



Alstonia scholaris (L.) R.Br.: Phytochemistry, Pharmacological Insights, Toxicology, and Emerging Nanomedicine Applications

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ABSTRACT

Alstonia scholaris (L.) R.Br., commonly known as the “scholar tree” or “devil’s tree,” is a medicinally significant evergreen species of the family Apocynaceae, widely distributed across South and Southeast Asia. Traditionally employed in Ayurveda, Unani, and Chinese medicine for respiratory ailments, fevers, diarrhea, and malaria, the plant has gained renewed scientific interest due to its diverse phytochemical profile. Its bark, leaves, and roots are rich in indole alkaloids, flavonoids, triterpenoids, and phenolic compounds, which underpin a broad spectrum of pharmacological activities including anticancer, antimicrobial, anti-inflammatory, antioxidant, hepatoprotective, and antidiabetic effects. Toxicological studies confirm relative safety at therapeutic doses, though high concentrations may induce mild hepatotoxicity. Recent advances in nanomedicine—such as nanoemulsions, polymeric nanoparticles, and silver nanoparticle formulations—have enhanced the bioavailability and efficacy of *A. scholaris* extracts, particularly in oncology and respiratory therapy. Despite promising preclinical evidence, clinical validation remains limited, underscoring the need for translational research. This review consolidates botanical, phytochemical, pharmacological, and toxicological insights into *A. scholaris*, highlighting its therapeutic potential and future prospects in drug development.

Keywords : *Alstonia scholaris*, Indole alkaloids, Phytochemistry, Nanomedicine, Pharmacological activities, Translational research

INTRODUCTION

Alstonia scholaris (L.) R.Br., commonly known as the “scholar tree” or “devil’s tree,” is a prominent evergreen species of the family Apocynaceae, distributed widely across South and Southeast Asia. Its bark has long been valued in traditional medicine, particularly within Ayurveda, Unani, and Chinese systems, for treating respiratory ailments, fevers, diarrhea, and malaria. Ethnobotanical records highlight its role as a febrifuge, tonic, and remedy for chronic pulmonary conditions [1]. Despite centuries of use, scientific investigations into its taxonomy, phytochemistry, and pharmacological potential remain scattered across diverse studies. The plant is taxonomically classified under the order Gentianales, genus *Alstonia*, and is distinguished by its latex-bearing bark and whorled leaves [2]. Phytochemical analyses reveal a rich composition of indole alkaloids, flavonoids, and triterpenoids, which underpin its reported antimicrobial, anti-inflammatory, and anticancer activities [3]. However, systematic consolidation of these findings is limited, creating a gap between traditional knowledge and modern biomedical validation. This review aims to synthesize current evidence on the botanical classification, chemical constituents, and therapeutic applications of *A. scholaris* bark, thereby providing a comprehensive foundation for future pharmacological exploration and drug development.



Figure 1: Taxonomical Classification

Geographical Distribution

This species exhibits a broad geographical distribution, being found throughout India, particularly in the sub-Himalayan tract, West Bengal, Bihar, Peninsular India, and the Andaman Islands, where it is frequently cultivated in public gardens and along roadsides. Its native range extends across South and Southeast Asia, encompassing southern China, the Indian subcontinent, Myanmar, Thailand, and Indonesia. The distribution further reaches Australasia, where it naturally occurs in northern Australia and is also cultivated as an ornamental tree. Moreover, its natural range stretches from Pakistan to China, underscoring its remarkable ecological adaptability to diverse climatic conditions [4].

Habitat

This species demonstrates considerable ecological versatility, occurring across diverse habitats and settings. It is commonly found in moist deciduous and evergreen forests, where it often forms part of the canopy layer. Beyond natural ecosystems, it is frequently cultivated in urban and rural landscapes, particularly along roadsides, in public parks, and in gardens, owing to its ornamental value and shade-providing qualities. The species thrives best under tropical to subtropical climatic conditions characterized by moderate to high rainfall. While it shows a preference for well-drained soils, it exhibits adaptability to a wide range of soil types. In terms of altitudinal distribution, it is widely encountered from lowland plains up to the sub-Himalayan regions, reflecting its broad ecological amplitude [5].

Morphological and Ecological Characteristics:

Alstonia scholaris is a medium-sized evergreen tree that typically grows between 12–18 m, though some specimens may reach up to 27 m. Its bark is rough, greyish-white externally and yellowish internally, exuding a bitter latex when injured. The leaves are thick, oblong, and blunt-tipped, arranged in whorls of 4–7. They are dark green above and pale beneath, often covered with a whitish bloom or pubescence. Structurally, the leaves possess numerous parallel nerves that converge into an intramarginal vein, giving them a coriaceous texture [6].

The tree produces small, fragrant, greenish-white flowers in branched, pubescent cymes. Each flower has a long corolla tube lined with hairs and oblong lobes that are rounded at the apex. Fruits are slender, cylindrical follicles measuring 30–60 cm in length, drooping in clusters. Upon dehiscence, they split open to release linear-oblong seeds fringed with silky hairs at both ends. Flowering and fruiting generally occur from March to July, often following drought conditions [7].

Ecologically, *A. scholaris* thrives in moist habitats across India, ranging from sub-temperate to dry tropical climates. It grows best in regions with 100–150 cm annual rainfall and prefers red alluvial soils with good aeration, though it can also adapt to black cotton soils, albeit with slower growth [8].



Figure 2 : Alstonia Scholaris Plant Parts

a) Tree b) Leaves c) Flower d) Bark e) Seed f) Fruit

Phytochemical Constituents :

Plant Part	Major Phytochemicals
Bark	Alkaloids (Echitamine, alstonine, scholaricine, picrinine), flavonoids, phenols, saponins, tannins, glycosides
Root Bark	Triterpenoids (α -amyrin acetate, lupeol), steroid (β -sitosterol)
Leaves	Alkaloids, flavonoids, steroids, triterpenoids, phenols; also show antioxidant and antimicrobial activity
Roots	Alkaloids, flavonoids, steroids, triterpenoids, phenols
Flowers	Volatile oils, alkaloids, flavonoids, steroids, triterpenoids, phenols

Pharmacological Activities:

- **Anticancer Activity**

The bark extract of *Alstonia scholaris* has demonstrated anticancer potential by mitigating radiation-induced biochemical alterations in mice, particularly through the regulation of cholesterol levels and reduction of lipid peroxidation. Furthermore, alcoholic extracts of *A. scholaris* have been reported to decrease the number of aberrant cells and significantly lower the overall frequency of chromosomal aberrations in vivo [9].

- **Antimicrobial Activity**

Methanolic extract of the *A. scholaris* bark was found to be active on Gram positive bacteria i.e. *Bacillus coagulans* and gram negative bacteria i.e. *Escherichia coli* [10].



- **Anti-inflammatory & Analgesic Activity**

Flavonoids and terpenoids in *A. scholaris* contribute to its anti-inflammatory and pain-relieving properties. demonstrated that leaf extracts reduced inflammation in experimental models, supporting its use in respiratory disorders like asthma and bronchitis [11].

- **Antioxidant Activity**

Phenolic compounds in *A. scholaris* have been shown to scavenge free radicals, reducing oxidative stress. high antioxidant activity in leaf extracts, suggesting protective effects against degenerative diseases [12].

- **Hepatoprotective Activity**

Extracts of *A. scholaris* have demonstrated protective effects on liver tissue. bark extracts reduced toxin-induced liver damage in experimental models, highlighting its potential in hepatoprotective therapy [13].

- **Antidiabetic Activity**

Alkaloids and saponins from *A. scholaris* have been linked to hypoglycemic effects. extracts lowered blood glucose levels in animal models, supporting its potential as an antidiabetic agent [14].

- **Antimutagenic & Antifertility Activity**

Recent work has also explored the plant's antimutagenic and antifertility effects. extracts reduced mutagenic activity and influenced fertility parameters, though these findings require further clinical validation [15].

Ethnobotanical Uses:

The medicinal applications of *Alstonia scholaris* have been well documented across classical systems such as Ayurveda, Unani, and Siddha. Traditionally, the plant has been employed in the management of respiratory ailments like asthma, as well as systemic conditions including jaundice and malaria [16]. Among local communities, decoctions prepared from the bark have been widely used to alleviate chronic diarrhea, fever, and various respiratory disorders. In addition to bark preparations, the leaves and latex of the plant have been applied externally for the treatment of wounds, ulcers, and diverse skin infections, reflecting its broad ethnomedicinal relevance [17]. These practices highlight the deep cultural integration of *A. scholaris* in traditional healthcare and provide a foundation for modern pharmacological investigations.

Toxicology and clinical Evidence

Acute Toxicity

Acute toxicity studies in rodents have shown that *Alstonia scholaris* extracts are generally safe at therapeutic doses.

- Leaf extracts: oral administration of aqueous and ethanolic leaf extracts up to 2000 mg/kg body weight did not produce mortality or severe behavioral changes, indicating a relatively high LD50 value.
- Bark extracts: Similar studies found no lethal effects up to 1500 mg/kg, though higher doses produced mild gastrointestinal irritation and transient hepatotoxicity due to alkaloid content [18].

Sub-chronic Toxicity

Repeated administration over several weeks has revealed dose-dependent effects:

- 90-day sub-chronic study in rats, administering bark extract at doses of 250, 500, and 1000 mg/kg/day. Mild elevations in liver enzymes (ALT, AST) were observed at 1000 mg/kg, but no severe histopathological damage was noted.
- Hematological parameters remained within normal ranges at lower doses, suggesting safety at therapeutic levels [19].



Chronic Toxicity

Long-term exposure studies highlight the importance of monitoring organ function:

- Chronic administration of bark extract at 200–800 mg/kg/day for 6 months caused dose-dependent changes in hematological and biochemical parameters. At higher doses (≥ 600 mg/kg), mild hepatotoxicity and nephrotoxicity were observed, though these effects were reversible upon discontinuation.
- No carcinogenicity or mutagenicity was reported in chronic models [20].

Nanomedicine Approaches

- **Nanoemulsions:** Leaf and bark extracts of *A. scholaris* have been incorporated into nanoemulsion systems to improve solubility and stability of alkaloids and flavonoids. These formulations showed enhanced antioxidant and antimicrobial activity compared to crude extracts [21].
- **Polymeric Nanoparticles:** Encapsulation of *A. scholaris* alkaloids in biodegradable polymers (such as PLGA nanoparticles) has been investigated to achieve controlled release and targeted delivery, particularly for anticancer applications [22].
- **Silver Nanoparticles (AgNPs):** Biosynthesis of silver nanoparticles using *A. scholaris* leaf extract has been reported, with strong antimicrobial and cytotoxic properties. These green-synthesized nanoparticles demonstrated improved efficacy against bacterial strains and cancer cell lines [23].
- **Liposomal Formulations:** Preliminary studies suggest that liposomal encapsulation of *A. scholaris* extracts can enhance bioavailability and reduce toxicity, making them promising for respiratory and hepatoprotective applications [24].

Clinical & Preclinical Evidence

- Preclinical studies in rodents have shown that nano formulations of *A. scholaris* extracts reduce oxidative stress and inflammation more effectively than conventional extracts.
- In vitro studies confirm that nanoparticle-based delivery systems improve cytotoxicity against cancer cells while minimizing damage to normal cells.
- Clinical trials are still limited, but early formulations tested for respiratory disorders indicate improved patient tolerance and efficacy compared to crude extracts.

Conclusion

Alstonia scholaris represents a unique convergence of traditional ethnomedicine and modern pharmacological exploration. Its diverse phytoconstituents, particularly alkaloids and flavonoids, contribute to a wide range of therapeutic effects, from antimicrobial and anti-inflammatory actions to anticancer and hepatoprotective properties. Toxicological evaluations suggest that the plant is generally safe at therapeutic doses, though careful monitoring is warranted at higher concentrations. Emerging nanotechnology-based delivery systems have further expanded its biomedical potential, offering improved solubility, targeted delivery, and enhanced pharmacological activity. However, clinical evidence remains scarce, and rigorous trials are essential to establish safety, efficacy, and standardized formulations. Bridging the gap between traditional knowledge and modern biomedical validation will not only strengthen the therapeutic relevance of *A. scholaris* but also position it as a promising candidate for future drug discovery and integrative medicine.

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