



A comprehensive review on the phytochemistry and pharmacodynamics of *Alstonia scholaris* (L.) R. Br.

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ABSTRACT

Alstonia scholaris (L.) R. Br., a tropical plant belonging to Apocynaceae family had been a fruitful traditional medicine in ayurveda and was used in several ailments. *Alstonia scholaris* is rich in phytochemicals like alkaloids, terpenoids, flavonoids, iridoids and essential oils. These phytochemicals are isolated from roots, stem, bark, fruits, flowers and leaves of *Alstonia scholaris*. The pharmacological aspect of *Alstonia scholaris* shows its greater potential in treatment of bacterial and viral infection, inflammatory diseases, ulcers, rheumatism, diarrhoea, hyperuricemia, diabetes, malaria, neural and cardiovascular diseases. Apart from these, *Alstonia scholaris* have been found to show antioxidant, immunomodulatory, antidepressant, analgesic and anticancer properties including cytotoxicity against various cancers in vitro and in vivo conditions. However, even after showing such pharmacological relevance, the clinical and pre-clinical studies of *Alstonia scholaris* is negligible. This review provides insights to the existing knowledge of *Alstonia scholaris* and its requisite in further research, so that it can be used as a therapeutic drug in near future.

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1. Introduction

The role of medicinal plants in traditional medicine and also as raw material in pharmaceuticals has been unimaginable. Considering its vast extension, the use of therapeutic plants has been increasing all over the world. The World Health Organizations report states that at least 70% of Indians are regularly using therapeutic plants as traditional medicines for treating several diseases (WHO, 2019). The therapeutic plants have been fundamental to the Indian ethnomedicinity- Ayurveda, Sidha, Unani and Tibetan medicine, as well as other folk medicines. One such medicinal plant, *Alstonia scholaris* (L.) R. Br. (*A. scholaris*) has been known for its conventional uses and excellent pharmacological relevance. *A. scholaris* is a tropical evergreen tree belonging to the family of Dogbanes (Apocynaceae) having white coloured perfumed flowers (El-Fiki *et al.*, 2019). Commonly known the Devil's plant or Blackboard tree, *A. scholaris* was initially named as *Echites scholaris*. Later in 1811, Robert Brown renamed the genus

name to *Alstonia* to honour Prof. Charles Alston (Oktavia *et al.*, 2020). The species name scholaris was kept due to its importance in scholastics as it was used to make blackboards in school (Pandey *et al.*, 2020). The other names of *A. scholaris* are Saptaparna, Chatian, Milk wood, Phalagaruda and also known in various names as listed in Table 1 (Oktavia *et al.*, 2020).

2. Morphology and geographical distribution

A. scholaris is an epiphyte with a maximum height of 60 m having greyish brown rough bark, white milky latex, and rooting branches. The tree is rounded in shape with 4-8 whorled dense leaves. The leaves are dark green, thick, obovate to oblanceolate and narrow at the base, while the flowers are greenish white coloured, compact, umbel shaped, numerous and well scented (Figure 1). The flowering of *A. scholaris* in India is during December to March and fruiting is during May to July (Majid and Faraj, 2023). *A. scholaris* is found throughout in India, Sri-Lanka through mainland

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South-East Asia including Nepal, Thailand, Vietnam, Papua New Guinea, Southern China, Indonesia, Malaysia throughout Myanmar to northern Australia and Oceania Islands (Mahar *et al.*, 2022). It grows in evergreen as well as deciduous forests and even in plains. It can be cultivated in all climatic conditions of India, from tropical to sub-tropical regions with healthy growth at an annual rainfall of 100 to 150 cm, as it favours humid atmosphere (Tripathy *et al.*, 2019). *A. scholaris* flourishes well in red and black alluvial soil while it slugs down in rainy season due to wet soil condition (Bhandary, 2020).

3. Ethnomedical uses

The therapeutic application *A. scholaris* has been well mentioned by the name Saptaparna in the Ayurvedic text “Bhavaprakasha” which was earlier use to cure asthma, bleeding leprosy, phantom tumour, ulcers and gastric issues (Oktavia *et al.*, 2020). It also played vital role in the treatment of rheumatism, wounds, malaria, diabetes, cholera and dysentery. Moreover, *A. scholaris* was used an antipyretic and anthelmintic agent, along with major roles in stomach ache, hepatic diseases, skin rashes, swelling and urinary tract infection (Chhajed *et al.*, 2023). In the Yunnan province of China, *A. scholaris* was known as “Dai” which is used for the treatment of respiratory tract infection (Zhao *et al.*, 2021).

4. Phytochemistry

A. scholaris has been the interest of researchers due to its multi-therapeutic applications as it has rich phytochemical constituents. All the parts of the *A. scholaris* (roots, bark, leaves, stem, fruit and flower) have been chemically investigated by several researchers and found to be identified with flavonoids, alkaloids, iridoids, tannins and steroids (Ali *et al.*, 2021). Some other chemical constituents which were reported in *A. scholaris* includes coumarins, terpenoids, phlobatanins, saponins, simple phenolics, primary metabolites and secondary metabolites (Ali *et al.*, 2020). Till now more than 400 phytochemical constituents have been isolated and characterized from *A. scholaris* (Baliga, 2012). Majority of the constituents include alkaloids that are isolated from all parts of *A. scholaris* like roots, stem, bark, leaves flower and even fruits (Zhao *et al.*, 2021) (Table 2). However, out of all the constituents of *A. scholaris*, few have been found to be very important in terms of therapeutic properties (Figure 2).

5. Pharmacodynamics

5.1. Antimicrobial activity

Macabeo and others reported that the methanol extract of *A. scholaris*'s leaves, stem and root bark had an

antimycobacterial effect. Using the Microplate Alamar Blue Assay (MABA) at a concentration of 50 g/mL, in-vitro antituberculosis activity inhibits about 89% of *Mycobacterium tuberculosis* H37Rv (Tripathi *et al.*, 2019). This study was conducted to confirm the role of butanol bark extracts in *Mycobacterium tuberculosis* (Zhao *et al.*, 2021). The Luciferase reporter phage (LRP) and an in-vitro assay based upon inactivation of viability by a modus operandi similar to the neutralization assay were used to report the inhibition of *Mycobacterium tuberculosis*. Following six days of incubation, when the butanolic extract was given, the in-vitro bioassay results showed comprehensive susceptibility to the rapid expansion species of *Mycobacterium* as in contrast to control (Goel *et al.*, 2021). Another study reported that bark and leaf extract of *A. scholaris* shows ant-microbial activity against various pathogens of human (Bagheri *et al.*, 2020). Alstoscholarisine K, an indole isolated from gall-modulated leaves of *A. scholaris* has potent anti-microbial activity (Yu, 2021). Leaf extracts of *A. scholaris* also exhibits potent activity towards multi-resistant fungal and bacterial strains (Altaf *et al.*, 2019).

5.2. Antioxidant activity

A lot of investigations have been done on the phytochemical analysis and antioxidant activities of *A. scholaris*. The study discovered that, in comparison to butanolic and ethyl acetate extracts, aqueous bark extracts had the antioxidant activity at the peak level in DPPH and ABTS assays (Goel *et al.*, 2021). Antioxidant property of *A. scholaris* will help human being to fight against various disease and stay young and healthy for longer period. But this important property of *A. scholaris* is not known very well till now. So, this property of *A. scholaris* needs more investigation to help human beings with a better option with no side effects.

5.3. Anti-inflammatory, Analgesic, anti-ulcerogenic and anti-rheumatoid activity

It has been reported the antinociceptive and anti-inflammatory characteristics in *A. scholaris* by various scholars. According to the study, ethanolic extract significantly affects hot plate techniques and lessens the inflammatory response in inflammation induced by carrageenan (Sultana *et al.*, 2020). There was a noticeable antiulcerogenic effect of the ethanolic extracts. The leaves of *A. scholaris* are said to possess antioxidant and antiarthritic qualities by researchers. The results of this research indicate that ethanolic extracts have potent antiarthritic qualities, which may be related to their antioxidant, analgesic, anti-inflammatory and immunosuppressive characteristics (Khyade *et al.*, 2014).

Another study has demonstrated the analgesic, anti-inflammatory and antiulcerogenic qualities of *A. scholaris* fractions. The investigation concluded that although the DCM fraction lacked ulcerogenic properties, it did possess peripheral anti-inflammatory and analgesic properties. The effects of the ethyl acetate fractions were negligible (Banik and Das, 2023). In a study, the anti-inflammatory and analgesic properties of *A. scholaris* has been shown. The authors concluded that the three main alkaloids found in *A. scholaris* leaves—picrinine (Figure 2), vallesamine and scholaricine might have some kind of analgesic and anti-inflammatory effect that acts peripherally (Zhan *et al.*, 2023). In this investigation, the conventional mechanism behind the anti-complementary action of stem bark extracts was demonstrated in in-vitro condition. Treatment for rheumatoid arthritis may be benefited from the anticomplementary action of *A. scholaris* (Kanase and Mane, 2018).

5.4. Anti-viral activity

Researches have shown that *A. scholaris* exhibits potent activity against various viruses. According to a study, the total alkaloid (TA) of *A. scholaris* markedly decreased the production of cytokines and chemokines at the levels of mRNA and protein and significantly blocks replication of virus in A549 cells and U937-derived macrophages (Zhou *et al.*, 2020). Moreover, in A549 cells, TA inhibited the activation of signal transduction triggered by type I interferons (IFN) and pattern recognition receptor (PRR). Crucially, in a deadly PR8 mouse model, TA also improved lung histopathology, decreased viral titer, inhibited the production of proinflammatory cytokines and innate immune cell infiltration and raised the survival rate (Zhou *et al.*, 2020). Moreover, it was found that *A. scholaris* exhibits potent preventive activity against infection of SARS-CoV-2 in Hamster Model of Syrian (Rizvi *et al.*, 2023). More studied needed in this field for better therapeutic option.

5.5. Anti-diarrheal activity

A. Scholaris has been shown to have anti-diarrheal properties by several researchers. According to a study, the methanolic crude extract of *A. scholaris* exhibits spasmolytic and anti-diarrheal properties via blocking the calcium channel (Shah *et al.*, 2010). The results of this research indicate that the anti-diarrheal and spasmolytic effects of *A. scholaris* crude extract may be because of the existence of a compound resembling CCB (Oktavia *et al.*, 2020). The anti-diarrheal characteristics of *A. scholaris* is not well known by now, further investigations are required to see its therapeutic effect in diarrhoea.

5.6. Anti-hyperuricemia

Some studies have revealed that *A. scholaris* also exhibits potent anti-hyperuricemia activity. Interestingly it lowers the levels of serum uric acid in models of mice at the concentration of 100 mg/kg and 200 mg/kg (Hu, 2023). Additionally, it shows better activity in HK-2 cell model enhanced by monosodium urate by enhancing the excretion of uric acid at the dose of 5µM (Hu *et al.*, 2022). Scaffolds triterpenoids extracted from leaves of *A. scholaris* shows anti-hyperuricemic properties in both in-vitro and in-vivo condition (Hu, 2021). There is less research data about the anti-hyperuricemia activity of *A. scholaris* till now, so more research is needed in this area.

5.7. Anti-nociceptive activity

It has been reported that some plants have the potent activity against either nootropic mode or stress but *A. scholaris* is one of these plants having such both activities at a time. Methanol bark extract of this plant exhibits both these properties whereas the leaves ethanol extract possesses anti-anxiety activity without having any sedative or stimulant effects (Khyade *et al.*, 2014). A clinical study taking about 30 patients was also conducted to check the effects of *A. scholaris* on hypertension and in result it was found that it potently reduces the both the systolic and diastolic blood pressure and symptoms of psychological disorders (Khyade *et al.*, 2014). Now-a-days human beings are suffering from diseases related to CNSs and there are limited therapeutic options with higher side effects are available for it. Henceforth, in depth invention of anti-nociceptive property of *A. scholaris* will help human being significantly with less/no side effects.

5.8. Anti-malarial activity

Like other plants *A. scholaris* also has the potent killing activity against malarial parasite *Plasmodium*. Although this study is limited but some are reported. Mostly the bark and leaf extract show potent activity against *P. falciparum*. More specifically the methanol extract of bark shows promising anti-plasmodial activity in comparison to others (Singh *et al.*, 2023). Moreover, not enough data has been reported about the anti-malarial activity of *A. scholaris*. Hence more researches are needed in this field to get an ideal anti-malaria agent using different extracts of *A. scholaris*.

5.9. Antidepressant

A study on antidepressant provided an account of *A. scholaris*'s impact on stress and cognitive function in mice. After applying the methanolic bark extracts, they found that

all the stress-induced markers—cortisol, glucose, protein, triglycerides, and cholesterol are normalized (Sarkar *et al.*, 2021). As in current scenario antidepressant therapeutics seeks more attention so in depth study about the antidepressant property of *A. scholaris*, which will help a lot to us.

5.10. Anti-diabetic

The potential for hypoglycemia of *A. scholaris* triterpenes was investigated and documented in a study. The authors found lupeol and betulin (Figure 2) to have hypoglycemic action. Another study reported *A. scholaris* Linn. bark's hypoglycemic activity and antihyperlipidemic effects in diabetic rats produced by streptozotocin (Chhajed *et al.*, 2023). Because of its antidiabetic and antihyperlipidemic activity, the research revealed that the bark of *A. scholaris* has potential effects on lipid profile and may be useful in treating diabetes and related cardiovascular problems (Kanase and Mane, 2018). The antihyperlipidemic and antidiabetic properties of *A. scholaris* leaves were demonstrated by researchers. The study found that in diabetic rats produced by streptozotocin, the ethanolic extract of *A. scholaris* exhibited antihyperlipidemic and antioxidant potential in addition to its antidiabetic effect. Dita was the source of α -glucosidase blockers, as described by the study. It has been reported that an aqueous methanol extract from dried Devil tree leaves exhibits α -glucosidase inhibitory action (Oktavia *et al.*, 2020). In detailed study will give a new therapeutic agent using different extracts of *A. scholaris* in the field of diabetics.

5.11. Anti-bacterial activity

Rapid centrifugal chromatography was used in the preliminary isolation of the bioactivator Logenetin from *A. scholaris*, as described by a study. The authors discussed the separation of logenetin and how it combats both gram-positive and gram-negative bacteria (Qin *et al.*, 2015). Wang *et al.* claim that *A. scholaris* and *Leea tetramera* possess antibacterial qualities. They concluded that *A. scholaris* and *Leea tetramera*'s root bark sections were useless against the fungi they looked at (Wang *et al.*, 2016). However no sufficient data is available till now related to anti-bacterial activity of *A. scholaris*, so in detail study in this area will give new insight into this field.

5.12. Immunomodulatory activity

The medicinal plants show their medicinal property by acting on the immune system of host. Like others *A. scholaris* also exhibits significant immunomodulatory role by acting differentially on the immune system of host. Research has been shown that the combination of alkaloid

and triterpenes of *A. scholaris* enhances immunomodulatory action in C57BL/6 mice (Al-Rikabi, 2020). Its bark extract also has an immunomodulatory effect. At lower dose the aqueous extract promotes the cellular immunity while at higher dose it apprehends hypersensitivity reactions (Dangi *et al.*, 2018). In depth research regarding this subject will be benefited to mankind in future to boost immunity.

5.13. Anti-cancer and cytotoxic activity

Cancer is the first line disease in world today. Instead of having many treatment options its cure rate is still in worst condition. This is for therapy resistance and higher side effects. So, to overcome this situation now researchers are emphasizing on plant-based therapies as they have various pharmacological activities including anti-cancer activity and less/no side effects. Like other plants *A. scholaris* also exhibits potent cytotoxicity and anti-cancer activity against various cancers in both in-vitro and in-vivo conditions. It has also the ability of chemosensitization. It has been reported that triterpenoids and sterols isolated from leaf of the *A. scholaris* shows potent anti-proliferative activity against NSCLC (Wang, 2017). Additionally, normoterpenoid indole alkaloids from fruit of *A. scholaris* potently kills the stem cells of glioblastoma (Wang, 2018). Alstoniasidines A (1) and B (2) isolated from *A. scholaris* shows cytotoxicity against stem cells of glioma by promoting caspase-3 mediated extrinsic pathway through enhancing the levels of expression of tumor necrosis factor/TNF- α , interleukin 1/IL-1, and the cleaved caspase-3 and also apprehends the self-renewal property of stem cells of glioma (Wei, 2018). It has also been reported that *A. scholaris* competently regulates the stomach cancer of mice promoted by benzopyrene (Chhajed, 2023). Interestingly hydroalcoholic stem bark extract of *A. scholaris* has the capacity of chemomodulation in combination with berberine hydrochloride in mice having Ehrlich ascites carcinoma in a concentration dependent manner (Khyade, 2014). In A549 NSCLC cells alkaloids and triterpenoids from *A. scholaris* promotes apoptosis via lowering the levels of expression of pro-casp8 and Bcl-2 and up-regulating the expression of cleaved caspase 8 which leads to cell death (Feng *et al.*, 2013). According to a research, *A. scholaris* exhibits anti-mutagenic and anti-carcinogenic effects on peripheral human lymphocyte culture and albino mice bone marrow cells towards genotoxicity enhanced by methyl methane sulfonate (Ahmad *et al.*, 2016). However, there is no recent advances in the study of anti-cancer property of *A. scholaris*. Numerous studies are required in this area to give a novel and beneficial therapeutic regimen in the field of cancer with no side effects and higher cure rate.

6. Toxicity of *A. scholaris*

There are not much of studies which have reported the toxic potential of *A. scholaris*. However, in a study, the authors checked the acute and sub-acute toxicity of the bark extracts of *A. scholaris* by feeding to the mice. They reported the highest acute toxicity in summer season, while least was reported to be in winter season. Moreover, the sub-acute toxicity was checked at a dose of 120 mg/kg and 240 m/kg. The higher dose was found to be more toxic due to higher concentration of ephetamine from *A. scholaris* (Baliga, 2012).

7. Conclusion

A. scholaris is a well-known plant that is used to cure a variety of illnesses in traditional and folk medicine. 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 this reason, it appears important to substantiate the use of this plant for therapeutic purposes by conducting scientific validation of the pharmacological properties of its constituents. The precise mechanisms underlying different pharmacological characteristics remain unclear. For this reason, *A. scholaris* merits considerably more clinical study and research before it can be considered a medication of interest.

Table 1

Common names of *Alstonia scholaris* used in different languages of India

Language	Synonyms of <i>Alstonia scholaris</i>
English	Devil's tree, Black board tree, White cheese wood, Chalkwood tree, Milky pine, Milk wood, Pine, Dita bark, Birrba
Hindi	Saittan ka jhad, Chatian, Shaitan ped, Chitvan
Sanskrit	Saptaparna, Phalagaruda, Grahanashana, Madagandha, Grahashi, Kshalrya, Payasya, Jivani, Vishalavaka, Ayugmapama, Vishamachhda
Oriya	Silgandha, Chhanchania, Chhatiana
Bengali	Chattin
Kannada	Hale, Doddapala
Marathi	Salvin, Santhni
Tamil	Pala, Wedrase, Elilapillai, Mukumpalei
Telugu	Edakulapada
Gujrati	Saptaparni
Malayalam	Daivapala
Sindhi	Rukattana

Table 2

Phytochemical constituents of *A. scholaris*

Phytochemical Class	Compound	Part of <i>A. scholaris</i>	Reference
Alkaloids	5-Methoxyaspidophylline	Leaves	(Rudani <i>et al.</i> , 2020)
	5a-Methoxystictamine	Leaves	(Khyade <i>et al.</i> , 2014)
	5-Methoxystictamine	Leaves	(Khyade <i>et al.</i> , 2014)
	5-epi-Nareline ethyl ether	Leaves	(Chaudhary, 2022)
	6,7-seco-Angustilobine B	Leaves	(Macabeo <i>et al.</i> , 2005)
	17-O-Acetylechitamine	Barks	(Zhao <i>et al.</i> , 2023)
	18-Hydroxy-19,20-dehydro-7, 21-seco-uleine	Leaves	(Oktavia <i>et al.</i> , 2020)
	19-E-Vallesamine	Fruits	(Khyade <i>et al.</i> , 2014)

19-S-Scholaricine	Fruits	
19-E-Picrinine	Fruits	
19-E-Akuammidine	Fruits	
19-Epischolaricine	Leaves	(Zhao <i>et al.</i> , 2021)
19,20-(E)-Vallesamine	Leaves	(Khyade <i>et al.</i> , 2014)
19,20-Dihydrocondylocarpine	Leaves	(Alvi and Muzaffar, 1986)
19,20-E-Alstoscholarine	Leaves	(Oktavia <i>et al.</i> , 2020)
20(S)-Tubotaiwine	Leaves	(Jeet <i>et al.</i> , 2020)
Akuammicine	Roots	(Mahar <i>et al.</i> , 2022)
Akuammicine-N _b -methiodide	Roots	(Reddy, 2016)
Akuammicine-N _b -oxide	Roots	(Haridas <i>et al.</i> , 2016)
Akuammicine N-oxide	Barks	
Akuammiginone	Barks	(Salim <i>et al.</i> , 2004)
Alstonine	Leaves	(Bainsal <i>et al.</i> , 2021)
Alschomine	Leaves	(Qin <i>et al.</i> , 2023)
Akuammidine	Leaves	(Mahar <i>et al.</i> , 2022)
Angustilobine B N ⁴ -oxide	Leaves	(Krishnan <i>et al.</i> , 2019)
Angustilobine B	Leaves	
Angustilobine B acid	Leaves	
Echitamic acid	Barks	(Rudani <i>et al.</i> , 2020)
Echitamine	Barks	
Echitamidine N-oxide	Barks	
Echitamidine	Leaves	
Lagunamine	Leaves	(Lee and Sperry, 2022)
Losbanine	Leaves	(Majid and Faraj, 2023)
Manilamine	Leaves	(Elshaier <i>et al.</i> , 2022)
N ⁴ -Methyl angustilobine B	Leaves	(Macabeo <i>et al.</i> , 2005)
N ¹ -Methoxymethyl picrinine	Leaves	
N ^b -Methylscholaricine	Leaves	
Nareline	Leaves, Fruits	(Chaudhary, 2022)
Nareline methyl ether	Leaves	(Shrivastava <i>et al.</i> , 2016)
Picalinal	Leaves	(Qin <i>et al.</i> , 2023)
Picaline	Leaves	(Paul <i>et al.</i> , 2021)
Picrinine	Leaves, Flowers, Fruits	(Li <i>et al.</i> , 2019)
Quinoline	Leaves	(Yang <i>et al.</i> , 2015)
Rhazimanine		(Rudani <i>et al.</i> , 2020)
Scholarisine A	Leaves	(Zhan <i>et al.</i> , 2020)
Scholaricine	Leaves	
Strictamine	Flower, Fruits	(Hamdiani <i>et al.</i> , 2018)
Tubotaiwine oxide	Leaves	(Zhang <i>et al.</i> , 2023)
Vallesamine N ^b -oxide	Leaves	(Mohammed <i>et al.</i> , 2021)

Terpenoids and Sterols	3,28- β -Diacetoxy-5-olea-triterpene	Flower	(Dey, 2011)
	β -Sitosterol	Leaves	(Ghansenyuy <i>et al.</i> , 2023)
	β -amyrin	Flower	(Akbar <i>et al.</i> , 2020)
	<i>n</i> -Tetracosane	Leaves	(Singh <i>et al.</i> , 2020)
	α -Amyrin acetate	Barks, Flowers, Fruits	(Ali <i>et al.</i> , 2022)
	Alstonic acids A and B	Leaves	(Akbar, 2020)
	Betulin	Leaves, Flowers	(Ali <i>et al.</i> , 2021)
	Betulinic acid	Leaves, Flowers	(Akbar <i>et al.</i> , 2020)
	Lupeol acetate	Barks	(Ali <i>et al.</i> , 2021)
	Oleanolic acid	Leaves	(Wang <i>et al.</i> , 2017)
	Sweroside	Leaves	(Zengin <i>et al.</i> , 2023)
	Ursolic acid	Leaves, Flowers	(Wang <i>et al.</i> , 2017)
	Flavonoids	Quercetin	Leaves
Quercetin-3-O- β -D-galactopyranoside		Leaves	(Banik <i>et al.</i> , 2023)
(+)-lyoniresinol 3 α -O- β -D-glucopyranoside		Leaves	(Afreen <i>et al.</i> , 2021)
Kaempferol		Leaves	(Singh <i>et al.</i> , 2017)
Isorhamnetin		Barks	(Kawiwong <i>et al.</i> , 2020)
Apioglucosides		Stems	(Chanda and Ramachandra, 2019)
Isorhamnetin-3-O- β -D-galactopyranoside		Leaves	(Bainsal <i>et al.</i> , 2021)
Kaempferol-3-O- β -D-galactopyranoside		Leaves	(Singh <i>et al.</i> , 2017)
Iridoids	Alstonoside 1	Stems	(Nanditha <i>et al.</i> , 2020)
	Scholareins A-D	Barks	(Indradi <i>et al.</i> , 2023)
	Isoboonein	Barks	(Khyade <i>et al.</i> , 2014)
	Alyxialactone	Barks	(Khyade <i>et al.</i> , 2014)
	Loganin	Barks	(Feng <i>et al.</i> , 2008)
Essential oils	Loganetin	Stems	
	α -Terpineol	Flowers	(Singh <i>et al.</i> , 2020)
	Terpinen-4-ol	Flowers	
	Linalool	Flowers	
	2-Phenylethyl acetate	Flowers	
	Furanoid	Flowers	
Pyranoid	Flowers		



Alstonia scholaris plant



Leaves of *Alstonia scholaris*



Bark of *Alstonia scholaris*



Flower of *Alstonia scholaris*

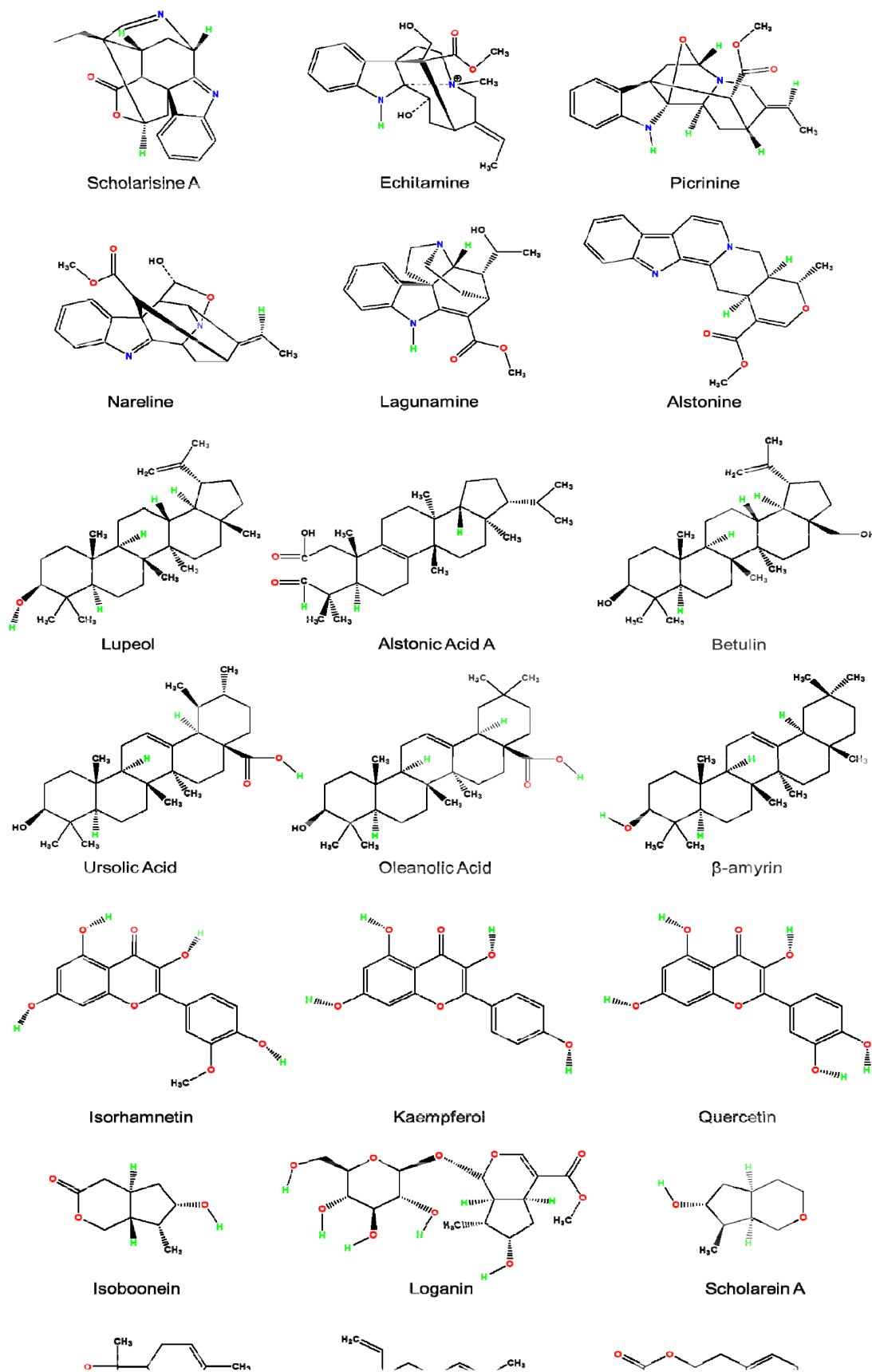


Figure 2: Structure of some phytochemicals isolated from *Alstonia scholaris*

References

- Afreen, S., Syed, W. and Banerjee, S. (2021). Herbal based drug discovery for skin and surgical infectious diseases. Biopharmacological activities of medicinal plants and bioactive compounds, Nova Science Publisher, New York: 101.
- Ahmad, M. S., S., Ahmad, A., Ali and M., Afzal (2016). Anticarcinogenic and antimutagenic activity of *Alstonia scholaris* on the albino mice bone marrow cells and peripheral human lymphocyte culture against methyl methane sulfonate induced genotoxicity. *Advanced Biomedical Research*. 30(5), 92-101.
- Akbar, A., A., Ms, S., Zikr-Ur-Rehman, M., Lateef and Z., Saeed (2020). Isolation And Biological Screening Of Secondary Metabolites From Stem Bark Of *Alstonia Scholaris* (L.) R. Br. *International journal of biology and biotechnology*. 17(1): 9-15.
- Akbar, S. (2020). *Alstonia scholaris* (L.) R. Br. (Apocynaceae). *Handbook of 200 Medicinal Plants: A Comprehensive Review of Their Traditional Medical Uses and Scientific Justifications*. Springer. 225-234.
- Al-Rikabi, M. A. (2020). Immunomodulatory Effect of Isolated Triterpenes from *Alstonia Scholaris* Linn. in Wistar Albino Rats. *International Journal of Pharmaceutical Research*. 15(4).
- Ali, M., E., Ali, H., Kausar, S., Zikr-Ur-Rehman, Z., Saify and M., Latif (2020). Secondary Metabolites from the Leaves and Defoliated Twigs of *Alstonia scholaris*. *Chemistry of Natural Compounds*. 56: 1132-1134.
- Ali, M. S., A., Ashfaq, M., Lateef, A., Sultan, S., Zikr-ur-Rehman and Z. S., Saify (2021). Phytochemical Screening and Biological Evaluation of Young Stems of *Alstonia scholaris*. *Journal of the Chemical Society of Pakistan*. 43(5):75-85.
- Ali, M. S., A., Sultan, M., Lateef and A., Ashfaq (2022). A New Flavone and Other Constituents from the Flowers and Fruits of *Alstonia scholaris*. *Chemistry of Natural Compounds*. 58(2): 233-236.
- Altaf, I. U. K., M. M., Hussain and R., Abdur (2019). Phytochemical and antimicrobial study of *Alstonia scholaris* leaf extracts against multidrug resistant bacterial and fungal strains. *Pakistan Journal of Pharmaceutical Sciences*. 32(4): 88-100.
- Alvi, K. and A., Muzaffar (1986). Isolation and ¹H/¹³C-NMR studies on 19, 20-dihydrocondylocarpine: an alkaloid from the leaves of *Ervatamia coronaria* and *Alstonia scholaris*. *Planta medica*. 52(04): 325-326.
- Bagheri, G., S. A., Ayatollahi, K., Ramírez-Alarcón, M., Fernández, B., Salehi, K., Forman, M., Martorell, M. H., Moghadam and J., Sharifi-Rad (2020). Phytochemical screening of *Alstonia scholaris* leaf and bark extracts and their antimicrobial activities. *Cellular and Molecular Biology Reports*. 66(4): 270-279.
- Bainsal, N., P., Aggarwal and K. S., Bora (2021). Phytochemical and Therapeutic Potential of *Alstonia scholaris* R. Br.-A Magical Traditional Plant. *Journal of Pharmaceutical Research International*. 33(56A): 41-51.
- Baliga, M. S. (2012). Review of the phytochemical, pharmacological and toxicological properties of *Alstonia scholaris* Linn. R. Br (Saptaparna). *Chinese journal of integrative medicine*. 9(3): 261-269.
- Banik, B. and M. K., Das (2023). Therapeutic Potential of *Alstonia scholaris* Latex in the Management of Inflammatory Diseases: An *in vitro* Approach. *Pharmacognosy Research*. 15(3): 478-483.
- Banik, B., M. K., Das, S., Das and S., De (2023). Anti-arthritis potential of latex of *Alstonia scholaris* (L.) R. Br.: an *in silico* and *in vivo* approach. *Nutrire*. 48(2): 40.
- Bhandary, M. J. (2020). *Alstonia scholaris* in the ethnomedicinal and religious tradition of Coastal Karnataka, India. *Biodiversitas Journal of Biological Diversity*. 21(4): 1569-1577.
- Chanda, S. and T., Ramachandra (2019). A review on some Therapeutic aspects of Phytochemicals present in Medicinal plants. *International Journal of Pharmacy Life Sciences*. 10(1): 221-213.
- Chaudhary, R. (2022). Ethnopharmacological review on versatile herbal medicament *Alstonia scholaris*. *Innov Pharm Pharmacother*. 10(2): 1-7.
- Chhajed, M., A., Jain, A., Pagariya, S., Dwivedi, N., Jain and V., Taile (2023). *Alstonia scholaris* Linn. R. Br.: An Assessment of its Botany, Conventional Utilization, Phytochemistry and Pharmacology. *J Pharmacognosy Reviews*. 17(33): 184-203.
- Dangi, R., N. K., Jain and A., Shaikh (2018). Immunomodulatory Activity of Different Extracts of Stem Bark of *Alstonia scholaris* Linn. *Journal of Drug Delivery Therapeutics*. 8(6-A): 106-110.
- Dey, A. (2011). *Alstonia scholaris* R. Br.(Apocynaceae): Phytochemistry and pharmacology: A concise review. *Journal of Applied Pharmaceutical Science* 1(6). 51-57.
- El-Fiki, M., A., El-Taher, A., EL-Gendy and M., Lila (2019). Morphological and anatomical studies on some taxa of family Apocynaceae. *Al-Azhar Journal of Agricultural Research*. 44(1): 136-147.
- Elshaier, Y. A., M. T., Nemr, M. S., Refaey, W. A., Fadaly and A., Barakat (2022). Chemistry of 2-vinylindoles: synthesis and applications. *New Journal of Chemistry*. 46(28): 13383-13400.

- Feng, L., Y., Chen, L., Yuan, X., Liu, J.-F., Gu, M.-H., Zhang and Y., Wang (2013). A combination of alkaloids and triterpenes of *Alstonia scholaris* (Linn.) R. Br. leaves enhances immunomodulatory activity in C57BL/6 mice and induces apoptosis in the A549 cell line. *Molecules*. 18(11): 13920-13939.
- Feng, T., X. H., Cai, Z. Z., Du and X. D., Luo (2008). Iridoids from the bark of *Alstonia scholaris*. *Helvetica Chimica Acta*. 91(12): 2247-2251.
- Ghansenyuy, S. Y., K. O., Eyong, P., Yemback, L., Mehreen, N. N., Vincent de Paul, M. S., Ali and G. N., Folefoc (2023). Lipoyxygenase inhibition and molecular docking studies of secondary metabolites from the leaves of *Alstonia scholaris*. *European Journal of Medicinal Chemistry Reports*. 9: 100-108.
- Goel, S., C. S., BR and Chandan (2021). Evaluation of Antioxidant and Antimicrobial Efficacy of *Camellia Sinensis* and *Alstonia Scholaris* Extracts on *Streptococcus Mutans* and *Lactobacillus Acidophilus*—An in Vitro Study. *Biomedical Pharmacology Journal*. 14(1): 455-465.
- Hamdiani, S., M. Al-As'ari, A. Satriani and S. Hadi (2018). Alkaloids from Pulau (*Alstonia scholaris* (L.) R. Br.) leaves of Lombok Island on the basis of GC-MS analysis. *AIP Conference Proceedings*, AIP Publishing.
- Haridas, N., S., Sreekumar and C., Biju (2016). Validation of Anti Tuberculosis Activity and Identification of Leads in *Alstonia scholaris* L.(R. Br.). *Journal of Pharmacy and Biological Sciences*. 11: 12-19.
- Hu, B.-Y., Y.-L. Zhao, D.-Y. Ma, M.-L. Xiang, L.-X. Zhao and X.-D. Luo (2022). Anti-hyperuricemic bioactivity of *Alstonia scholaris* and its bioactive triterpenoids in vivo and in vitro. *J Ethnopharmacol*. 290: 115049.
- Indradi, R. B., M. Muhaimin, M. I. Barliana and A. Khatib (2023). Potential Plant-Based New Antiplasmodial Agent Used in Papua Island, Indonesia. *Plants*. 12(9): 1813.
- Jeet, A., Y. Singh, P. Singh, R. Nimoriya, C. J. Bilung, S. Kanojiya, V. Tripathi and D. K. Mishra (2020). Strategies for indole alkaloids enrichment through callus culture from *Alstonia scholaris* (L.) R. Br. *Plant Growth Regulation*. 90: 383-392.
- Kanase, V. and D. J., Mane (2018). A pharmacognostic and pharmacological review on *Alstonia scholaris*. *Asian J Pharm Clin Res*. 11(12): 22-26.
- Kawiwong, J., A. Injard, A. Riankrasin, K. Kamonlakorn, P. Srisoithongsug, D. Pekthong and S. Parhira (2020). Chemical constituents and antioxidant activity of the *Alstonia scholaris* latex extract. 12th NPRU national Academic Conference.
- Khyade, M. S., D. M. Kasote and N. P. Vaikos (2014). *Alstonia scholaris* (L.) R. Br. and *Alstonia macrophylla* Wall. ex G. Don: A comparative review on traditional uses, phytochemistry and pharmacology. *Journal of Ethnopharmacology*. 153(1): 1-18.
- Krishnan, P., C.-W. Mai, K.-T. Yong, Y.-Y. Low and K.-H. Lim (2019). Alstobrogaline, an unusual pentacyclic monoterpene indole alkaloid with aldimine and aldimine-N-oxide moieties from *Alstonia scholaris*. *Tetrahedron Letters*. 60(11): 789-791.
- Lee, S. and J. Sperry (2022). Isolation and biological activity of azocine and azocane alkaloids. *Bioorganic Medicinal Chemistry*. 54: 116560.
- Li, R., M.-J. Zi, Z.-P. Gou, Y.-L. Zhao, W.-T. Zhang, F. Lu, W.-Y. Cao, Y.-P. Zhao, Q.-N. Li and Y. Zhao (2019). Pharmacokinetics and safety evaluation in healthy Chinese volunteers of alkaloids from leaf of *Alstonia scholaris*: a multiple doses phase I clinical trial. *Phytomedicine*. 61: 152828.
- Macabeo, A. P. G., K. Krohn, D. Gehle, R. W. Read, J. J. Brophy, G. A. Cordell, S. G. Franzblau and A. M. Aguinaldo (2005). Indole alkaloids from the leaves of Philippine *Alstonia scholaris*. *Phytochemistry*. 66(10): 1158-1162.
- Mahar, R., N. Manivel, S. Kanojiya, D. K. Mishra and S. K. Shukla (2022). Assessment of Tissue Specific Distribution and Seasonal Variation of Alkaloids in *Alstonia scholaris*. *Metabolites*. 12(7): 607-615.
- Majid, A. and H. R. Faraj (2023). A review Study of the Chemical Constituents and Pharmacological Activities of *Alstonia scholaris* linn. *University of Thi-Qar Journal of Science* 10(1).
- Mohammed, A. E., Z. H. Abdul-Hameed, M. O. Alotaibi, N. O. Bawakid, T. R. Sobahi, A. Abdel-Lateff and W. M. Alarif (2021). Chemical diversity and bioactivities of monoterpene indole alkaloids (MIAs) from six Apocynaceae genera. *Molecules*. 26(2): 488.
- Nanditha, R., J. Saravanan, T. Praveen, S. Deepa and E. Rymbai (2020). Evaluation of anti-cancer, antioxidant and antimicrobial activities of *Alstonia scholaris* L. *Research Journal of Pharmacy Technology*. 13(9): 4153-4157.
- Oktavia, R., S. Misfadhila and H. Rivai (2020). Overview of traditional, phytochemical, and pharmacological uses of pulau (*Alstonia scholaris*). *World Journal of Pharmacy Pharmaceutical Sciences*. 9(8): 334-354.
- Pandey, K., C. Shevkar, K. Bairwa and A. S. Kate (2020). Pharmaceutical perspective on bioactives from *Alstonia scholaris*: ethnomedicinal knowledge, phytochemistry, clinical status, patent space, and future directions. *Phytochemistry reviews*. 19: 191-233.

- Paul, A. T., G. George, N. Yadav, A. Jeswani and P. S. Auti (2021). Pharmaceutical Application of Bio-actives from *Alstonia* Genus: Current Findings and Future Directions. *Bioactive Natural Products for Pharmaceutical Applications*: 463-533.
- Qin, X.-J., Y.-L. Zhao, P.-K. Lunga, X.-W. Yang, C.-W. Song, G.-G. Cheng, L. Liu, Y.-Y. Chen, Y.-P. Liu and X.-D. Luo (2015). Indole alkaloids with antibacterial activity from aqueous fraction of *Alstonia scholaris*. *Journal of Ethnopharmacology*. 71(25): 4372-4378.
- Qin, Y., Y. J. He, Y. L. Zhao, Z. S. Zhou, Z. J. Wang, Y. Y. Zhu and X. D. Luo (2023). Targeted quantitative analysis of monoterpene indole alkaloids in *Alstonia scholaris* by ultra high performance liquid chromatography coupled with quadrupole time of flight mass spectrometry. *Journal of Separation Science*. 2200843.
- Reddy, D. S. (2016). Phytochemical analysis of active constituents of *Alstonia scholaris* and their cytotoxicity in vitro. *International Journal of Pharmaceutical Sciences Research*. 7(8): 3262.
- Rizvi, Z. A., U. Madan, M. R. Tripathy, S. Goswami, S. Mani, A. Awasthi and M. Dikshit (2023). Evaluation of ayush-64 (a polyherbal formulation) and its ingredients in the Syrian hamster model for SARS-CoV-2 infection reveals the preventative potential of *Alstonia scholaris*. *J Pharmaceuticals*. 16(9): 1333.
- Rudani, M., Y. Chhotala, R. Prajapati, G. Sailor and V. Jain (2020). *Alstonia scholaris*: A potent asian medicinal plant (A comprehensive phytopharmacological review). *Pharma Science Monitor*. 11(1): 19-39.
- Salim, A. A., M. J. Garson and D. J. Craik (2004). New Indole Alkaloids from the Bark of *Alstonia scholaris*. *Journal of natural products*. 67(9): 1591-1594.
- Sarkar, K. K., M. M. Rahman, A. A. E. Shahriar, T. Mitra, M. Golder, M. N. H. Zilani and B. Biswas (2021). Comparative neuropharmacological and cytotoxic profiles of *Alstonia scholaris* (*L.*) and *Mimusops elengi* (*L.*) leaves. *Advances in Traditional Medicine*. 21(3): 499-506.
- Shah, A. J., S. A. Gowani, A. J. Zuberi, M. N. Ghayur and A. H. Gilani (2010). Antidiarrhoeal and spasmolytic activities of the methanolic crude extract of *Alstonia scholaris* *L.* are mediated through calcium channel blockade. *Phytotherapy Research: An International Journal Devoted to Pharmacological Toxicological Evaluation of Natural Product Derivative*. 24(1): 28-32.
- Shrivastava, N., M. Datar and R. Saxena (2016). Pharmacognostic Evaluation and Physio-Chemical Analysis of *Alstonia scholaris* Bark. *Biosciences Biotechnology Research Asia*. 7(1): 429-431.
- Singh, A., K. Daniel, S. K. Jain and S. Vengrulkar (2023). Phytochemical Screening and in Vitro Anti-Plasmodium Falciparum Activity of *Alstonia Scholaris*. *Current Science*. 3(4): 351-356.
- Singh, H., R. Arora, S. Arora and B. Singh (2017). Ameliorative potential of *Alstonia scholaris* (*Linn.*) *R. Br.* against chronic constriction injury-induced neuropathic pain in rats. *BMC Complementary Alternative Medicine*. 17(1): 1-9.
- Singh, M. K., S. Singh, S. Yadav, P. K. Kashyap, S. T. Ram, M. P. Darokar and S. Verma (2020). Chemical composition and antibacterial activity of floral volatile oil of *Alstonia scholaris* (*L.*) *R. Br.* from India. *Journal of Medicinal and Aromatic Plant Sciences*. 42(3-4): 234-240.
- Sultana, N., M. S. Qazi and M. Kamal (2020). New anti-inflammatory triterpene esters and glycosides from *Alstonia scholaris*. *Anti-Inflammatory and Anti-Allergy Agents in Medicinal Chemistry*. 19(4): 370-386.
- Tripathi, S. K., A. K. Mahakud and B. K. Biswal (2019). A green approach towards formulation, characterization, and antimicrobial activity of poly (Lactic-co-Glycolic) acid-*Alstonia scholaris* based nanoparticle. *Materials Research Express*. 6(9): 095325.
- Tripathy, M., B. Pasayat, A. Tripathy and N. Bhol (2019). Seasonal Incidence of Gall Forming Psyllid *Pseudophacopteron tuberculatum*, Crawford Infesting *Alstonia scholaris* *R. Brown* at Bhubaneswar, Odisha. *Journal of Tree Sciences*. 37(2): 14-21.
- Wang, C.-M., H.-T., Chen, Z.-Y., Wu, Y.-L., Jhan, C.-L., Shyu and C.-H., Chou (2016). Antibacterial and synergistic activity of pentacyclic triterpenoids isolated from *Alstonia scholaris*. *Molecules*. 21(2): 139(48): 17281-17284.
- Wang, C.-M., K.-L. Yeh, S.-J. Tsai, Y.-L. Jhan and C.-H. Chou (2017). Anti-proliferative activity of triterpenoids and sterols isolated from *Alstonia scholaris* against non-small-cell lung carcinoma cells. *Molecules*. 22(12): 2119.
- WHO (2019). WHO global report on traditional and complementary medicine 2019. World Health Organization. W. H. Organization, World Health Organization.
- Yang, X.-W., X.-D. Luo, P. K. Lunga, Y.-L. Zhao, X.-J. Qin, Y.-Y. Chen, L. Liu, X.-N. Li and Y.-P. Liu (2015). Scholarisines H-O, novel indole alkaloid derivatives from long-term stored *Alstonia scholaris*. *Tetrahedron Letters*. 71(22): 3694-3698.
- Zengin, G., M. El-Raey, W. El-Kashak, G. E.-S. Batiha, D. Althumairy, S. Alamer, N. M. Mostafa and O. A. Eldahshan (2023). Sweroside: An iridoid glycoside of potential neuroprotective, antidiabetic and antioxidant

- activities supported by molecular docking. *Amino Acids*. 1-10.
- Zhan, G., F. Zhang, K. Yang, T. Yang, R. Zhou, W. Chen, J. Zhang, X. Zhang and Z. Guo (2023). Alsolarines A and B, two rearranged monoterpene indole alkaloids from *Alstonia scholaris*. *Organic Biomolecular Chemistry*. 21(40): 8190-8196.
- Zhan, R., S.-Z. Du, Z.-H. Duan, Y. Nian and Y.-G. Chen (2020). Scholarinine A, a N3 type caged-monoterpene indole alkaloid as Cav3. 1 T-type calcium channel inhibitor from *Alstonia scholaris*. *Tetrahedron Letters*. 61(1): 151354.
- Zhang, F., K. Yang, H. Liu, T. Yang, R. Zhou, X. Zhang, G. Zhan and Z. Guo (2023). Structurally diverse monoterpene indole alkaloids with vasorelaxant activities from the branches of *Alstonia scholaris*. *Phytochemistry reviews*. 209: 113610.
- Zhao, M.-x., J. Cai, Y. Yang, J. Xu, W.-y. Liu, T. Akihisa, W. Li, T. Kikuchi, F. Feng and J. Zhang (2023). Traditional uses, chemical composition and pharmacological activities of *Alstonia R. Br.* (Apocynaceae): A review. *Arabian Journal of Chemistry*: 104857.
- Zhao, Y.-L., Z.-P. Gou, J.-H. Shang, W.-Y. Li, Y. Kuang, M.-Y. Li and X.-D. Luo (2021). Anti-microbial effects in vitro and in vivo of *Alstonia scholaris*. *Natural Products and Bioprospecting*. 11: 127-135.
- Zhao, Y.-L., S.-B. Pu, Y. Qi, B.-F. Wu, J.-H. Shang, Y.-P. Liu, D. Hu and X.-D. Luo (2021). Pharmacological effects of indole alkaloids from *Alstonia scholaris* (L.) R. Br. on pulmonary fibrosis in vivo. *Journal of Ethnopharmacology*. 267: 113506.
- Zhou, H.-X., R.-F. Li, Y.-F. Wang, L.-H. Shen, L.-H. Cai, Y.-C. Weng, H.-R. Zhang, X.-X. Chen, X. Wu and R.-F. Chen (2020). Total alkaloids from *Alstonia scholaris* inhibit influenza a virus replication and lung immunopathology by regulating the innate immune response. *Phytomedicine*. 77: 153272.