Alstonia scholaris Linn. R. Br.: An Assessment of its Botany, Conventional Utilizaton, Phytochemistry and Pharmacology

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ABSTRACT

Alstonia scholaris, a plant that belongs to the Apocynaceae family and is widely used around the world, exhibits pharmacological properties that are advantageous to human health. It is a widely used plant that has been used in traditional medicine for a very long time. Rheumatism, antileprosy, ulcer, antiseptics, different chronic inflammatory skin conditions, rheumatoid arthritis discomfort, broad-spectrum tonic, antidysentery, and vulnerary agents have all been successfully treated with A. scholaris. Along with treating fatigue, antipyretic, anticholeric, malaria fever, irregular and unbalanced menstruation, hepatic problems, diabetes, and dysentery, it has also been beneficial in treating these other conditions. It possesses astringent, analgesic, anti-inflammatory, and anti-diabetic effects. Additionally, it has cytotoxic, radioprotective CNS, anti-arthritic, anti-cancer, antioxidant, anti-malarial, and anti-cancer effects. The numerous derivative metabolites were taken into account in the pioneering research on phytochemical analysis from the various plant sections. The plant displayed an abundance of metabolites, including tocopherols, polyunsaturated fatty acids, carboxylic acids, proteins, and carbohydrates. With a variety of biological functions, it also shown pharmaceutical efficacy. This evaluation seeks to acquaint the reader with the plant by adding to a clear overview of the botanical distinctiveness, typical uses, phytochemistry, and biological and pharmacological activities.

Keywords: A. scholaris, Traditional medicine, Phytoconstituents.

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INTRODUCTION

Traditional medicine is a collection of information, acquaintances, skills (ability to apply learned knowledge), and performances based on theories, viewpoints, and understanding of various ethnic groups, whether they are understandable or not, and used for maintaining and securing wellbeing as well as for the treatment, mitigation, identification, and management of physical or mental illnesses. Because it is safe, affordable, and pharmacologically effective, conventional medicine is widely utilised to treat a wide range of illnesses in most nations.^[1,2]



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Alstonia, a member of the Apocynaceae family, is a well-known medicinal plant. This medicinal plant is widely used by humans all over the world to treat a variety of ailments. *A. scholaris* has successfully treated a variety of inflammatory chronic skin diseases, rheumatic pain, general tonic, antidysenteric agent, vulnerary agents, fatigue, anti-fever, anticholeric, malaria fever, unbalanced menses, hepatic disorders, diabetes, anthelmintic, stomach upset, bone fracture, skin disorders, aphrodisiac, emmenagogue, inflammation, and urinary infections.^[3-7]

It has astringent, anti-diabetic, analgesic, and anti-inflammatory properties. It also has anti-malarial, antioxidant, anti-cancer, and cytotoxic properties, as well as radioprotective CNS and anti-arthritic properties.^[8]

Plant Profile

The Devils tree is known by several local and common names^[3-9]

Language	Vernacular Names of Saptaparna
English	Dita; Devils tree; White Cheese wood
Sanskrit	Saptaparna
Hindi	Chatiun; chitvan; saitan ka jhad; Saptaparni
Gujarati	Saptaparni
Malayalam	Daivapala
Kannada	Doddapala
Tamil	MukumPalai; Elilaippala
Telugu	Edakulapala
Marathi	Saptaparni
Bengali	Chattin
Unani	Kashim

History

In history, Linnaeus named the plant systematically as Echites scholaris. Conversely, to admiration to Dr. Charles Alston (1685-1760), the Botany Professor at Edinburgh University, great scientific writer and King's garden custodian at Holyrood and amongst the few botanists who refused to accept the Linnaean taxonomic classification after its establishement. The common nomenclature was altered to Alstonia, while the genus name Scholaris was kept to indicate its utilization in schools in South East Asia, where its wood is conventionally utilised to craft slates and blackboards. The further synonyms of the plant comprise Tabernaemontana alternifolia Burm, Pala scholaris (L.) Roberty and Echites pala Buch-Ham ex Spreng.[3-10] Since the leaves are originate in swirls of seven; this plant is referred as sapthaparna or saptaparni (sapta meaning seven and parna or parni meaning leaves in Sanskrit). The leaves arrangement if A. scholaris is depicted in Figure 1.

Cultivation

A. scholaris is resilient tree and it has a preference of well-drained soils. It achieves adulthood in 8 to 10 years. Its propogation can be done by number of methods include cuttings (which root effortlessly in soil), air-layering and implanting (cleave and upturned T-grafting) and seeds (gathered from matured unsplited shells). It worked as moderator plant for *Pauropsylla tuberculata*, a category of psyllid that manufactures galls above folio exterior which appears an unattractive pocket. Sowing of seeds is one of the best propogation methods for elevating the harvest; generally no pre-treatment is necessary to grow the crop. Throughout summer, fruits may be collected prior to splitting of slender and stiff pods. Seeds are fluffy however incapable to disperse

effortlessly and involuntarily. It may be cultivated under a variety of climatic situations in India, from tropical to sub-tropical. On the other hand, it flourishes healthy in vicinity having annual rainfall around 100 to 150 cm, since it favors a reasonably moist environment. The species thrives in the well-aerated red alluvial soil. It may also develop in black cotton soils; however its augmentation is sluggish because of the wet soil conditions that triumph during the rainy season.^[3-10]

Botanical Descriptions

Parts Used

Each and every one components of the plant counting matured fruits, leaves, trunk, and flora can be utilized for the management of various diseases.^[3-8]

Morphology

A. scholaris, an epiphyte with climbing and rooting branches. The *A. scholaris* is a middle-sized to large, glabrous tree that can grow up to 20 metres tall and 10 metres wide in urban areas, and up to 50 to 60 metres tall in its natural habitat. Rounded, denser, pagoda-shaped, and multi-tiered mature crowns are visible (Figure 2).

Its adolescent twigs are abundantly lenticellate, rectangular flakes appeared on peeling off, and its full-grown outer bark is grayish-pale brown, smooth-scaly. Internal bark has a cream, golden, or straw hue and is covered in a lot of milky and bitter saps. The bark has a strong bitter flavour and almost no scent.

The tops of the leaves are glossy, while the bottoms are dull. The leaves are leathery, barely obovate to very scarcely spathulate with cuneate base and curved tip, and have 25 to 50 pairs of lateral veins that occur at an angle of 80-90° to the midvein. Cymes are intense and pubertal, with a stretched peduncle of 4 to 7 cm (1.6 to 2.8 inches). Pedicels are typically as long or shorter than the calyx.

The corolla is white and tubular, overlapping toward the left, 6-10 mm (0.24-0.39 inches); the lobes are mostly ovate or mostly obovate, 2-4.5 mm (0.079-0.177 inches); the lobes are predomintly oval or mostly obovate in shape, 2 to 4.5 mm (0.079 to 0.177 in). The ovaries appear inconspicuous and pubescent. Follicules have a distinct, linear appearance. Flowers bloom between September and October. The fragrance of the blossoms is strikingly similar to that of the Raatrani (*Cestrum nocturnum*) flower, which blooms at night (Figure 3).

A. scholaris seeds have an oblong shape and have ciliated edges, and ending in clumps of hair 1.5 to 2 cm (0.59 to 0.79 in) (Figure 4 a, b).

Fruits that mature from green to brown and have thin, linear, dehiscent follicles that are 20–40 (-63) cm long and 3-5 mm



Figure 1: Arrangement of leaves of A. scholaris.

wide that are generated in pendulous pairs. Seeds are many, tiny, smooth, tufted on the tips, and wind-dispersed (Figure 5).

The plant is mostly native to the Indian subcontinent, Bangladesh, Sri Lanka, Nepal, Bhutan, Pakistan, Southeast Asia, including Indonesia, the Philippines, Malaysia, Laos, Cambodia, Papua New Guinea, Vietnam, Myanmar, Thailand, China, Yunnan, and Guangxi, as well as Australia and Queensland. However, it can frequently be seen in the state of West Bengal in India. It also occurs in Maharashtra, Karnataka, Kerala, Tamil Nadu, Bihar, Goa, and the Andaman and Nicobar Islands in other parts of India.^[3-13]

Taxonomic arrangement of A. Scholaris Linn. R. Br.

Taxonomy	Alstonia scholaris	
Kingdom	Planta, Vegetal, Plants	
Subkingdom	Tracheobionta, Vascular Plants	
Division	Mangoliophyta, Flowering Plant	
Class	Mangoliopsida, Dicotyledon	
Subclass	Asteridae	
Order	Gentianales	
Family	Apocynaceae	
Tribe	Plumeriae	
Subtribe	Alstoniinae	
Genus	Alstonia	
Identifications of phytochemicals constituents		

Phytochemical constituents^[14-26] and pharmacognostic^[27-32] analysis of this species have been reported by numerous researchers.



Figure 2: A. scholaris tree.



Figure 3: Flowers of A. scholaris.

In general *A. scholaris* is a plant that encloses alkaloids, flavonoids, coumarin derivatives, leucoanthocyanin, reducing sugars, simple

phenolics, steroids, saponins and tannins. The extract of Leaves comprises of different elements for example Cu, Zn, Fe, Ca, Cr, Mn and Cd.^[33]

Primary and secondary metabolites were found in the current plant according to previous phytochemical screening. Some of the numerous secondary metabolites from the various plant components have been discovered by preliminary phytochemical screening. Table 1 lists compounds that were extracted from oils and other extracts of different *A. scholaris* sections.

Investigation of phytochemicals of the *A. scholaris* affirms the occurrence of a variety of phytoconstituents for example alkaloids, cardiac glycosides, flavonoids, terpenoids, tannins, saponin, catechin, coumarin, phenolic compounds, glycoside and steroidal xanthoprotein, proteins, reducing sugars, carbohydrates,



Figure 4: Seeds of A. scholaris.



Figure 4b: Fruits of A. scholaris.

phytosterols, fats and fixed oils, gums and mucilages in accordance with classic procedures in its different extracts as shown in Table 2.

Alkaloids are amongst the major components of the species. Amongst different alkaloids, Echitamine, Echitamine chloride, Rhazine, Nareline, Pseudo Akuammigine, lagumamine (19- hydroxytubotaiwine), angustilobine B acid, losbanine (6,7-seco-6-norangustilobine B), tubotaiwine, its oxide, 6,7-secoangustilobine B; 17-O-Acetyl echtamine, echitamine, manilamine, N4-methylangustilobine B, vallesamine, angustilbine β -N4-oxide, 20(s)tubotaiwine and 6,7-secoangustilobine Scholarine, Scholaricine, Dihydrocondylocarpine, Β, 19.20-Z-Vallesamine and 19.20-E-Vallesamine, Picrinine, Alschomine and Isoalschomine, Mataranine A and B, monoterpenoid indole alkaloids, Picralinal of picralima group, Picrinine-type alkaloids, N 1-methoxymethyl Picrinine, corialstonine and corialstonidine etc. have been reported.

Correspondingly, it has been establish to enclose additional alkaloidal derivatives viz. picrinine, alschomine, 19-epischolaricine, nareline, N- β -methylscholarcine, N- α -methyl burnamine and vallesamin-N- β -oxide and angustilobine.^[76]

The other species of genus of Alstonia i.e. *A. glaucescens* have been accounted to contains indole alkaloids like 17-O-acetyl-Nb-demethyl echitamine, echitamidine-N-Oxide, echitaminic acid, sweroside, echitamidine, Nb-demethyl echitamine, 20-epi-19-echitamidine, *N*-bdemethylechtamine-*N*-oxide and echitamine.^[77] Among the further components, a novel flavanone glucoside Iso-okanin-7-O-alpha-lrhamnopyranoside, and a secoiridoid glucoside Alstonoside, (Thomas *et al.*, 2008)^[73] have been recorded.

Leaves of *A. scholaris* showed the existence of quercetin, isorhamnetin, isorhamnetin-3-*O*- β -*D*-galactopyranoside, ursolic acid, betulin, betulinic acid, alstonic acid A&B, stigmasterol, β -sitosterol, scholaricine, alstonamine, alschomine, angustilobine-B acid, akuammidine, rhazimanine, losbanine, lagunamine. It has been further reported that *A. scholaris* leaves contails the combinations of erythrodiol (1a), uvaol (1b), and betulin (1c); oleanolic acid (2a) and ursolic (2b); β -amyrin acetate (3b) and α -amyrin acetate (3b); β -sitosterol (4a) and stigmasterol (4b); squalene (5); β -sitosteryl-3 β -glucopyranoside-6'-*O*-fatty acid esters (6); and chlorophyll a (7). The checal structures of compound 1-7 are presented in Figure 5.

The bark contains alkaloids echitamine, ditamine, losbanine, picrinine, alstonine, and alstonosides. Stem Bark of *A. scholaris* constitutes 17-*O*-acetylechitamine, akuammiginone, echitaminic acid, echitamine, echitamidine *N*-oxide, scholarisines B-G, alstonoside, isoboonein, loganin, scholareins A-D.^[3-7]

Flowers of *A. scholaris* reported the presence of strictamine, picrinine, ursolic acid, amyrin acetate, linoleic acid,

 3β -Acetate-24-nor-urs-4, 12-diene ester triterpenes, 3,28- β -Diacetoxy-5-oleatriterpene, linalool, α -terpineol.

Despite the fact that methanolic and acetone extracts of every plant part were found to contain significant amounts of total phenolic compounds ranging from 111.1 to 238.5 mg GAE/g extract, absolute ethanol was found to be an effective solvent for isolating the phenolic compounds from different fractions of *A. scholaris.* Figures 6 and 7, respectively, depict the structure and absolute stereochemistry of the isolated (-)-alstoscholarisines A-E and (+)-alstoscholarisines F-J. They noted the presence of steroidal components, anthraquinone derivatives, tannins, phenolic compounds, terpenoids, saponins, and alkaloidal components.

Bioactivity and Pharmacological Properties *Traditional uses*

It is applied as astringent, antiseptics, used in rheumatism, antileprotic, ulcer, and to treat different inflammatory persistent skin disorders, general tonic, and rheumatoid pain. It also been used as anticholeric, antidysentery, antipyretic, antimalarial, vulnerary agents, aphrodisiac, antidiabetes, anthelmintic in conjunction with it also useful in stomachache, emmenagogue, fatigue, hepatic disease, irregular menses, skin diseases, swelling, bone fracture, urinary tract infections.^[3-13]

The milky juice is useful on ulcers and on rheumatic pains; mixed with oil and dropped in the ear it alleviates otitis. The bark tincture acts in some cases as a potent galactogogue.

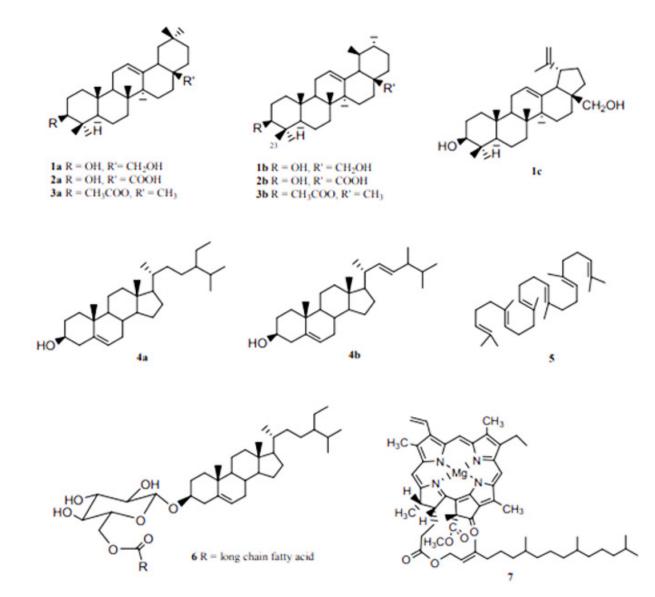


Figure 5: Chemical structure of erythrodiol (1a), uvaol (1b), betulin (1c), oleanolic acid (2a), ursolic (2b), β-amyrin acetate (3b), α-amyrin acetate (3b), β-sitosterol (4a), stigmasterol (4b), sualene (5), β-sitosteryl-3β-glucopyranoside-6*-O-fatty acid esters (6), chlorophyll a (7) from the leaves of *A. scholaris*.

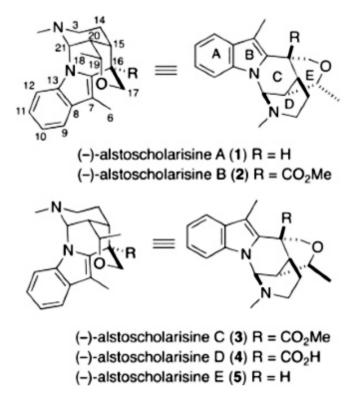


Figure 6: Structure and absolute stereochemistry of (-)-alstoscholarisines A-E.

Literature evaluation has exposed that extracts and isolated compounds of *A. scholaris* confirms antidiabetic, analgesic and antiinflammatory, antimalarial, antioxidant, anticancer and cytotoxic activity, radio protective CNS activity and antiarthritic activity.^[7]

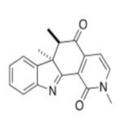
Antidiabetic activity

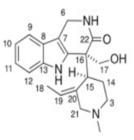
Hypoglycemic potential of triterpenes from *A. scholaris* was studied and reported by Ragasa *et al.* They discovered hypoglycemic activity in betulin and lupeolus acetate.^[78]

Hypoglycemic activity and antihyperlipidemic effects on diabetic induced by streptozotocin in rats by *A. scholaris* Linn. bark was reported by Bandawane and co-workers. The research suggested that the bark having important effects on lipid profile and *A. scholaris* bark potential in diabetes and associated cardiovascular impediments because of its antidiabetic and antihyperlipidemic activity.^[79]

Arulmozhi and co-workers depicted antidiabetic and antihyperlipidemic potential of *A. scholaris* Linn. R. Br. Leaves. The study concluded that ethanolic extract of *A. scholaris*, along with the antidiabetic activity, it also having antihyperlipidemic and antioxidant potential in diabetic rats induced by streptozotocin.^[80]

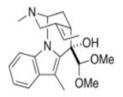
Anurakkun *et al.*, reported α -Glucosidase blockers isolated from Dita. The inhibitory activity of α -glucosidase has been observed in aqueous methanol extract from dried leaves of Devil tree.





(+)-alstoscholarisine F (6)

N 3 14 21 | 15 18 12 13 N 19 NR 11 2 13 N 19 NR 11 2 16 17 OH



(+)-alstoscholarisine J (10)

(+)-alstoscholarisine G (7)

(+)-alstoscholarisine H (8) R = H (+)-alstoscholarisine I (9) R = CO₂Me

Figure 7: Structure and absolute stereochemistry of (+)-alstoscholarisines F-J.

Active principles were equipped from rat small intestine acetone powder, isolated and recognized against α -Glucosidase.^[81]

Antidepressant

A. scholaris and its effects on stress and cognition in mice were described by Kulkarni and Juvekar. They came to the conclusion that the methanolic bark extracts normalised all the stress-induced indicators, including cortisol levels, carbohydrate, protein, triglycerides, and cholesterol, when administered.^[82]

Antibacterial Activity

Maurya *et al.*, reported the preparatory isolation of the *A. scholaris*' Logenetin, a bioactivator using rapid centrifugal chromatography. They reported isolation of Logenetin and its effects against gram positive and negative organism.^[83-84]

According to Khan *et al.*, *Leea tetramera* and *A. scholaris* have antibacterial properties. They came to the conclusion that the root bark portions of *A. scholaris* and *L. tetramera* were ineffective against the fungi examined.^[85-86]

Antimycobacterial activity

A. scholaris's leaves, stem bark, and root bark were extracted in methanol, and Macabeo and others claimed that this had an antimycobacterial effect. Approximately 89% of Mycobacterium tuberculosis H_{37} Rv is blocked by *in-vitro* antituberculosis activity utilising the Microplate Alamar Blue Assay (MABA) at a dosage of 50 g/mL.^[87]

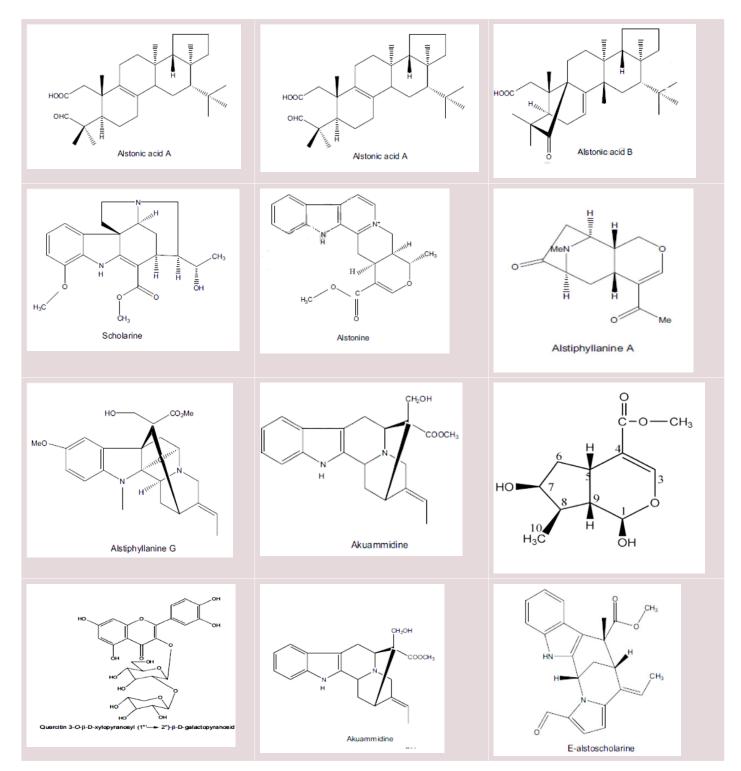
The current study^[88] was conceded out to discover the vulnerability to butanol extracts of bark of *A. scholaris* of *Mycobacterium tuberculosis*. To report the inhibition of *Mycobacterium tuberculosis*, Luciferase reporter phage (LRP)

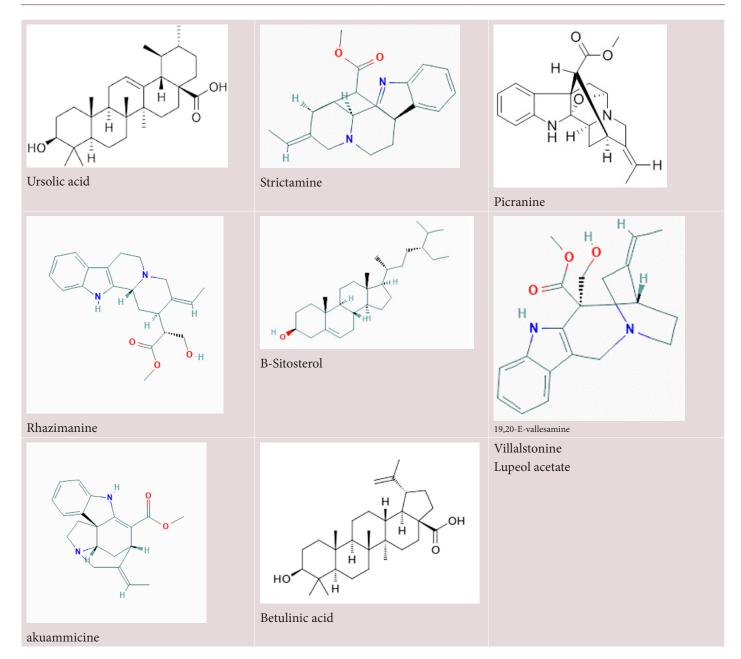
Part used	Extract/Oil	Chemical Constituents	Ref.
Flower extract		One of the oleanane types, 3,28- β -diacetoxy-5-olea-triterpene, 3 β -hydroxy-24-nor -urs-4,12,28-triene triterpene, 3 β -acetate-24-nor-urs-4,12-diene ester triterpene, along with two identified triterpenes viz., α -amyrin acetate and ursolic acid.	[14]
Flower	Volatile oil	Most important components be 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 components accomodate greater than 90% of oxygenated compounds, which committed to its aromatic odor.	[15]
	Column fraction	<i>n</i> -Hexacosane, lupeol, β -amyrin, palmitic acid and ursolic acid	[16]
	Column fraction	Picrinine and strictamine	[17]
	Root bark	Two triterpenoids, α -amyrin acetate and lupeol and a steroid, β -sitosterol	[18]
	Trunk bark	A novel indole alkaloid, akuammiginone, and a new glycosidic indole alkaloid, echitamidine-N-oxide-19- O - β - d -glucopyranoside, along with the five recognized alkaloids, echitaminic acid, akuammicine N -oxide, N -demethylalstogustine N -oxide, echitamidine- N -oxide, and N -demethylalstogustine	[19]
Bark	Alkaloidal extract	Six newer monoterpenoid indole alkaloids, scholarisines B-G collectively with 15 reported derivatives	[20]
	Bark	Triterpenoids α-amyrin acetate and lupeol	[21]
	Ethanolic extracts	Four novel 11-noriridoids namely, scholareins A-D, together with three reported analogues, isoboonein, alyxialactone and loganin	[22]
	Alcoholic extracts	17-O-acetylachitamine and echitamine	[23]
Leaves	Leaves extract	The eight elements, Ca, Mg, Cu, Fe, Zn, Cr, Cd and Mn were isolated from the leaves extract of <i>A. scholaris</i> based on conventional analytical procedures and distributed into water soluble and water insoluble state through microporous filtering film	[24]
	Column fraction	Iridoids, leucoanthrocyanins, flavonoids, alkaloids coumarins, simple phenolics, reducing sugars, steroids, tannins and saponins	[25]
	Methanolic extracts	A new indole alkaloid, akuammidine-N-oxide together akuammidine	[26]
	Leaves extracts	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	[27]
	Methanol percolate	Lagunamine (19-hydroxytubotaiwine), angustilobin B acid and losbanine (6,7-seco-6-norangustilobine B) together with tubotaiwine, its oxide and 6,7-seco-angustilobine	[28]
	Leaves extract	19-epischolaricine, N -methyl scholaricine, N -methylburnamine and valle samine N -oxide	[29]
	<i>n</i> -hexane extract	The predominant <i>N</i> -alkanes were C31 (46.43%) and C33 (21.85%), while C29 (6.16%), C32 (4.28%), C25 (3.74%) were moderately abundant. The C17 (0.39%) and C22 (0.44%) n-alkanes were present only in minor amounts.	[30]
	Hydro-alcoholic extract	2,3-secofernane triterpenoids. Alstonic acid A and B, together with an indole alkaloid, <i>N</i> -methoxymethyl picrinine.	[31]
	Column fraction	Megastigmane-3 β , 4 α , 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]

Table 1: Compounds isolated from oils and various extracts of different parts of Alstonia scholaris.

Part used	Extract/Oil	Chemical Constituents	Ref.
	Leaves extract	Forteen compounds were collected and the structures were explicated as: cycloeucalenol, β -amyrin-3-palmitate, α -amyrin acetate, 3-lupenol, lupen-3- palmitate, β -sitosterol, squalene, α -tocopherol, α -tocopherolquinone, bis(2-ethylhexyl)phthalate, dibutyl phthalate, 1-hydroxy-3,5-dimethoxyxanthone, 7,3',4'-trimethoxyl-5-hydroxylflavones, 3,5,7,4'-tetrahydroxyl flavones-3- O - β - d -glucoside	[35]
	Ethanolic extract	Monoterpenoid indole alkaloids having skeleton arrangement and two supplementary carbons, named <i>E</i> -alstoscholarine and <i>Z</i> -alstoscholarine	[36]
	Leaves extract	Ursolic acid determined by HPTLC	[37]
	Alcoholic extracts	Three new akuamillan type indole alkaloids, i.e. 5-methocystrictamine (=methyl (5β, 16R, 19E)-5methoxyakuaramilan-17-oate, methyl (16R, 19E)-1,2-dihydro-16-(hydr oxymethyl)-5-oxoakuammilan-17-oate, and methyl (2β, 16R, 19E)-4,5-didehydro-1,2-dihydro-2-hydroxy-16-(hedroxymethyl)akuammilan-4-ium-17-oate chloride	[38]
	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 identified indole alkaloids, (e)-vallesamine, angustilobine B N4-oxide, (<i>S</i>)-tubotaiwine, and 6,7-seco- angustilobine B	[39]
	Leaves extract	Three novel indole alkaloids, nareline ethyl ether, 5-epi-nareline ethyl ether and scholarine- $N(4)$ oxide, along with picrinine and sclolaricine, the nareline methyl ether	[40]
	Leaves extract	Picrinine and akuammidine	[41]
	Alcoholic extracts	Picrinal	[42]
	Alcoholic extract	Alstonamine, novel indole alkaloid and rhazimanine, sitsirikine category indole alkaloid	[43]
	Methanolic extract	Racemic mixture of 19,20- <i>E</i> -vallesamine and 19,20- <i>Z</i> -vallesamine	[44]
	Leaves extract	19,20-Dihydrocondylacarpine	[45]
	Ethanolic extract	A new alkaloid, scholaricine, has been isolated. It was elucidated as 2-demethylscholarine	[46]
	Ethanolic extract	A new alkaloid designated scholaricine. It was (±)12-methoxyechitamidine	[47]
	Leaves extract	alkaloid-a, a newer indole alkaloid, along with echitamine and echitamidine	[48]
Fruit	Pod	N-formylscholarine, a novel indole alkaloid, along with strictamine, picrinine and nareline indole alkaloid picrinine, strictamine and nareline	[49]
Truit	Methanolic extract	Alkaloids, 19- <i>E</i> -Picrinine, 19- <i>E</i> -akuammidine, 19- <i>E</i> -vallesamine and 19- <i>S</i> -scholaricine	[50]
Root	Bark	Ψ -akuammigine, akuammicine; akuammicine-N-methiodide; akkuammicine-N-oxide; indole alkaloids; N-demethylechitamine, tubotaiwine	[51]
Stem	Hydro- alcoholic extract	Alstonoside; a newer secoiridoid glucoside, along with formononetin-7-O- β - <i>d</i> -apiofuranosyl-(1 \Rightarrow 6)- β - <i>d</i> -glucopyranoside and biochanin-A-7-O- β - <i>d</i> -apiofuranosyl-(1 \Rightarrow 6)- β - <i>d</i> -glucopyranoside; two isoflavone apioglucosides	[52]
	Bark	0.200% total alkaloids, 0.07% steroids and 0.44% resins	[53]
Trunk	Bark	Akuammiginone; novel indole alkaloid and echitamidine- <i>N</i> -oxide-19- <i>O</i> - β - <i>d</i> -glucopyranoside; novel glycosidic indole alkaloid along with the five recognized alkaloids, echitaminic acid, <i>N</i> -demethylalstogustine- <i>N</i> -oxide, akuammicine- <i>N</i> -oxide, echitamidine- <i>N</i> -oxide and <i>N</i> -demethylalstogustine	[54]
Seed	<i>n</i> -Hexane extract	Oil of mature seed contains oleic acid (65.66%), linoleic acid (12.15%, palmitic acid (13.77%) and stearic acid (8.42%)	[55]

Table 2: Structures of compounds isolated from Alstonia scholaris Linn. R. Br.





assay and an *in-vitro* assay based on viability inactivation by a modus operandi analogous to the neutralisation assay was used. When administered with the butanolic extract after 6 days of incubation, the *in-vitro* bioassay findings demonstrated complete vulnerability to the quick growth Mycobacterium species as compared to control.

Immunomodulatory activity

Inducing apoptosis in the A549 Cell Line and enhancing immunomodulatory activity in C57BL/6 Mice are two effects of combining the alkaloids and triterpenes of *A. scholaris* (Linn.) R Br leaves. These findings offer early proof that triterpenes and alkaloids both have immune modulation and apoptosis-inducing properties, and that their combination has a more potent effect than each class alone.^[40,42] Pule (*A. scholaris*) bark extracts have an immunostimulatory effect. At dosages of 50 and 100 mg/kg body weight in this investigation, the aqueous extract had no impact on the amount of primary antibodies. The aqueous extract stimulated cellular immunity at a dose of 50 mg/kg body weight while inhibiting the delayed type of hypersensitive reaction at a dose of 100 mg/kg b.w.^[89]

Retinoid-Induced Skin Irritation Inhibition Activity

A. scholaris Linn. R. Br. both *in-vitro* and *in-vivo* dramatically decreases retinoid-induced skin sensitivity. The findings indicated that *A. scholaris* is a potential substance that may improve the anti-aging properties of retinoids while minimising their capacity to irritate skin.^[90]

Part used	Phytoconstituents	Activity reported	Ref.
Bark	Ditamine, echitamine, echitenine, echicaoutchin, echicerin, echitin, echitein, echiretin, ditain, ditamine, losbanine, 6,7-seco angustilobine B, Nb - demethyl	Tonic, aphrodisiac, febrifuge, stimulant, expectorant, alterative, carminative, anti- periodic, astringent and stomach ache. Used to treat leprosy, dyspepsia, malarial fever, Leishmania infection.	[121]
	echitmaine, 17-Oacetyl echitamine, picraline deacetyl, lupeol and β-sitosterol.	 Stimulant, carminative, stomachic, bitter tonic, astringent, aphrodisiac, expectorant, febrifuge, alterative and antiperiodic. Bark in Ayurveda-febrifuge, alterative, tonic and gastrointestinal sedative. Infusion, Tincture-galactogogue. Fresh bark extract in milk-leprosy, dyspepsia. Amritashtakapachana-valuable in debility, after effects of fever, chronic diarrhoea, dysentery and catarrhal fever. Decoction (Pachan) - After effects of Malaria, distinct drop in fever. Philippines – Fever and dysentery. Cambodia-Astringent, antidysenteric and emmenogogue. Chronic plaudism with enlargement of spleen and liver. Unani: Ingredient of 'Kashim'. Homoeopathy: Malarial fever, anaemia, indigestion, general debility and other stomach ailments. Ayush- 64: Microfilaraemia. Ethanolic extract of Stem bark: Antileishmanial activity. Used in treatment of chronic diarrhoes, dysentery and bowel 	[122]
		movements	[read]
Latex of bark	Caoutchouc and resins	Pimple, dental caries, pyorrhea.	[121]
		Used in ulcers, sores, tumors, and in rheumatoid pain, Mixed with oil and dropped into ears, relieves earache.	[123]
Tender Leaves	Picrinine, nareline, akuammidine, picralinal, akuammigine, betulin, ursolic acid, β - sitosterol, flavonoids, phenolic acids, scholarine.	Leaves pulverized to make poultice in treatment of ulcers. Used in snake bite and scorpion bite.	[4]
Leaves	Alschomine, isoalschomine, tubotaiwine, Nb -oxide, lagunamine, Nb – methyl	Used in treatment of ulcer, rheumatic pain, asthma and diabetes.	[2,3]
	scholaricine, pseudoakkuammigine Nb oxide, akuammidine, Na-methyl burnamine, picraline, picrinine, picrarinal, areline, angustilobine B acid, 6,7-seco angustilobine B, losbanine, vallesamine, vallesamine Nb oxide, 6, 7 seco-19, 20 α-epoxy angustilobine B.	Used against beri-beri, congestion of liver, dropsy and ulcers.	[123]
Flower	Picrinine, strictamine, tetrahydroalstonine, n-hexacosane, lupeol, β-amyrin, palmitic acid, ursolic acid	Used in asthma and other respiratory problems.	[2,3]
Roots	Picraline diacetyl	Used in enlarged liver with pain.	[2,3]

Table 3: Biological activities of parts of A. scholaris.

Anticancer activity

On several types of carcinomas, the chemopreventive impact of various extracts of *A. scholaris* was investigated.^[77,91-104] The antitumor efficacy of the *A. scholaris* alkaloid fraction was assessed *in-vitro* and *in-vivo*. The antineoplastic activity of HeLa cells treated with ethanolic extracts increased over time in a time-dependent manner; the maximum activity was shown after the cells were exposed to the extracts for 24 hr.^[92]

Activity	Part/extract	Animal model/cell line	Ref.
Antituberculosis	Methanol extract of leaf, stem bark and root bark	The mice treated daily with rifampicin + MEAS or rifampicin + MEMI against Mycobacterium TB H_{37} Rv showed an 85% survival rate in the synergistic groups. The recovery rates for mice given MEAS 200 mg/kg daily were 62.5%.	[124]
	Butanolic extract of bark	Susceptibility of <i>M. tuberculosis</i>	[125]
Antibacterial	The methanol and acetone extract of <i>A. scholaris</i>	image27Bacterial strain: the Gram-positive bacteria were <i>S. aureus</i> (ATCC9144) (SA), <i>M. luteus</i> (ATCC4698) (ML), <i>K. pneumoniae</i> (ATCC15380) (KP), <i>B. subtilis</i> (ATCC 6051) (BS), and <i>P. aeruginosa</i> (ATCC25668) (PA); <i>E. aerogens</i> (ATCC13048) (EA), <i>S. typhi</i> (NCTC 8394) (ST) and <i>S. paratyphi A</i> (SPA) were Gram-negative bacteria	[126]
	Logenetin	They reported isolation of Logenetin and its effects against gram positive and negative organism.	[127]
	Leaf and Bark	Pronounced antibacterial activity against Methicillin Resistant <i>S. aureus</i> (MRSA) and the clinical strain Providence stuartii. Antibacterial activity was also tested against a large group of Gram positive and Gram-negative bacteria and it was found to reside maximum in the butanol and ethyl acetate fractions of methanol extract of leaf and bark	[128]
	The crude methanolic extracts of the leaves, stem and root barks of <i>A</i> . <i>scholaris</i>	The micro-organisms used were A. niger, A. rubrum, A. versicolor, A. vitis, C. albicans, C. trpicallis, C. cladospriods, P. notatum, T. mentagrophytes, T. tronsrum	[129]
	Leaf powder extracted with petroleum ether, chloroform, ethyl acetate and methanol	The micro-organisms used were <i>E. coli</i> , <i>S. typhi</i> , <i>S. aureus</i> , <i>K. pnuemoniae</i> , <i>Shigella dysenteriae</i> , <i>A.s niger</i> and <i>A. flavus</i>	[33]
	Trunk bark	Two Gram-positive bacteria including <i>B. subtilis</i> and <i>S. pyogenes</i> and four Gram-negative bacteria including <i>E. coli, K. pneumoniae, P. aeruginosa</i> and <i>Proteus mirabilis</i>	[130]
	Roots, stem bark and leaves of various solvent (Hexane, Benzene, Isopropanol, Ethyl acetate, Methanol and Water) extracts	Gram positive (<i>S. aureus, B. cereus</i> and <i>Lactococcus lactis</i>) as well as Gram negative bacteria (Aeromonas sp., <i>E. aerogenes,</i> <i>E. coli, P. aeruginosa</i> and <i>P. mirabilis</i>)	[84]
Antifungal	butanol fractions of <i>A</i> . <i>scholaris</i> and the root bark of <i>Leea tetramera</i>	They concluded that the none of the fractions were active against the fungi tested	[129]
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	[131]
	Hydro-alcoholic extract of bark	Male Swiss albino mice were studied for radiation-induced hematological and biochemical alterations Dose tolerance of <i>Alstonia scholaris</i> extract (ASE), Dose reduction factor (DRF), Endogenous colonies in spleen, LPx and GSH were studied in Swiss albino mice	[132] [133]
	Bark	Radiation-induced biochemical alteration in mice by ameliorated cholesterol and lipid peroxidation	[134]

Table 4: Pharmacological activities reported from different parts/extract of Alstonia scholaris.
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Activity	Part/extract	Animal model/cell line	Ref.
Anticancer	Bark extract	Skin carcinogenesis in Swiss albino mice	[91]
	Alkaloid fraction	<i>In-vitro</i> and <i>in-vivo</i> evaluation of anticancer activity. Treatment of Cultured human neoplastic cell lines (HeLa, HepG2, HL60, KB and MCF-7) and in Ehrlich ascites carcinoma (EAC) bearing mice. HeLa cells with 25 µg/mL of ethanolic extracts resulted in a time dependent increase in the antineoplastic activity and the greatest activity was observed when the cells were exposed to ethanolic extracts for 24 h	[92]
	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)	[93]
	Different extracts from stem bark	HeLa cell lines	[94]
Cytotoxic	Different extracts from stem bark Echitamine chloride	The benzo(a)pyrene induced for stomach carcinogenesis in mice. The ASE treatment not only reduced the frequency of splenocytes bearing one MN but also cells bearing multiple MN indicating the efficacy of ASE in inhibiting mutagenic changes induced by BaP. HeLa, HepG2, HL60, KB and MCF-7 cell lines <i>in-vitro</i> and in mice bearing EAC	[95]
	Methanol extracts of root barks of <i>A. macrophylla</i> , <i>A. glaucescens</i> , and <i>A.</i> <i>scholaris</i> , collected from Thailand	Human lung cancer cell lines, MOR-P (adenocarcinoma) and COR-L23 (large cell carcinoma), using the SRB assay	[96]
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	[97]
Chemomodulatory activity	<i>A. scholaris</i> extract (ASE) studied in combination with berberine hydrochloride (BCL)	EAC bearing mice	[98]
	Combination of 120 mg/ kg of ASE with 25 mg/kg of CPA was most effective	Mice transplanted with EAC	[99]
	Hydro-alcoholic extract	Benzo(a)pyrene (BaP) induced forestomach carcinoma in female mice	[100]
	Hydro-alcoholic extract	Enhancement of the cytotoxic effects of echitamine chloride by vitamin A EAC cell cultures	[101]
	Echitamine chloride	Modulation of the impaired drug metabolism in sarcoma-180 bearing mice	[102]
Radiosensitizing effect	Alkaloid fraction of <i>A</i> . <i>scholaris</i>	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	[103]
	Echitamine chloride from bark of <i>A. scholaris</i>	Inhibition of glycolysis and respiration of sarcoma 180 cells	[104]

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antiasthmatic and expectorant activitiesfractions and main alkaloids of A. scholaris leafmodels including annomin or suffur dioxid induced mice couphing and citric activity was investigated on guinea pigs' bronchoconstriction induced by histamine. The expectorant activity was evaluated by the volume of phenol red in mice'sBroncho-vasodilatory activityEthanolic extract of leavesGuinea pig trachea, leum[119]Broncho-vasodilatory activityEthanolic extract of leavesGuinea pig trachea, leum[119]Anti-inflammatory and analgesicThe leaf extractThe analgesic activities were investigated using acetic acid induced writhing, hotplate and formalin tests in mice. The antiinflammatory activities were investigated using acetic acid induced writhing, stopen induced are edema and carrageenan induced air pouch formation in mice, and COX-1, -2 and 5-LOX inhibition[135]Analgesic and antipyreticBenzene and methanolic scholaris leaf, three main alkaloids, fraction of Alstonia scholaris leaf, three main alkaloids, picrinine, vallesamine analgesic effect peripherally based on several in-vivo assays.[136]Anti-nociceptive and antipyreticBenzene and methanolic strates of the flowers and fruitsThe study indicated that have significant effects in hot plate the antipyretic activity of the flower and induced mice while the antipyretic activity of the flower and induced sind educed sind and evolution of koots[137]Anti-nociceptive and ruitsEthanolic extract of RootsActic acid induced mice and scholaris kas and reduces inflammatory response in carrageenan induced inflammatory. immunosuppressant activities[137]Anti-nor	Activity	Part/extract	Animal model/cell line	Ref.
activityEthanolic extract of leavesBroncho-vasodilatory activity mediated presumably by prostaglandins calcium antagonism and endothelium-derived relaxing factor(s).[119]Anti-inflammatory and analgesicThe leaf extractThe analgesic activities were investigated using acetic acid induced writhing, hotplate and formatin tests in mice. The antiinflammatory activities were determined <i>in-vivo</i> and <i>in-viro</i> , including xylene induced ear edema and carrageenan induced air pouch formation in mice, and COX-1, -2 and 5-LOX inhibition[44]Alkaloidal fraction of leavesThey concluded that the alkaloids fraction of Alstonia scholaris leaf, three main alkaloids, pricinine, vallesamine and scholaris leaf, three main alkaloids, pricinine, vallesamine analgesic effect peripherally based on several <i>in-vivo</i> assays.[41]Analgesic and antipyreticBenzene and methanolic extracts of the flowers and fruitsThe analgesic activity of the flower and fruits were studied using the writhing assay and the tail fick assay in mice while fruits[135]Anti-nociceptive and anti-inflammatory activityEthanolic extract flowers and induced inflammatory activity of the flower and fruits[137]Anti-arthritic activityEthanolic extract of leavesA scholaris has prominent antiarthritic activity which methods and reduces inflammatory response in carrageenan induced inflammatory. immunosuppressant activity on human complement and polymorphonuclear fleukocyt	Anti-tussive, antiasthmatic and expectorant activities	fractions and main alkaloids of <i>A. scholaris</i>	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	[118]
Anti-inflammatory and analgesicThe leaf extractThe analgesic activities were investigated using acetic acid induced writhing, hotplate and formalin tests in mice. The antiinflammatory activities were determined <i>in-vivo</i> and <i>in-vitro</i> , including xylene induced are determined <i>in-vivo</i> and <i>in-vitro</i> , and <i>induced xitro</i> [135]Analgesic and antipyreticAlkaloidal fraction of leavesThe analgesic activity of the flower and fruits were studied 	Broncho-vasodilatory	Ethanolic extract of leaves	Guinea pig trachea, ileum	[119]
analgesicinduced writhing, hotplate and formalin tests in mice. The antiinflammatory activities were determined <i>in-vivo</i> and <i>in-vivo</i> , and <i>in-vivo</i> , and <i>in-vivo</i> , and <i>in-vivo</i> , and <i>in-vivo</i> .induced withing, hotplate and formalin tests in mice. The antiinflammatory activities were determined <i>in-vivo</i> and <i>in-vivo</i> .induced withing, hotplate and formalion in mice, and corrageenan induced air pouch formation in mice, and corrageenan induced that the alkaloids picrinine, vallesamine and scholaricine, may produce the anti-inflammatory and analgesic effect peripherally based on several <i>in-vivo</i> assays.[44]Anti-nociceptive and anti-inflammatory activityThe analgesic activity of the flower and fruits were studied the antipyretic activity of the inflorescence of <i>A. scholaris</i> was studied by yeast induced pyrexia in rats.[137]Anti-nociceptive and anti-inflammatory activityEthanolic extract of leavesA. scholaris has prominent antiarthritic activity which may be attributed to its analgesic, antiinflammatory, immunosuppressant activities[138]Anti-arthritic activityEthanolic extractsThe attributed to its analgesic, antiinflammatory, immunosuppressant activity on could help treat rheumatoid arthritis.[14]Antiulcerogenic activityEthanolic extra	activity	Ethanolic extract of leaves	prostaglandins calcium antagonism and endothelium-derived	[119]
leavesscholaris leaf, three main alkaloids, picrinine, vallesamine and scholaricine, may produce the anti-inflammatory and analgesic effect peripherally based on several <i>in-vivo</i> assays.Analgesic and antipyreticBenzene and methanolic extracts of the flowers and fruitsThe analgesic activity of the flower and fruits were studied using the writhing assay and the tail fick assay in mice while the antipyretic activity of the inflorescence of A. scholaris was studied by yeast induced pyrexia in rats.[136]Anti-nociceptive and anti-inflammatory activityEthanolic extract RootsThe study indicated that have significant effects in hot plate methods and reduces inflammatory response in carrageenan induced inflammation.[122]Anti-arthritic activityEthanolic extract of leaves activityA. scholaris has prominent antiarthritic activity which may be attributed to its analgesic, antiinflammatory, immunosuppressant activities[114]Anti-arthritic activityEthanolic extractThe ethanolic extracts had significant antiucerogenic activity via the classical pathway. The anticomplementary action could help treat rheumatoid arthritis.[114]Antiulcerogenic activityEthanolic extract of leavesThe study concluded that DCM fraction having peripheral analgesic activity wint hack of ulcerogenic activity with lack of ulcerogenic activity with lack of ulcerogenic property. The ethyl acetate fractions didn't show any significant effects.[80]Wound healingEthanolic and aqueousExcision, incision and dead space wound healing models[139]	Anti-inflammatory and analgesic	The leaf extract	induced writhing, hotplate and formalin tests in mice. The antiinflammatory activities were determined <i>in-vivo</i> and <i>in-vitro</i> , including xylene induced ear edema and carrageenan induced air pouch formation in mice, and	[135]
antipyreticextracts of the flowers and fruitsusing the writhing assay and the tail fick assay in mice while the antipyretic activity of the inflorescence of A. scholaris was studied by yeast induced pyrexia in rats.[137]Anti-nociceptive and 			<i>scholaris</i> leaf, three main alkaloids, picrinine, vallesamine and scholaricine, may produce the anti-inflammatory and	[44]
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anti-inflammatory activitymethods and reduces inflammatory response in carrageenan induced inflammation.Image: Carrageenan induced inflammation.Anti-arthritic activityEthanolic extract of leavesA. scholaris has prominent antiarthritic activity which may be attributed to its analgesic, antiinflammatory, immunosuppressant activities[138]Stem bark extractThe activity on human complement and polymorphonuclear leukocytes was reported. In this study, stem bark extracts 			Acetic acid induced writhing and tail immersion test.	[137]
may be attributed to its analgesic, antiinflammatory, immunosuppressant activitiesThe activity on human complement and polymorphonuclear leukocytes was reported. In this study, stem bark extracts demonstrated <i>in-vitro</i> anticomplementary activity via the classical pathway. The anticomplementary action could help treat rheumatoid arthritis.[114]Antiulcerogenic activityEthanolic extractsThe ethanolic extracts had significant antiulcerogenic activity. Ite analgesic activity and antiinflammatory activity with lack of ulcerogenic property. The ethyl acetate fractions didn't show any significant effects.[80]Wound healingEthanolic and aqueousExcision, incision and dead space wound healing models[139]	Anti-nociceptive and anti-inflammatory activity	Ethanolic extract	methods and reduces inflammatory response in carrageenan	[122]
leukocytes was reported. In this study, stem bark extracts demonstrated <i>in-vitro</i> anticomplementary activity via the classical pathway. The anticomplementary action could help treat rheumatoid arthritis.Image: The ethanolic extracts had significant antiulcerogenic activityAntiulcerogenic activityEthanolic extractsThe ethanolic extracts had significant antiulcerogenic activity.[122]Ethanolic extract of leavesThe study concluded that DCM fraction having peripheral analgesic activity and antiinflammatory activity with lack of ulcerogenic property. The ethyl acetate fractions didn't show any significant effects.[139]	Anti-arthritic activity	Ethanolic extract of leaves	may be attributed to its analgesic, antiinflammatory,	[138]
Ethanolic extract of leavesThe study concluded that DCM fraction having peripheral analgesic activity and antiinflammatory activity with lack of ulcerogenic property. The ethyl acetate fractions didn't show any significant effects.[80]Wound healingEthanolic and aqueousExcision, incision and dead space wound healing models[139]		Stem bark extract	leukocytes was reported. In this study, stem bark extracts demonstrated <i>in-vitro</i> anticomplementary activity via the classical pathway. The anticomplementary action could help	[114]
analgesic activity and antiinflammatory activity with lack of ulcerogenic property. The ethyl acetate fractions didn't show any significant effects.139Wound healingEthanolic and aqueousExcision, incision and dead space wound healing models[139]	Antiulcerogenic activity	Ethanolic extracts	The ethanolic extracts had significant antiulcerogenic activity.	[122]
		Ethanolic extract of leaves	analgesic activity and antiinflammatory activity with lack of ulcerogenic property. The ethyl acetate fractions didn't show	[80]
	Wound healing		Excision, incision and dead space wound healing models	[139]

Activity	Part/extract	Animal model/cell line	Ref.
Antidiabetic and antihyperlipidemic	Ethanolic extract of leaves	Streptozotocin induced diabetic rat, also possess antihyperlipidemic and antioxidant activities	[80]
	Bark	Streptozotocin induced diabetic rats. The bark having significant effects on lipid profile and potential of <i>A. scholaris</i> bark in diabetes as well as related cardiovascular complications due to its anti-diabetic and anti-hyperlipidemic properties	[79]
Antidiabetic	Leaf powder	Powder of leaves of <i>A. scholaris</i> causes a significant decrease in blood glucose level in human volunteers with Non-insulin dependent diabetes mellitus	[140]
α-Glucosidase inhibitors	Aqueous methanol extract of leaves	Active principles against α -Glucosidase, prepared from rat small intestine acetone powder, were isolated and identified	[81]
Antihypertension	Decoction of bark	In patients with essential hypertension	[141]
Antidiarrheal and spasmolytic activities	Methanolic crude extract	Method used was castor oil induced diarrhea for <i>in-vivo</i> antidiarrheal activity and rabbit jejunum <i>in-vitro</i> model for spasmolytic activity. Antidiarrhoeal and spasmolytic effects, mediated possibly through the presence of CCB-like constituent(s).	[115]
	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	[116]
	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	[117]
Immunostimulating	Bark extracts	BALB/c mouse	[89]
<i>In-vitro</i> antioxidant and free radical scavenging	Fraction from ethanolic etract of leaves	1,1-diphenyl-2-picryl-hydrazil (DPPH) free radical scavenging, metal ion chelating, hydrogen peroxide scavenging, superoxide anion radical scavenging, and ferric thiocyanate reducing	[105]
	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	[106]
	Methanolic extract of leaves	DPPH assay and plasmid nicking assay	[107]
	aqueous extracts of bark	The study revealed highest antioxidant activity as compared to butanolic and ethyl acetate extracts in DPPH and ABTS assays.	[108]
	Flowers and fruits	The study revealed <i>in-vitro</i> model system like DPPH assay and Beta carotene Assay	[109]
Nitric oxide Scavenging	Ethanolic extract of bark	No scavenging activity	[110]
Stress and cognition	Methanolic extract of bark	Restraint stress model in mice, passive avoidance model and elevated plus maze model	[82]
Anti-anxiety activity	Ethanolic extract of leaves	Elevated plus maze, open field, hole board, light dark, mirror chamber and foot shock induced aggression models	[142]

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Activity	Part/extract	Animal model/cell line	Ref.
Anti-malarial	Methanol extracts prepared from various parts of <i>A. scholaris, A.</i> <i>macrophylla</i> and <i>A. glaucescens</i>	Anti-plasmodial activity against multidrug resistant K1 strain of Plasmodium falciparum cultured in human erythrocytes	[143]
	The petroleum ether extract and methanol extract of the bark	Antimalarial activity in mice infected with Plasmodium berghei	[144]
Anti-fertility	Lupeol acetate isolated from benzene extract of <i>A</i> . <i>scholaris</i>	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	[145]
	α-Amyrin acetate isolated from plant	Male albino rats used to study the effect on fertility.	[146]
	Bark extract	Drug showed significant antifertility effect in male rat at this dose level. The primary site of action may be meiotic germ cells	[147]
Antileishmanial	Plant extract	Plants were evaluated for antileishmanial activity with <i>Leishmania donovani</i> infected hamsters	[148]
Hepatoprotective	Plant extract	Liver injuries induced by carbon tetrachloride (CCl_4), β -d-galactosamine, acetaminophen and ethanol were investigated by means of serum biochemical and histopathologic examinations	[149]
Toxicological profile	Different doses up to 2000 mg/kg	The acute and sub-acute toxic effects of various doses of hydro-alcoholic extract of <i>A. scholaris</i> (ASE) were studied in mice and rats	[120]
	Hydro-alcoholic extract	Hematological analysis revealed a dose-dependent decrease in RBC, WBC, haemoglobin, neutrophils, and monocytes, as well as a significant increase in lymphocytes, eosinophils, and basophils. The presence of echitamine may explain the observed toxic effect of ASE.	[150]
Teratogenic effect	Hydro-alcoholic extract	The teratogenic effect was studied in the pregnant Swiss albino mice on Day 11 of gestation	[150]

It was discovered that sapthaparna was efficient at controlling the benzo(a)pyrene induced stomach cancer in mice. Additionally, it has been shown that the ASE therapy decreased the frequency of both cells and splenocytes containing numerous MN, demonstrating the effectiveness of ASE in preventing mutagenic alterations brought on by BaP. The frequency of BaP-induced MN in the treated mice's splenocytes was considerably decreased by either pre- or post-treatment with ASE.^[100]

Antioxidant activity^[105-110]

A. scholaris's phytochemical analysis and antioxidant activities were reported by Antony *et al.* In DPPH and ABTS assays, the study found that aqueous bark extracts had the highest antioxidant activity when compared to butanolic and ethyl acetate extracts.^[108]

Analgesic, anti-inflammatory, antirheumatoid and antiulcerogenic activity

A. scholaris Linn. was found to have antinociceptive and antiinflammatory properties, according to Arulmozhi and colleagues. The study indicated that ethanolic extract have significant effects in hot plate methods and reduces inflammatory response in carrageenan induced inflammation. The ethanolic extracts had significant antiulcerogenic activity.^[111]

According to Arulmozhi *et al.*, the leaves of *A. scholaris* Linn. R. Br. have antiarthritic and antioxidant properties. According to the findings of this study, ethanolic extracts have strong antiarthritic properties that may be due to their analgesic, antiinflammatory, immunosuppressant, and antioxidant properties.^[112] *A. scholaris* fractions have been shown to have analgesic, antiinflammatory, and antiulcerogenic properties by Arulmozhi *et al.* The investigation came to the conclusion that the DCM fraction

lacked ulcerogenic properties but had peripheral analgesic and antiinflammatory activities. There were no discernible impacts from the ethyl acetate fractions.^[112]

A. scholaris has been shown to have anti-inflammatory and analgesic properties by Xiao-Dong Luo *et al.* They came to the conclusion that the three primary alkaloids in the *A. scholaris* leaf, picrinine, vallesamine, and scholaricine, may have a peripherally acting anti-inflammatory and analgesic effect.^[113]

The activity of the stem bark extract of *Alstonla boonei* de wild on human complement and polymorphonuclear leukocytes was described by Labadie *et al.* Stem bark extracts in this study have *in-vitro* anticomplementary action that is mediated by the conventional mechanism. Rheumatoid arthritis treatment may benefit from the anticomplementary activity.^[114]

Antidiarrhoeal and Spasmolytic Activities

Varoius researchers reported the antidiarrhoeal properties of *A. scholaris*.^[115-117] The antidiarrheal and spasmolytic effects of the methanolic crude extract of *A. scholaris* L. were described by Shah *et al.* and are mediated via calcium channel blocking. The study's findings suggest that the crude extract of *A. scholaris* has antidiarrheal and spasmolytic properties, which may be mediated by the presence of a compound similar to CCB (s).^[115]

Antitussive, antiasthmatic and expectorant

The anti-tussive, anti-asthmatic, and expectorant properties of *A. scholaris* were reported by Xiao-Dong Luo *et al.* They discovered that the alkaloids fraction of the *A. scholaris* leaf was an antitussive, antiasthmatic, and expectorant activity component. It may also be a useful lead material for the development of respiratory disorders drugs. The primary anti-tussive and anti-asthmatic chemical, picrinine, could be used to check the quality of goods made from *A. scholaris* leaf.^[118]

According to *Shabana et al., A. scholaris* leaves have broncho-vasodilatory properties. They discovered that the *A. scholaris* leaves have broncho-vasodilatory activity that is apparently mediated by prostaglandins calcium antagonism and endothelium-derived relaxing factor (s).^[119]

The acute toxicity and long-term safety of the hydro-alcoholic extract of Sapthaparna in mice and rats were reported by Jagetia *et al.* When compared to untreated controls, they discovered that the total protein, albumin, DNA, RNA, cholesterol, glucose, glutathione, and total thiols in the 240 mg/kg ASE-treated mice decreased. RBC, WBC, haemoglobin, neutrophils, and monocytes all showed dose-dependent declines in the haematological study, while lymphocytes, eosinophils, and basophils significantly increased. The toxic impact of ASE that has been noticed may be brought on by echitamine.^[120]

Table 3 provides a review of the biological activities of isolated chemicals, while Table 4 lists the pharmacological actions of *A. scholaris.*

CONCLUSION

An ethnopharmacological approach is needed for thorough analysis of plants used in traditional medicine. As the plant A. scholaris has grown in popularity globally and has gotten quite wild in many regions of the world, it has been utilised as traditional medicine for decades. As the extracts from the various A. scholaris sections and their separated components display encouraging biological properties, there is need for more investigation. This has made natural product-based drug research interesting bio resource. Despite the plant's high traditional value and several biological functions, a thorough phytochemical investigation has not yet been adequately investigated. Consequently, a phytochemical examination of the A. scholaris plant is required. The plant A. scholaris has a wide range of pharmacological activities, and many of its isolated compounds have not been studied for their pharmacological activity. For these reasons, it seems worthwhile to scientifically validate the pharmacological properties of A. scholaris constituents, which will support the plant's long history of use by tribal people as a medicine.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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