Review Article

Alstonia scholaris: It's Phytochemistry and pharmacology

Abstract

Complementary therapies based on herbal medicines are the world's oldest form of medicine and recent reports suggest that such therapies still enjoy vast popularity, especially in developing countries where most of the population does not have easy access to modern medicine. *Alstonia scholaris* (L.) R.Br (Apocynaceae) is an evergreen tropical tree native to Indian sub-continent and South East Asia, having grayish rough bark and milky sap rich in poisonous alkaloid. It is reported to contain various iridoids, alkaloids, coumarins, flavonoids, leucoanthocyanins, reducing sugars, simple phenolics, steroids, saponins and tannins. It has been reported to possess antimicrobial, antiamoebic, antidiarrheal, antiplasmodial, hepatoprotective, immunomodulatory, anticancer, antiasthmatic, free radical scavenging, antioxidant, analgesic, anti-inflammatory, antiulcer, antifertility and wound healing activities. In other parts of the world, it is used as a source cure against bacterial infection, malarial fever, toothache, rheumatism, snakebite, dysentery, bowl disorder, etc. Reports on the pharmacological activities of many isolated constituents from *A. scholaris* (L.) R.Br are lacking, which warrants further pharmacological studies.

Key words:
Alstonia scholaris (L.) R.Br, echitamine, pharmacology, phytochemistry, review

Introduction

Complementary therapies based on herbal medicines are the world's oldest form of medicine and recent reports suggest that such therapies still enjoy vast popularity, especially in developing countries where most of the population does not have easy access to modern medicine.[1] The traditional Indian system of medicine, Ayurveda, which means the science of life, is one of the world's oldest systems of medicines. Ayurveda mainly uses plant-based formulas developed through the experimentation and experiences of doctors for centuries.[2]

Alstonia scholaris (L.) R.Br (Apocynaceae) is an evergreen tropical tree native to Indian sub-continent and South East Asia, having grayish rough bark and milky sap rich in poisonous alkaloid. This plant is a native of India, Sri Lanka, Pakistan, Nepal, Thailand, Burma, Malaysia, South East Asia, Africa, Northern Australia, Solomon Islands, and Southern China.[3-8] The plant is a large evergreen tree, growing up to 17–20 m in height, with a straight often fluted and buttressed bole, about 110 cm in diameter. Bark is grayish brown, rough, lenticellate abounding, bitter in taste secreting white milky latex. Leaves are 4–7 in a whorl, coriaceous, elliptic-oblong. Flowers are small, greenish white, many in umbellate panicles, corolla tube is short, very strongly scented. Fruits have follicles, 30–60 cm long. Seeds are papillose with brownish hair at each end.[4(80-83),5(111-114)] The bark, also called dita bark, is traditionally used by many ethnic groups of North East India and other parts of the world as a source cure against bacterial infection, malarial fever, toothache, rheumatism, snakebite, dysentery, bowl disorder, etc. Also, the latex is used in treating coughs, sores and fever.[4,9,10] 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.[3]

Access this article online	
Website: http://www.cysonline.org	Quick Response Code
DOI: 10.4103/2229-5186.82970	

Pawan Kaushik, Dhirender Kaushik, Neha Sharma, A. C. Rana[1]

Department of Pharmacology, Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra, Haryana, [1]Rayat college of Pharmacy, Ropar, Punjab, India

Address for correspondence:
Dr. Dhirender Kaushik,
Institute of Pharmaceutical Sciences,
Kurukshetra University, Kurukshetra, Haryana, India.
E-mail: dkaushik.apti@gmail.com

Table 1: Important chemical constituents from different parts of *Alstonia scholaris*

Part used	Extract/oil	Chemical constituent	Ref.
Flower	Flower extract	3β-acetate-24-nor-urs-4,12-diene ester triterpene and 3β-hydroxy-24-nor-urs-4,12,28-triene triterpene and one of the oleanane types, 3,28-β-diacetoxy-5-olea-triterpene together with two known triterpenes, α-amyrin acetate and ursolic acid	[14]
	Volatile oil	Principal constituents were linalool (35.7%), *cis*- and *trans*-linalool oxides (furanoid and pyranoid) (14.7%), α-terpineol (12.3%), 2-phenylethyl acetate (6.3%) and terpinen-4-ol (5.6%). The volatile concentrate contained more than 90% of oxygenated compounds, which contributed to its fragrant odour	[15]
	Column fraction	*n*-hexacosane, lupeol, palmitic acid, β-amyrin and ursolic acid	[16]
	Column fraction	Picrinine and strictamine	[17]
Bark	Root bark	Two triterpenoids, α-amyrin acetate and lupeol, and a steroid, β-sitosterol	[18]
	Trunk bark	A new indole alkaloid, akuammiginone, and a new glycosidic indole alkaloid, echitamidine-*N*-oxide 19-*O*-β-D-glucopyranoside, together with the five known alkaloids, echitaminic acid, echitamidine *N*-oxide, *N*-demethylalstogustine *N*-oxide, akuammicine *N*-oxide, and *N*-demethylalstogustine	[19]
	Alkaloidal extract	Six new monoterpenoid indole alkaloids, scholarisines B–G together with 15 known analogues, were isolated from the bark of *A. scholaris*	[20]
	Bark	Triterpenoids α-amyrin acetate and lupeol	[21]
	Ethanolic extracts	Four new 11-noriridoids, namely, scholareins A–D, along with three known derivatives, isoboonein, alyxialactone, and loganin	[22]
	Alcoholic extracts	17-*O*-acetylechitamine and echitamine	[23]
		Contain scholarisine I and scholarisine II	[24]
Leaves	Leaves extract	The eight elements, Cu, Zn, Fe, Mg, Ca, Cr, Mn and Cd, were extracted from the leaves of *A. scholaris* based on traditional analytical flowchart program and separated into water-soluble state and suspension state by microporous filtering film	[25]
	Column fraction	Iridoids, alkaloids, coumarins, flavonoids, leucoanthocyanins, reducing sugars, simple phenolics, steroids, saponins and tannins	[26]
	Methanolic extract	A new indole alkaloid, akuammidine-*N*-oxide together with akuammidine	[27]
	Leaves extract	Eight flavonoids were isolated and identified: kaempferol, quercetin, isorhamnetin, kaempferol-3-*O*-β-D-galactopyranoside, quercetin-3-*O*-β-D-galactopyranoside, isorhamnetin-3-*O*-β-D-galactopyranoside, kaempferol-3-*O*-β-D-xylopyranosyl-(2-1)-*O*-β-D-galactopyranoside, quercetin-3-*O*-β-D-xylopyranosyl-(2-1)-*O*-β-D–galactopyranoside	[28]
	Methanol percolate	Lagunamine (19-hydroxytubotaiwine), angustilobin B acid and losbanine (6,7-seco-6-nor-angustilobine B) together with tubotaiwine, its oxide and 6,7-seco-angustilobine B	[23]
	Leaves extract	19-epischolaricine, *N*-methylscholaricine, *N*-methylburnamine and vallesamine *N*-oxide	[29]
	n-Hexane extract	The predominant *n*-alkanes were C_{31} (46.43%) and C_{33} (21.85%), while C_{29} (6.16%), C_{32} (4.28%), C_{25} (3.74%) were moderately abundant. The C_{17} (0.39%) and C_{22} (0.44%) *n*-alkanes were present only in minor amounts	[30]
	Hydro-alcoholic extract	2,3-Secofernane triterpenoids, alstonic acids A and B, together with an indole alkaloid, *N*-methoxymethyl picrinine	[31]
	Column fraction	Megastigmane-3β, 4α, 9-triol and 7-megastigmene-3,6,9-triol	[32]
	Ethanolic extract	Unprecedented cage-like alkaloid, scholarisine A	[33]
	Ethanolic extract	Four picrinine-type monoterpenoid indole alkaloids, 5β-methoxyaspidophylline, picrinine, picralinal and 5-methoxystrictamine	[34]
	Leaves extract	Fourteen compounds were obtained and the structures were elucidated as: cycloeucalenol, α-amyrin acetate, β-amyrin-3-palmitate, lupen-3-ol, lupen-3-palmitate, β-sitosterol, squalene, α-tocopherol, α-tocopherolquinone, bis(2-ethylhexyl) phthalate, dibutyl phthalate, 1-hydoxy-3,5-dimethoxyxanthone, 7,3′,4′-trimethoxyl-5-hydoxylflavone, 3,5,7,4′-tetrahydoxyl-flavone-3-*O*-β-D-glucoside	[35]
	Ethanolic extract	Monoterpenoid indole alkaloids with a skeleton rearrangement and two additional carbons, named *E*-alstoscholarine and *Z*-alstoscholarine	[36]

Contd...

Table 1: ***Contd/-***

Part used	Extract/oil	Chemical constituent	Ref.
	Leaves extract	The structures of these isolated compounds were found to be quercetin 3-*O*-β-D-xylopyranosyl (1″→2″)-β-D-galactopyranoside and (−)-lyoniresinol 3-*O*-β-D-glucopyranoside	[37]
	Leaves extract	Ursolic acid determined by HPTLC	[38]
	Alcoholic extract	Three new akuamillan-type indole alkaloids, i.e. 5-methoxystrictamine (=methyl (5β,16*R*,19*E*)-5-methoxyakuaramilan-17-oate, methyl (16*R*,19*E*)-1,2-dihydro-16-(hydroxymethyl)-5-oxoakuammilan-17-oate, and methyl (2β,16*R*,19*E*)-4,5-didehydro-1,2-dihydro-2-hydroxy-16-(hydroxymethyl) akuammilan-4-ium-17-oate chloride	[39]
	Methanolic extract	The first seco-uleine alkaloids, manilamine (18-hydroxy-19,20-dehydro-7,21-seco-uleine) and N4-methyl angustilobine B, together with the known indole alkaloids, (*E*)-vallesamine, angustilobine B N4 oxide, (*S*)-tubotaiwine, and 6,7-seco-angustilobine B	[40]
	Leaves extract	Three new indole alkaloids, nareline ethyl ether, 5-epi-nareline ethyl ether and scholarine-*N*(4)oxide, in addition to nareline methyl ether, picrinine and scholaricine	[41]
	Leaves extract	Picrinine and akuammidine	[42]
	Alcoholic extract	Picralinal	[43]
	Alcoholic extract	A new indole alkaloid, alstonamine, and a sitsirikine type indole alkaloid, rhazimanine	[44]
	Methanol extract	A new alkaloid, 19,20-*Z*-vallesamine, along with 19,20-*E*-vallesamine	[45]
	Leaves extract	19,20-Dihydrocondylocarpine	[46]
	Ethanolic extract	A new alkaloid, scholaricine, has been isolated. It was elucidated as 2 (demethylscholarine)	[47]
	Ethanolic percolate	A new alkaloid designated scholaricine. It was (±)12-methoxyechitamidine	[48]
	Leaves extract	A new indole alkaloid, alkaloid-a, together with echitamine and echitamidine	[49]
Fruit	Pod	A new indole alkaloid, *N*-formylscholarine, together with picrinine, strictamine and nareline Indole alkaloid picrinine, strictamine and nareline	[50]
	Methanolic extract	Alkaloids 19-*E*-picrinine, 19-*E*-akuammidine, 19-*E*-vallesamine and 19-*S*-scholaricine	[51]
Root	Bark	ψ-akuammigine; akuammicine; akuammicine-*N*-methiodide; akuammicine-*N*-oxide; indole alkaloids; *N*-demethylechitamine, tubotaiwine	[52]
Stem	Hydro-alcoholic extract	A new secoiridoid glucoside, named alstonoside, together with two isoflavone apioglucosides, formononetin 7-*O*-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside and biochanin A 7-*O*-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside	[53]
	Bark	0.200% total alkaloids, 0.07% steroids and 0.44% resins	[54]
Trunk	Bark	A new indole alkaloid akuammiginone and a new glycosidic indole alkaloid echitamidine-*N*-oxide19-*O*-β-D-glucopyranoside together with the five known alkaloids, echitaminic acid, echitamidine-*N*-oxide, *N*-demethylalstogustine *N*-oxide, akuammicine *N*-oxide and *N*-demethylalstogustine	[55]
Seed	*n*-Hexane extract	Oil of mature seed contains oleic acid (65.66%), linoleic acid (12.15%), palmitic acid (13.77%) and stearic acid (8.42%)	[56]

A. scholaris (L.) R.Br has been used in traditional systems of medicine for treating various ailments. The ripe fruits of the plant are used in syphilis and epilepsy. It is also used as a tonic, antiperiodic, and anthelmintic. The milky juice of *A. scholaris* (L.) R.Br has been applied to treat ulcers. The bark is the most intensively used part of the plant and is used in many compound herbal formulas.[4] It is a bitter tonic, alternative, and febrifuge and is reported to be useful in the treatment of malaria, diarrhea, and dysentery.[4,7,8,11] Recently, the leaf extract has also been found to own antimicrobial properties.[12] *A. scholaris* (L.) R.Br has also been reported to inhibit liver injuries induced by carbon tetrachloride, beta-D-galactosamine, acetaminophen, and ethanol as remarked by the reduced elevation of levels of serum transaminases and histopathologic changes such as cell necrosis and inflammatory cell infiltration.[13]

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. The other synonyms of the plant include *Tabernaemontana alternifolia* Burm, *Echites pala* Buch-Ham ex Spreng, and *Pala scholaris* (L.) Roberty.[3,4(pp1308- 1315),5(pp337-346)-8] In Sanskrit, the plant is referred to as *phalagaruda*, *sapthaparna*, and *saptaparni* (*sapta* means 7 and *parna* or *parni* means leaves) because the leaves are found in whorls of 7 [Figure 1].

Table 2: Pharmacological activities reported from *Alstonia scholaris*

Activity	Part/extract	Animal model/cell lines	Ref.
Antituberculosis	Methanol extract of leaf, stem bark and root bark of *A. scholaris*	*In vitro* antituberculosis activity (89% inhibition against *Mycobacterium tuberculosis* H37Rv at 50 μg/mL) using Microplate Alamar Blue Assay (MABA)	[57]
Antibacterial	The methanol and acetone extract of *A. scholaris*	Bacterial strain: the Gram-positive bacteria were *Staphylococcus aureus* (ATCC9144) (SA), *Micrococcus luteus* (ATCC4698) (ML), *Klebsiella pneu-moniae* (ATCC15380) (KP), *Bacillus subtilis* (ATCC 6051) (BS), and *Pseudomonas aeruginosa* (ATCC25668) (PA); *Enterobacter aerogens* (ATCC13048) (EA), *Salmonella typhi* (NCTC 8394) (ST) and *Salmonella paratyphi* A (SPA) were Gram-negative bacteria	[58]
	The crude methanolic extracts of the leaves, stem and root barks of *A. scholaris*	The microorganisms used were *Aspergillus niger, Aspergillus rubrum, Aspergillus versicolor, Aspergillus vitis, Candida albicans, Candida trpicallis, Clasdosporium cladospriods, Penicillium notatum, Trychophyton mentagrophytes, Trychophyton tronsrum*	[59]
	A. scholaris leaf powder is extracted with petroleum ether, chloroform, ethyl acetate and methanol	The microorganisms used were *Escherichia coli, Salmonella typhi, Staphylococcus aureus, Klebsiella pnuemoniae, Shigella dysenteriae, Aspergillus niger and Aspergillus flavus*	[26]
	Trunk bark	Two Gram-positive bacteria including *Bacillus subtilis* and *Streptococcus pyogenes* and four Gram-negative bacteria including *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Proteus mirabilis*	[60]
Radioprotective	Bark	Male Swiss albino mice were studied for cytogenetic alterations in the form of chromosomal aberrations and micronuclei induction in bone marrow by exposing them to 2.5 Gy gamma radiations	[61]
	Hydro-alcoholic extract of bark	Male Swiss albino mice were studied for radiation-induced hematological and biochemical alterations	[62]
		Dose tolerance of *Alstonia scholaris* extract (ASE), Dose reduction factor (DRF), Endogenous colonies in spleen, LPx and GSH were studied in Swiss albino mice	[63]
	A. scholaris extract (ASE) of bark	Radiation-induced biochemical alteration in mice by ameliorated cholesterol and lipid peroxidation	[64]
Anticancer	Bark extract	Skin carcinogenesis in Swiss albino mice	[65]
	Alkaloid fraction	Cultured human neoplastic cell lines (HeLa, HepG2, HL60, KB and MCF-7) and in Ehrlich ascites carcinoma (EAC) bearing mice	[66]
	Ethanolic leaves extract	Human cell lines, i.e. lung cancer cells (A-549), oral cancer cells (K3), breast cancer lines (MCF-7), neuroblastoma cancer lines (SW-N-MC), colon cancer cells (SW-620)	[67]
	Echitamine chloride, a plant alkaloid from *A. scholaris*	Rats have been used to examine the anticancer effects on methylcholanthrene-induced fibrosarcoma	[68]
	EAC bearing mice from bark of *A. scholaris*	EAC bearing mice	[69]
	Ethanolic extract of stem of *A. scholaris* (ASE)	EAC bearing mice	[70]
	Different extracts from stem bark	HeLa cell lines	[71]
Cytotoxic	Echitamine chloride	HeLa, HepG2, HL60, KB and MCF-7 cell lines *in vitro* and in mice bearing EAC	[72]
	Methanol extracts of root barks of *Alstonia macrophylla, Alstonia glaucescens,* and *A. scholaris*, collected from Thailand	Human lung cancer cell lines, MOR-P (adenocarcinoma) and COR-L23 (large cell carcinoma), using the SRB assay	[73]
Alteration in phosphatase activity	Bark extract	Exposed to gamma radiation at the source to surface distance (SSD) of 77.5 cm to deliver the dose rate of 1.32 Gy/min	[74]
Chemomodulatory activity	*A. scholaris* extract (ASE) was studied in combination with berberine hydrochloride (BCL)	EAC bearing mice	[75]
	Combination of 120 mg/kg of ASE with 25 mg/kg of CPA was most effective	Mice transplanted with EAC	[76]
	Hydro-alcoholic extract of *A. scholaris* (ASE)	Benzo(a)pyrene (BaP) induced forestomach carcinoma in female mice	[77]

Contd...

Table 2: ***contd/-***

Activity	Part/extract	Animal model/cell lines	Ref.
	Enhancement of the cytotoxic effects of echitamine chloride by vitamin A	EAC cell cultures	[78]
	Echitamine chloride	Modulation of the impaired drug metabolism in sarcoma-180 bearing mice	[79]
Radiosensitizing effect	Alkaloid fraction of *A. scholaris*	Evaluated in various neoplastic cell lines, namely, HeLa, HePG2, HL60, MCF-7, and KB exposed to 0, 0.5, 1, 2, 3, and 4 Gy of γ-radiation	[80]
	Echitamine chloride from bark of *A. scholaris*	Inhibition of glycolysis and respiration of sarcoma-180 cells	[81]
Anti-tussive, anti-asthmatic and expectorant activities	Ethanolic extract, fractions and main alkaloids of *A. scholaris* leaf	The anti-tussive activity 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' bronchoconstriction induced by histamine. The expectorant activity was evaluated by the volume of phenol red in mice's tracheas	[82]
Broncho-vasodilatory activity	Ethanolic extract of *A. scholaris* (Apocynaceae) leaves	Guinea pig trachea, ileum	[83]
Anti-inflammatory and analgesic	The leaf extract	The analgesic activities were investigated using acetic acid-induced writhing, hot-plate and formalin tests in mice. The anti-inflammatory activities were determined *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	[84]
Wound healing	Ethanolic and aqueous extract of leaves	Excision, incision and dead space wound healing models	[85]
Antidiabetic and antihyperlipidemic	Ethanolic extract of the leaves of *A. scholaris*	Stz induced diabetic rat	[86]
Antidiabetic	Leaf powder of *A. scholaris*	Powder of leaves of *A. scholaris* causes a significant decrease in blood glucose level in human volunteers with Non-insulin dependent diabetes mellitus	[87]
Antihypertension	Decoction of bark	In patients with essential hypertension	[88]
Antidiarrheal and spasmolytic activities	Methanolic crude extract of *A. scholaris*	Method used was castor oil induced diarrhea for *in vivo* antidiarrheal activity and rabbit jejunum *in vitro* model for spasmolytic activity	[89]
	Antidiarrheal formulation	Charcoal suspension (10%) was used to study the effect of kutajarishta on percent intestinal transit, while its effect on electrolyte, mainly potassium secretion, was studied using glibenclamide in castor oil induced diarrhea	[90]
	Aqueous and the alcoholic bark extracts	Castor oil induced diarrhea. Parameters under study were number of diarrheal episodes and mean wt. of stools of mice	[91]
Immunostimulating	Bark extracts	BALB/c mouse	[92]
In vitro antioxidant and free radical scavenging	Fraction from ethanolic etract of leaves of *A. scholaris*	1,1-diphenyl-2-picryl-hydrazil (DPPH) free radical scavenging, metal ion chelating, hydrogen peroxide scavenging, superoxide anion radical scavenging, and ferric thiocyanate reducing	[93]
	Methanolic extract of fruit and flower	Extract showed significant antioxidant activity by inhibition of DPPH and superoxide production. Free radical scavenging activity is due to the presence of flavonoid	[94]
	Methanolic extract of leaves	DPPH assay and plasmid nicking assay	[95]
Nitric oxide Scavenging	Ethanolic extract of bark	NO scavenging activity	[96]
Stress and cognition	Methanolic extract of bark of *A. scholaris*	Restraint stress model in mice, passive avoidance model and elevated plus maze model	[97]
Anti-anxiety activity	Ethanolic extract of *A. scholaris* leaves (EEAS)	Elevated plus maze, open field, hole board, light dark, mirror chamber and foot shock induced aggression models	[98]
Antimalarial	Methanol extracts prepared from various parts of *A. scholaris, A. macrophylla* and *A. glaucescens*	Antiplasmodial activity against multidrug-resistant K1 strain of *Plasmodium falciparum* cultured in human erythrocytes	[99]
	The petroleum ether extract and methanol extract of the bark of *A. scholaris*	Antimalarial activity in mice infected with *Plasmodium berghei*	[100]
Antifertility	Lupeol acetate isolated from benzene extract of *A. scholaris*	Body weights, weight of reproductive organs, i.e. testes, epididymis, seminal vesicle and ventral prostate, were observed. Testicular sperm count, epididymal sperm count and motility were also evaluated using male albino rats	[101]
	α-Amyrin acetate isolated from the plant *A. scholaris*	Male albino rats	[102]

Contd...

Table 2: ***contd/-***

Activity	Part/extract	Animal model/cell lines	Ref.
	A. scholaris bark extract	Drug showed significant antifertility effect in male rat at this dose level. The primary site of action may be meiotic germ cells	[103]
Antileishmanial	*A. scholaris* plant extract	Plants were evaluated for antileishmanial activity with *Leishmania donovani* infected hamsters	[104]
Hepatoprotective	*A. scholaris* plant extract	Liver injuries induced by carbon tetrachloride (CCl4), β-d-galactosamine, acetaminophen and ethanol were investigated by means of serum biochemical and histopathologic examinations	[105]
Toxicological profile	Different doses up to 2000 mg/kg	The acute and sub-acute toxic effects of various doses of hydro-alcoholic extract of *A. scholaris* (ASE) were studied in mice and rats	[106]
Teratogenic effect	Hydro-alcoholic extract of *A. scholaris*	The teratogenic effect was studied in the pregnant Swiss albino mice on Day 11 of gestation	[107]

Figure 1: *Alstonia scholaris* with fruit pods

Taxonomical classification of *A. scholaris* Linn. R.Br

Taxonomy	*Alstonia scholaris*
Kingdom	Plantae, Planta
Subkingdom	Tracheobionta, vascular plants;
Division	Magnoliophyta, Flowering plants
Class	Magnoliopsida, Dicotyledon
Subclass	Asteridae
Order	Gentianales

Phytochemistry

A. scholaris Linn. is known to be a rich source of alkaloids and there is interest among the scientists to use this for therapeutic purposes. Amongst the chemical classes present in medicinal plant species, alkaloids stand as a class of major importance in developing new drugs because alkaloids own a great variety of chemical structures and have been identified [Table 1] as being responsible for the pharmacological properties of medicinal plants. Almost all the parts of plant (bark, flower, root) are found to contain active principles [Table 1].

Pharmacology

Following are the pharmacological activities of the plant; it has been investigated scientifically in animal models to validate the potential of the plant in cure of variety of ailments as shown in [Table 2].

Acknowledgment

We would like to thank Director, Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra, for providing the necessary facilities for completion of this work.

References

1. World Health Organization. WHO Traditional Medicine Strategy 2002–2005. World Health Organization Document, WHO/EDM/TRM/2002.1. Geneva, Switzerland: World Health Organization; 2002.
2. Mukherjee PK, Wahile A. Integrated approaches towards drug development from Ayurveda and other Indian system of medicines. J Ethnopharmacol 2006;103:25-35.
3. Anonymous. The Wealth of India: Raw Materials, Vol 43. New Delhi, India: Council of Scientific and Industrial Research; 1960.
4. Nadkarni AK. Indian Materia Medica. 3rd ed. Mumbai, India: Popular Press; 1976.
5. Kirtikar KR, Basu BD. Indian Medicinal Plants. Vol 2. Dehradun, India: Bhushen Singh Mahendra Pal Singh; 1935.
6. Satyavati GV, Gupta AK, Tandon N. Medicinal Plants of India. New Delhi, India: Indian Council of Medical Research; 1987.
7. Warrier PK, Nambiar VPK, Ramankutty C. Indian Medicinal Plants. Hyderabad, India: Orient Longman; 1996.
8. CHEMEXCIL. Selected Medicinal Plants of India. Bombay, India: Basic Chemicals, Pharmaceutical and Cosmetic Export Promotion Council; 1992. p .205-7
9. Bhattacharjee, SK. Handbooks on Medicinal Plant, 4th Rev. Edition, Jaipur, India: Pointer publishers; 2004.
10. Kumar S. Medicinal Plants of North-East region, 1st Ed Rajasthan, India: Scientific Publishers; 2002.
11. Sathyavathi GV, Gupta AK, Tandon N. Medicinal Plants of India. New Delhi, India: Indian Council of Medical Research; 1987;2:230-9.
12. Omoregbe RE, Ikuebe OM, Ihimire IG. Antimicrobial activity of some medicinal plants extracts on Escherichia coli, Salmonella paratyphi and Shigella dysenteriae. Afr J Med Med Sci 1996;25:373-5.
13. Lin SC, Lin CC, Lin YH, Supriyatna S, Pan SL. The protective effect of *Alstonia scholaris* R. Br. on hepatotoxin- induced acute liver damage. Am J Chin Med 1996;24:153-64.
14. Sultana N, Saleem M. Phytochemical studies on *Alstonia scholaris*.

Zeitschrift fur Naturforschung - Section B. J Chem Sci 2010;65:203-10.

15. Dung NX, Ngoc PH, Rang DD, Nhan NT, Klinkby N, Leclercq P. Chemical composition of the volatile concentrate from the flowers of Vietnamese *Alstonia scholaris* (L.) R.Br, Apocynaceae. J Essent Oil Res 2001;13:424-6.
16. Dhar DN, Suri SC, Dwivedi P. Chemical examination of the flowers of *Alstonia scholaris.* Planta Med 1977;31:33-4.
17. Dutta SC, Bhattacharya SK, Ray AB. Flower alkaloids of *Alstonia scholaris*. Planta Med 1976;30:86-9.
18. Hemalatha K, Satyanarayana D, Subrahmanyam EV. Phytochemical constituents of root bark of *Alstonia scholaris*. R. Br. Asian J Chem 2008;20:5405-8.
19. Salim AA, Garson MJ, Craik DJ. New indole alkaloids from the bark of *Alstonia scholaris.* J Nat Prod 2004;67:1591-4.
20. Feng T, Cai XH, Zhao PJ, Du ZZ, Li WQ, Luo XD. Monoterpenoid indole alkaloids from the bark of *Alstonia scholaris.* Planta Med 2009;75:1537-41.
21. Chakravarti D, Chakravarti RN, Ghose R. Triterpenes of *Alstonia scholaris* (dita-bark). Experientia 1957;13:277.
22. Feng T, Cai XH, Du ZZ, Luo XD. Iridoids from the bark of *Alstonia scholaris.* Helv Chim Acta 2008;91:2247-51.
23. Yamauchi T, Abe F, Padolina WG, Dayrit FM. Alkaloids from leaves and bark of *Alstonia scholaris* in the Philippines. Phytochemistry 1990;29:3321-5.
24. Cai XH, Shang JH, Feng T, Luoa XD. Novel alkaloids from *Alstonia scholaris* Zeitschrift fur Naturforschung - Section B. J Chem Sci 2010;65:1164-8.
25. Ye YQ, Wu N, Yang LJ, Nian X, Zhang DY, Gao YT. Speciation analysis of eight metal elements in the leaves of *Alstonia scholaris* by flame atomic adsorption spectrometry. Guang Pu Xue Yu Guang Pu Fen Xi. 2009;29; 3416-9.
26. Khyade MS, Vaikos NP. Phytochemical and antibacterial properties of leaves of *Alstonia scholaris* R. Br. Afr J Biotechnol 2009;8:6434-6.
27. Hirasawa Y, Miyama S, Kawahara N, Goda Y, Rahman A, Ekasari W, *et al*. Indole alkaloids from the leaves of *Alstonia scholaris.* Heterocycles 2009;79:1107-12.
28. Hui T, Sun T, Zhu L, Guo W, Rao G. Flavonoids in leaves of *Alstonia scholaris.* Zhongguo Zhong Za Zhi 2009;34:1111-3.
29. Yamauchi T, Abe F, Chen RF, Nonaka GI, Santisuk T, Padolina WG. Alkaloids from the leaves of *Alstonia scholaris* in Taiwan, Thailand, Indonesia and the Philippines. Phytochemistry 1990;29:3547-52.
30. Dutta M, Laskar S. Hydrocarbons in the surface wax of the leaves of *Alstonia scholaris* (Linn.) R.Br. Orient J Chem 2009;25:437-9.
31. Wang F, Ren FC, Liu JK. Alstonic acids A and B, unusual 2, 3-secofernane triterpenoids from *Alstonia scholaris.* Phytochemistry 2009;70:650-4.
32. Xu Y, Feng T, Cai XH, Luo XD. A new C13-norisoprenoid from leaves of *Alstonia scholaris*. Chin J Nat Med 2009;7:21-3.
33. Cai XH, Tan QG, Liu XP, Feng T, Du ZZ, Li WQ, *et al*. A cage-monoterpene indole alkaloid from *Alstonia scholaris.* Org Lett 2008;10:577-80.
34. Cai XH, Liu YP, Feng T, Luo XD. Picrinine-type alkaloids from the leaves of *Alstonia scholaris.* Chin J Nat Med 2008;6:20-2.
35. Deepthi SR, Remya R, Thankamani V. Antibacterial activity studies and phytochemical screening on the methanol extract of *Alstonia scholaris* R. Br. Res J Biotechnol 2008;3:40-3.
36. Cai XH, Du ZZ, Luo XD. Unique monoterpenoid indole alkaloids from *Alstonia scholaris.* Org Lett 2007;9:1817-20.
37. Anurakkun J, Bhandari N, Kawabata. α-Glucosidase inhibitors from Devil tree (*Alstonia scholaris*). Food Chem 2007;103:1319-23.
38. Shetty P, Mangaonkar K, Sane RT. HPTLC determination of ursolic acid in *Alstonia scholaris* R. Br. J Planar Chromatogr - Mod TLC. 2007;20:65-8.
39. Zhou H, He HP, Luo XD, Wang YH, Yang XW, Di YT, *et al*. Three new indole alkaloids from the leaves of *Alstonia scholaris.* Helv Chim Acta 2005;88:2508-12.
40. Macabeo AP, Krohn K, Gehle D, Read RW, Brophy JJ, Cordell GA, *et al*. Indole alkaloids from the leaves of Philippine *Alstonia scholaris.* Phytochemistry 2005;66:1158-62.
41. Kam TS, Nyeoh KT, Sim KM, Yoganathan K. Alkaloids from *Alstonia scholaris.* Phytochemistry 1997;45:1303-5.
42. Ghosh R, Roychowdury P. The structure of an Alkaloid, Picrine, from *Alstonia scholaris.* Acta Cryst 1988;44:2151-4.
43. Rastogi RC, Kapil RS, Popli SP. Picralinal - A key alkaloid of picralima group from *Alstonia scholaris* R. Br. Experientia 1970;26:1056.
44. Rahman A, Alvi KA. Indole alkaloids from *Alstonia scholaris.* Phytochemistry 1987;26:2139-42.
45. Rahman A, Alvi KA, Abbas SA, Voelter W. Isolation of 19,20-Z-Vallesamine and 19,20-E-Vallesamine from *Alstonia scholaris.* Heterocycles1987;26:413-9.
46. Rahman A, Alvi KA, Muzaffar A. Isolation and 1H/13C-NMR studies on 19,20-dihydrocondylocarpine: An alkaloid from the leaves of *Ervatamia coronaria* and *Alstonia scholaris.* Planta Med 1986;4:325-6.
47. Rahman A, Asif M, Ghazala M, Fatima J, Alvi KA. Scholaricine, an alkaloid from *Alstonia scholaris.* Phytochemistry 1985;24:2771-3.
48. Banerji A, Siddhanta AK. Scholarine: An indole alkaloid of *Alstonia scholaris.* Phytochemistry 1981;20:540-2.
49. Chatterjee A, Mukherjee B, Ray AB, Das B. The alkaloid of the leaves of *Alstonia scholaris* R. Br. Tetrahedron Lett 1965;6:3633-7.
50. Jain L, Pandey MB, Singh S, Singh AK, Pandey VB. A new indole alkaloid from *Alstonia scholaris.* Nat Prod Res 2009;23:1599-02.
51. Jain L, Singh S, Pandey MB, Pandey VB. Alkaloids of *Alstonia scholaris.* J Indian Chem Soc 2009;86:758-60.
52. Wongseripipatana S, Chaisri L, Sritularak B, Likhitwitayawuid K. Indole Alkaloids from the Fruits of *Alstonia scholaris*. Thai J Pharm Sci 2004;28: 173-80.
53. Boonchuay W, Court WE. Minor alkaloids of *Alstonia scholaris* root. Phytochemistry 1976;15:821.
54. Thomas PS, Kanaujia A, Ghosh D, Duggar R, Katiyar CK. Alstonoside, a secoiridoid glucoside from *Alstonia scholaris* Indian Journal of Chemistry - Section B. Org Med Chem 2008;47:1298-302.
55. Ansari MM, Khan SA. Pharmacognostical studies on the bark of *Alstonia scholaris* R.Br. (Chatiun). Hamdard Med 2006;49:95-103.
56. Dutta M, Senn S, Laskar S. Fatty acid composition of *Alstonia scholaris* (Linn.) R. Br. seed oil having some antibacterial principles. Biosci Biotechnol Res Asia 2010;7:481-4.
57. Macabeo AP, Krohn K, Gehle D, Read RW, Brophy JJ, Franzblau SG, *et al*. AM. Activity of the extracts and indole alkaloids from *Alstonia scholaris* against Mycobacterium tuberculosis H37Rv.Philipp Agric Sci 2008;91:348-51.
58. Gami B, Parabia F. Screening of methanol and acetone extract for antimicrobial activity of some medicinal plants species of Indian folklore. Int J Res Pharm Sci 2011;2:69-75.
59. Khan MR, Omoloso AD, Kihara M. Antibacterial activity of *Alstonia scholaris* and *Leea tetramera.* Fitoterapia 2003;74:736-40.
60. Hussain A, Zaman MK, Ramteke AM. Antibacterial activity of trunk bark of *Alstonia scholaris*. Asian J Pharm Clin Res 2010;3:46-7.
61. Jahan S, Goyal PK. Protective effect of *Alstonia scholaris* against radiation-induced clastogenic and biochemical alterations in mice. J Environ Pathol, Toxicol Oncol 2010;29:101-11.
62. Gupta U, Jahan S, Chaudhary R, Goyal PK. Amelioration of radiation-induced hematological and biochemical alterations by *Alstonia scholaris* (a medicinal plant) extract. Integr Cancer Ther 2008;7:155-61.
63. Jahan S, Gupta U, Chaundhary R, Goyal PK. Prophylactic use of *Alstonia scholaris* (Sapthaparna) against gamma irradiation. Pharmacol Online 2009;1:160-75.
64. Gupta U, Chaudhary R, Goyal PK. Post-treatment effects of *Alstonia scholaris* extract against radiation-induced biochemical alterations in Swiss albino mice. Iran J Radiat Res 2010;8:169-77.
65. Jahan S, Chaudhary R, Goyal PK. Anticancer activity of an indian medicinal plant, *Alstonia scholaris*, on skin carcinogenesis in mice. Integr Cancer Ther 2009;8:273-9.
66. Jagetia GC, Baliga MS. Evaluation of anticancer activity of the alkaloid fraction of *Alstonia scholaris* (Sapthaparna) *in vitro* and *in vivo*. Phytother Res 2006;20:103-9.
67. Sharma V, Mallick S A, Tiku AK. Anticancer Activity of Devil Tree (*Alstonia scholaris* Linn.) Leaves on Human Cancer Cell Lines. Indian J Agric Biochem 2010;23:63-5.
68. Kamarajan P, Sekar N, Mathuram V, Govindasamy S. Antitumor effect of echitamine chloride on methylcholonthrene induced fibrosarcoma in rats. Biochem Int 1991;25:491-8.

69. Jagetia GC, Baliga MS, Venkatesh P, Ulloor JN, Mantena SK, Genebriera J, *et al*. Evaluation of the cytotoxic effect of the monoterpene indole alkaloid echitamine *in-vitro* and in tumour-bearing mice. J Pharm Pharmacol 2005;57:1213-9.
70. Jagetia GC, Baliga MS. Effect of *Alstonia scholaris* in enhancing the anticancer activity of berberine in the Ehrlich ascites carcinoma-bearing mice. J Med Food 2004;7:235-44.
71. Jagetia GC, Baliga MS. The effect of seasonal variation on the antineoplastic activity of *Alstonia scholaris* R. Br. in HeLa cells. J Ethnopharmacol 2005;96:37-42.
72. Jagetia GC, Baliga MS, Venkatesh P, Ulloor JN, Mantena SK, Genebriera J, *et al*. Evaluation of the cytotoxic effect of the monoterpene indole alkaloid echitamine *in-vitro* and in tumour-bearing mice. J Pharm Pharmacol 2005;57:1213-9.
73. Keawpradub N, Houghton PJ, Eno-Amooquaye E, Burke PJ. Activity of extracts and alkaloids of Thai Alstonia species against human lung cancer cell lines. Planta Med 1997;63:97-101.
74. Gupta U, Chaudhary R, Goyal PK. Alterations in phosphatases activity in blood of mice by *Alstonia scholaris* extract after gamma irradiation. Pharmacol Online 2010;2:752-60.
75. Jagetia GC, Baliga MS. Effect of *Alstonia scholaris* in enhancing the anticancer activity of berberine in the Ehrlich ascites carcinoma-bearing mice. J Med Food 2004;7:235-44.
76. Jagetia GC, Baliga MS. Modulation of antineoplastic activity of cyclophosphamide by *Alstonia scholaris* in the Ehrlich ascites carcinoma-bearing mice. J Exp Ther Oncol 2003;3:272-82.
77. Jagetia GC, Baliga MS, Venkatesh P. Effect of Sapthaparna (*Alstonia scholaris* Linn) in modulating the benzo(a)pyrene-induced forestomach carcinogenesis in mice. Toxicol Lett 2003;144:183-93.
78. Viswanathan S, Ramamurthy N, Subramanian S, Mathuram V, Govindasamy S. Enhancement of the cytotoxic effects of Echitamine chloride by vitamin A: An *in vitro* study on Ehrlich ascites carcinoma cell culture. Indian J Pharmacol 1997;29:244-9.
79. Saraswathi V, Mathuram V, Subramanian S, Govindasamy S. Modulation of the impaired drug metabolism in Sarcoma-180 bearing mice by echitamine chloride Cancer Biochem Biophys 1999;17:79-88.
80. Jagetia GC, Baliga MS. Treatment with *Alstonia scholaris* Enhances Radiosensitivity *In vitro* and *In vivo*. Cancer Biother Radiopharm 2003;18:917-29.
81. Saraswathi V, Ramamoorthy N, Subramaniam S, Mathuram V, Gunasekaran P, Govindasamy S. Inhibition of glycolysis and respiration of sarcoma-180 cells by echitamine chloride. Chemotherapy 1998;44:198-205.
82. Shang JH, Cai XH, Zhao YL, Feng T, Luo XD. Pharmacological evaluation of *Alstonia scholaris*: Anti-tussive, anti-asthmatic and expectorant activities. J Ethnopharmacol. 2010;129:293-8.
83. Channa S, Dar A, Ahmed S. Atta-Ur-Rahman. Evaluation of *Alstonia scholaris* leaves for broncho-vasodilatory activity. J Ethnopharmacol 2005;97:469-76.
84. Shang, JH, Cai XH, Feng T, Zhao YL, Wang JK, Zhang LY, *et al*. Pharmacological evaluation of *Alstonia scholaris*: Anti-inflammatory and analgesic effects. J Ethnopharmacol 2010;129:174-81.
85. Arulmozhi S, Rasal VP, Sathiyanarayanan L, Ashok P. Screening of *Alstonia scholaris* Linn. R.Br. for wound healing activity. Opem 2007;7:254-60.
86. Arulmozhi S, Mazumder PM, Lohidasan S, Thakurdesai P. Antidiabetic and antihyperlipidemic activity of leaves of *Alstonia scholaris* Linn. R.Br. Eur J Integrative Med 2010;23-32
87. Akhtar SM, Bano H. Hypoglycemic effect of powdered *Alstonia scholaris*(Satona). Prof Med J 2002;9:208-71.
88. Bhogayata K, Sharma PP, Patel BR. A cilinical evaluation of saptaparna (*Alstonia scholaris* L., R. Br.) on Essential Hypertension. Ayu 2009;30: 318-22.
89. Shah AJ, Gowani SA, Zuberi AJ, Ghayur MN, Gilani AH. Antidiarrhoeal and spasmolytic activities of the methanolic crude extract of *Alstonia scholaris* L. are mediated through calcium channel blockade. Phytother Res 2010;24:28-32.
90. Juvekar AR, Patil RS, Joglekar SN, Shamkuwar PB, Shirodkar BJ. Mechanism of antidiarrhoeal activity of kutajarishta an ayurvedic formulation. Indian Drugs 2000;37:478-80.
91. Patil RS, Juvekar AR, Joglekar SN, Shamkuwar PB, Nimbkar SR. Study of antidiarrhoeal activity of *Alstonia scholaris* bark. Indian Drugs 1999;36:463-5.
92. Iwo MI, Soemardji AA, Retnoningrum DS, Sukrasno, U UM. Immunostimulating effect of Pule (*Alstonia scholaris* L. R.Br., Apocynaceae) bark extracts. Clin Hemorheol Microcirc 2000;23:177-83.
93. Arulmozhi S, Mazumder PM, Narayanan LS, Thakurdesai PA. *In vitro* antioxidant and free radical scavenging activity of fractions from *Alstonia scholaris* Linn. R.Br. Int J Pharm Tech Res 2010;2:18-25.
94. Ravi Shankar K, Ramesh KV, Naveena P. Free radical scavenging activity of the flower and fruit extracts of *Alstonia scholaris*. Biosci Biotechnol Res Asia 2008;5:493-4.
95. Arvind K, Rajbir K, Saroj A. Free radical scavenging potential of some Indian medicinal plants. J Med Plants Res 2010;4;2034-42.
96. Arulmozhi S, Mazumder PM, Ashok P, Sathiya Narayanan L. *In vitro* antioxidant and free radical scavenging activity of *Alstonia scholaris* Linn. R.Br. Iran J Pharmacol Ther 2007;6:191-6.
97. Kulkarni MP, Juvekar AR. Effect of *Alstonia scholaris* Linn. R.Br on stress and cognition in mice. Indian J Exp Biol 2008;47:47-52.
98. Arulmozhi S, Mazumder PM, Kangralkar VA, Narayanan LS, Thakurdesai P. Anti-Anxiety activity of *Alstonia scholaris* linn. R.Br. Pharmacol Online 2008;3:761-75.
99. Keawpradub N, Kirby GC, Steele JC, Houghton PJ. Antiplasmodial activity of extracts and alkaloids of three alstonia species from Thailand. Planta Med1999;65:690-4.
100. Gandhi M, Vinayak VK. Preliminary evaluation of extracts of *Alstonia scholaris* bark for *in vivo* antimalarial activity in mice. J Ethnopharmacol 1990;29:51-7.
101. Gupta RS, Bhatnager AK, Joshi YC, Sharma MC, Khushalani V, Kachhawa JB. Induction of antifertility with lupeol acetate in male albino rats. Pharmacol 2005;75:57-62.
102. Gupta RS, Bhatnager AK, Joshi YC, Sharma R, Sharma A. Suppression of fertility in male albino rats following α-amyrin acetate administration. Pharm Biol 2004;42:98-104.
103. Gupta RS, Sharma R, Sharma A, Bhatnager AK, Dobhal MP, Joshi MP, *et al*. Effect of *Alstonia scholaris* bark extract on testicular function of winstar rats. Asian J Androl 2002;4:175-8.
104. Singha UK, Guru PY, Sen AB, Tandon JS. Antileishmanial activity of traditional plants against Leishmania donovani in golden hamsters. Int J Pharm 1992;30:289-95.
105. Lin SC, Lin CC, Lin YH, Supriyatna S, Pan SL. The protective effect of *Alstonia scholaris* R. Br. on hepatotoxin-induced acute liver damage. Am J Chin Med 1996;24:153-64.
106. Baliga MS, Jagetia GC, Ulloor JN, Baliga MP, Venkatesh P, Reddy R, *et al*. The evaluation of the acute toxicity and long term safety of hydroalcoholic extract of Sapthaparna (*Alstonia scholaris*) in mice and rats. Toxicol Lett 2004;151:317-26.
107. Jagetia GC, Baliga MS. Induction of Developmental Toxicity in Mice Treated with *Alstonia scholaris* (Sapthaparna) in Utero. Birth Defects Res B Dev Reprod Toxicol 2003;68:472-8.

How to cite this article: Kaushik P, Kaushik D, Sharma N, Rana AC. Alstonia scholaris: It's Phytochemistry and pharmacology. Chron Young Sci 2011;2:71-8.

Source of Support: Nil, **Conflict of Interest:** None declared