012, Khan et al., 2003, Misra et al., 2011, Thankamani et al., 2011, Varshney and Goyal, 1995).*

#### 4.10 Antivenom Activity

Goshet al. investigated the venom neutralising potential of *A. scholaris* where he found that when the bark extract of this plant was administered to viper snaked poisoned swiss albino mice models, it significantly reduced the biochemical and histopathological changes like apoptosis, vacuole formation in cytoplasm, cell size changes in liver and kidney tubule necrosis. Local symptoms related with snake poison envenomation are characterized by pain, swelling, haemorrhage and necrotic damage at the site of the bite and these symptoms are significantly decreased by aqueous *A. scholaris* extract at 200mg/kg BW (Gosh et al., 2018).

### 5. CONCLUSION

The plant *A. scholaris* has ethnobotanical uses which have been validated in few pharmacological investigations. Various parts of this plant like bark, stem, root, and leaves have been reported to have anticancer, antimicrobial, hepatoprotective activity. *A. scholaris* has been found to be rich in phytoconstituents. Phytochemicals isolated from this plant may possess pharmacological potential which need to be studied in *in silico*, *in vitro* and *in vivo* model.

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