ISSN 2063-5346

Studies on Anti-Asthmatic Activities in Alstonia Scholaris

Rupak Kumar Swain[1], Dr Manisha[2], Dr. Meera Indracanti[3], Dr. B. Padma[4], Dr. Biman Kumar Sarma[5]

Article History: Received: 15.03.2023 Revised: 20.04.2023 Accepted: 26.05.2023

ABSTRACT:

In various medical systems, numerous herbal remedies have been used to treat and manage various diseases. In various traditional medical practices, the plant Alstonia scholaris has been used to treat human diseases and ailments. It is said to contain phenolic acids, flavonoids, and various alkaloids. It has been shown to have antimicrobial, antiamoebic, antiplasmodial, hepatoprotective, immunomodulatory, anticancer, antiasthmatic, antioxidant, analgesic, anti-inflammatory, anti-ulcer, anti-fertility, and wound healing properties. Additionally, there are reports indicating that this plant is traditionally used for its cardiotonic, anti-diabetic, and anti-arthritic properties. There are no reports of pharmacological activities for many Alstonia scholaris isolated constituents, which would support their subsequent pharmacological studies.

Keywords: Medicinal Plants; Ayurveda; Therapeutics; Elixir of life.

[1]Assistant Professor, Department of Pharmacology, Roland Institute of Pharmaceutical Sciences, Berhampur, Odisha.
[2]Associate Professor and Head of Botany Department, Chinmaya Degree College, BHEL, Haridwar (Affiliated to Hemwati Nandan Bahuguna Garhwal University, Srinagar, Garhwal)
[3]Professor, Department of Medical Biotechnology, School of Allied Health Sciences, Malla Reddy University, Hyderabad 500100
[4]Assistant Professor, University Post Graduate College, Secunderabad Osmania University
[5]Assistant Professor, Department of Zoology, Rangapara College

INTRODUCTION

Plants have been useful to humans as valuable components of medicines, seasonings, beverages, cosmetics, and dyes for thousands of years, helping to improve human health and quality of life. The idea that plants contain natural substances that can improve health and treat illness is the foundation of herbal medicine. Global attention to plant research has grown in recent years, and a lot of evidence has emerged demonstrating the enormous potential of medicinal plants used in various traditional systems. The use of natural remedies is receiving a lot of attention right now. Furthermore, plant extract was the source of many Western drugs. There are a lot of herbs that are mostly used to treat problems with the cardiovascular system,

liver, central nervous system, digestive system, and metabolism. They may be useful in the treatment or management of a variety of diseases as a drug or supplement due to their potential to have a significant therapeutic effect. The isolated compound(s) and extracts of herbal drugs or medicinal plants have demonstrated a wide range of biological activities. In folklore, such have been and continue to be utilized as food supplements or medicines for a variety of disorders. Ethnopharmacological research on such medicinally important plants and herbs continues to pique the interest of researchers all over the world.

Alstonia scholaris, one of these plants, attracts the attention of researchers all over the world because of its pharmacological activities, which range from fighting malaria to fighting cancer. Alstonia scholaris Linn. R.Br. belongs to the family Apocynaceae, and it grows in both evergreen and deciduous forests as well as on plains all over India. The plant can be found abundantly in West Bengal and South India, in the sub-Himalayan region from the Yamuna eastward to 3000 feet above sea level. From India and Sri Lanka to mainland South-East Asia and southern China, Malaysia, northern Australia, and the Solomon Islands, it is widespread throughout the Asia-Pacific region. The wood is a non-durable hardwood that can be used for light indoor construction and the production of pulp and paper. The wood is called "scholaris" because it was used in school blackboards. In the Indian, British, and French pharmacopoeias, the bark is officially recognized.

The plant is a massive evergreen tree that can grow up to 20 meters tall and has a bole that is about 110 centimeters in diameter and is frequently fluted and buttressed. The bark is rough, grayish-brown, and covered in bitter, white, milky latex; leaves ranging from 4 to 7, coriaceous, oblong to elliptic, pale beneath; small, greenish-white flowers in umbellate panicles; the short corolla tube has a strong scent; fruits with follicles that are 30-60 cm long; papillose seeds with brownish hairs on each end

Echites scholaris L., Echites pala Ham., are the plant's synonyms. Burm's Tabernaemontana alternifolia Alipauen, Andarayan, Bita, Dalipauen, Dirita, Dita, Ditaa, Dilupaon, Lava, Lipauen, Oplai, Pasuit, Pulai, Tanitan, Tangitang, Milky pine, Devil tree, Shaitan wood, Saittan ka jat, Hale, Satween, Elilappalai, Saptaparna, and Phalagaruda are all other names for the plant. India uses Alstonia scholaris's bark, leaves, and milky exudates.

Phytochemistry

Alstonia scholaris Linn. is a well-known source of alkaloids, and scientists are interested in using it for therapeutic purposes. Alkaloids are one of the chemical classes found in medicinal plant species. Because they have a wide range of chemical structures and have been found to be responsible for the pharmacological properties of medicinal plants, alkaloids are a major part of the process of developing new drugs. However, only a small number of the approximately 180 alkaloids that were isolated have been tested for biological activities to this point. The bark, flower, and root of almost every plant are found to contain active principles. The commercial formulation Ayush 64 makes use of the species A.scholaris. This plant's bark contains the alkaloid ditamine and echitamine, as well as echitenine, echicaoutchin, an amorphous yellow mass, echicerin in acicular crystals, echitin in crystallized scales, echitein in rhombic prisms (a crystallisable acid), and echiretin, an amorphous

Traditional uses of Alstonia scholaris Linn. R.Br., (1 – 3)

Part	Constituents	Traditional Uses
Bark	Ditamine, echitamine, echitenine, echicaoutchin, echicerin, echitin, echitein, echiretin, ditain, ditamine, losbanine, 6,7-seco angustilobine B, N^b-demethyl echitmaine, 17-O-acetyl 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:** Microfilaræmia **Ethanolic extract of Stem bark:** Antileishmanial activity.
Milky Juice or latex of Bark	caoutchouc and resins	Dental caries, pimple, pyorrhea. Applied to ulcers and rheumatic pains. Mixed with oil and dropped into ears, relieves earache.
Tender Leaves	picrinine, nareline, akuammidine, picralinal,akuammigine, betulin, ursolic acid, β - sitosterol, flavonoids, phenolic acids, scholarine.	Roasted, pulverized and made to a poultice which is used as a local stimulant to unhealthy ulcers. Administered to women after confinement, used in snake – bite and scorpion bite.

substance that resembles an alkaloid, a fatty acid, The drug's febrifuge properties were attributed to an uncrystallisable bitter principle known as ditain.

Dung et al. used hexane to extract the fresh plant material, hydrodistilled the combined extracts into a slight and wet residue, and used high-resolution GC and GC/MS to analyze the results. Linalool (35.7%), cis and trans linalool oxides, alpha-terpineol, and terpinen-4-ol were identified as the primary components.

Scholaricine, an anilinoacrylate alkaloid with a proposed structure of 2-(demethylschoarine), was isolated from Alstonia scholaris leaves by Atta-ur-Rahman et al. They also reported that the leaves of Alstonia scholaris contained the alkaloid 19, 20-dihydrocondylocarpine. From Alstonia scholaris, Atta-ur-Rahman et al. also isolated 19, 20-Z- and 19, 20-E- Vallesamine. Tatsuo Yamauchi et al. extracted lagunine (19-hydroxytubotaiwine), angustilobine B acid, and losbanine (6,7-seco-6-nor-angustilobine B) from the leaves of Philippine A. scholaris. They also extracted tubotaiwine, its oxide, and 6,7- seco-angustilobine B. Together with echitamine, 17-O-acetylechitamine was extracted from the plant's bark.

From the (pH 5) alkaloid extract of Philippine Alstonia scholaris leaves, Macabeo et al. reported the isolation and structural elucidation (MS and NMR) of the first seco-uleine alkaloids manilamine (18-hydroxy-19,20-dehydro-7,21-seco-uleine) and N4-methyl angustilobine B, in addition to the known indole alkaloids 19,20-(E)-val

A number of alkaloids were isolated from the leaves of A. scholaris by Tatsuo Yamauchi et al. The structures of 19-epischolaricine, Nb-methylscholaricine, Na-methylburnamine, and vallesamine Nb oxide were identified using spectroscopic and chemical approaches. They said that picrinine, nareline, and alschomine were the main alkaloids in the leaves of plants from Taiwan and Thailand that shared similar alkaloid patterns.

Toh-Seok Kam et al. isolated the indole alkaloids nareline ethyl ether, 5-epi-nareline ethyl ether, scholarine-N4-ioxide, picrinine, and scholaricine from the leaf extract of A. scholaris. Atta-ur-Rahman et al. also isolated another indole alkaloid, alstonamine

PHARMACOLOGY

Traditional Uses

The bark is bitter, astringent, acrid, thermogenic, digestive, laxative, anthelmintic, febrifuge, antipyretic, depurative, galactogogue, stomachic, cardiotonic, and tonic. It also acts as a digestive, tonic, and a heart tonic. It helps with fever, malarial fever, abdominal disorders, dysentery, dyspepsia, leprosy, skin diseases, pruritus, tumors, chronic and foul ulcers, asthma, bronchitis, cardiopathy, helminthiasis, agalactia, and debility. It also helps with diarrhoea, dysentery, dyspepsia, and leprosy. The milky, bitter liquid is beneficial for ulcers, vitiated vata conditions, and otalgia.

1 to 2 ounces of the preparation infusion, of tincture, one to two drachms diluted in water, and five to ten grains of ditanin administered two to three times per day. In cases of leprosy, an

extract made from fresh bark is administered in milk. It is additionally utilized as an anthelmintic.

Rheumatoid arthritis and ulcers are treated with milky juice; It alleviates earache when mixed with oil and sprayed into the ear. In some cases, the bark tincture is a potent galactogogue.

After giving birth, women are given fresh ginger root or zedoary juice along with the leaves. The medication is additionally utilized in instances of snake-chomp. Galactopoietics, CNS depressants, anticancer, antituberculosis, antidysentric, and antimalarials are among the plant's active constituents.

Antiasthmatic activity

Bronchodilatory activity of the ethanol extract of Alstonia scholaris leaves in anaesthetized rats was reported by Channa et al (29). In vitro preparations of guinea-pig trachea did not confirm this property, indicating that bronchodilation is not due to the direct tracheal smooth muscle relaxation. The vasodilatory activity of the extract was reported to be independent of adrenergic or muscarinic receptors or prostaglandins but was mainly via endothelial-derived relaxing factor, nitric oxide. The extract inhibited the spontaneous movements of rabbit jejunum and contractile effects of acetylcholine and histamine on guinea-pig ileum. Additionally, the extract caused marked reduction of barium chloride-, potassium chloride- and calcium chloride-induced contraction on guinea-pig ileum and pulmonary artery, implying a direct interference of plant extract with the influx of calcium ions into cells. However, the extract had no detectable effect on mobilization of intracellular calcium. These results coupled with the in vivo effects of ethanol extract reveal that the Alstonia scholaris leaves possess broncho-vasodilatory activity mediated presumably by prostaglandins, calcium antagonism and endothelium-derived relaxing factor(s).

Pharmacological Activities of Isolated Constituents

Echitamine Chloride:

According to the findings of Saraswathi et al., the indole alkaloid echitamine chloride (EC), which was extracted from the bark of Alstonia scholaris, has a highly promising effect against cancer. In sarcoma-180-induced mice, the effect of this drug on the microsomal drug detoxifying system was investigated. It was able to alter the impaired drug detoxifying system that was observed in the sarcoma-180 bearing mice when administered subcutaneously at a dosage of 5 mg/kg body weight.

Additionally, it was discovered that echitamine chloride had an effect on mitochondrial and cellular respiration, resulting in a smaller energy reservoir and the death of S-180 cells.

They have also reported that vitamin A increased the cytotoxic effects of echitamine chloride on Ehrlich ascites carcinoma cells grown in vitro. Similar to adiramycin, mitomycin – C, and bleomycin, they claim a free radical-dependent mechanism for tumoricidal action.

Echitamine chloride's anticancer effects on methylcholanthrene-induced fibrosarcoma were examined by Saraswathi et al. and found to be significant reductions in tumor growth. After echitamine chloride treatment, the altered activities of plasma and liver transaminases, gamma-glutamyl transpeptidase, and lipid peroxidation in fibrosarcoma have returned to near normal levels. After echitamine chloride treatment, both the lower levels of glutathione in the liver and the lower activities of catalase, superoxide dismutase, and glutathione peroxidase have returned to near normal levels.

Alstonine:

It has been determined that the primary component of a plant-based remedy is the indole alkaloid alstonine. Alstonine demonstrated in vivo antimalarial activity in a preliminary

evaluation carried out by Wright et al.

Traditional psychiatrists in Nigeria use it to treat mental illnesses. The traditional application of alstonine is remarkably compatible with its profile in experimental animals, despite the fact that it is certainly challenging to compare the very concept of mental disorders across cultures. Alstonine exhibits significant differences from the more recent atypical antipsychotics, despite having a psychopharmacological profile that is closer to those of the more recent ones in mouse models. According to Meldrum and Ozawa et al., alstonine has clear anxiolytic activity, mediated by 5-HT2A/2C serotonin receptors, indicating effectiveness against schizophrenia's negative symptoms; It disrupts the glutamate system in a way that matches its positive effects on schizophrenia.

Alstonine lacks the pro-convulsant property that is common to many antipsychotics, which is a significant advantage for chronic use in epileptic schizophrenic patients in particular. The major drawback of many antipsychotics is that they do not have significant additional pyramidal effects because they do not have any direct effects on the dopaminergic system.

Alstonine's anticancer activity was reported by Beljanski and Beljanski, who were able to successfully treat a sizeable portion of Swiss mice bearing Ehrlich ascites carcinoma cells and BALB/C mice inoculated with transplantable YC8 lymphoma ascites cells. Alstonine could only partially stop the growth of some solid tumors. Additionally, Beljanski reported that alstonine could distinguish DNA from healthy tissue from DNA from cancer. When DNA from various cancerous tissues or cells is used as a template, it stops DNA in vitro synthesis. Alstonine's ability to form an alkaloid-cancer DNA complex is the cause of its reported inhibitory effect.

Conclusion

The ethnopharmacological approach is required for a thorough investigation of the plants that are utilized in traditional medicine. The interest in plants as a potential source of new drugs has grown as a result of the recently developed methods for isolation, characterization, and pharmacological testing. Since many isolated compounds of Alstonia scholaris have not been studied for their pharmacological activity, it seems worthwhile to scientifically validate the pharmacological properties of Alstonia scholaris constituents, which will substantiate the tribal people's use of this plant for medicinal purposes over centuries. The plant Alstonia scholaris has a wide range of pharmacological activities.

References

A.K. Nadkarni. K.M. Nadkarni’s Indian Materia Medica, Vol. I, Popular Prakashan, Bombay, 80-83 (1976).

A.P. Macabeo, K. Krohn, D. Gehle, R.W. Read, J.J. Brophy and G.A. Cordell. Indole alkaloids from the leaves of Philippine Alstonia scholaris. Phytochemistry 66(10): 1158 – 62 (2005).

Atta-ur- Rahman, A. Muzaffar and N. Doulatabadi. Isolation and 1H/13C-NMR studies on 19, 20-dihydrocondylocarpine – an alkaloid from the leaves of Ervatamia coronaria. Phytochemistry 25(7): 1781 – 83 (1986).

Atta-ur-Rahman and K.A. Alvi. Indole alkaloids from Alstonia scholaris. Phytochemistry 26(7): 2139-42 (1987).

Atta-ur-Rahman, K.A. Alvi, S.A. Abbas and W. Voelter. Isolation of 19, 20-Z- Vallesamine and 19, 20 – E – Vallesamine from Alstonia scholaris. Heterocycles 26(2): 413 – 419 (1987).

Atta-Ur-Rahman, M. Asif, Ghazala, J. Fatima and K.A. Alvi. Scholaricine, an alkaloid from Alstonia scholaris. Phytochemistry 24(11): 2771-73 (1985).

Atta-ur-Rahman. Isolation, structural and synthetic studies on the chemical constituents of medicinal plants of Pakistan. Pure and Appl. Chem. 58(5): 663 – 73 (1986).

B. Costall and R.J. Naylor. Behavioural interactions between 5-hydroxytryptophan, neuroleptic agents and 5-HT receptor antagonists in modifying rodent responding to aversive situations. British J. Pharmacol. 116: 2989 – 99 (1995).

B.S. Meldrum. Neurotransmission in epilepsy. Epilepsia 36: S30 – 35 (1995).

B.S. Meldrum. The role of glutamate in epilepsy and other CNS disorders. Neurology 44 (Suppl. 8): S14 – 23 (1994).

C.Y. Lim-Sylianco, A.P. Jocano and C.M. Linn. Antimutagenicity of twenty Philippine plants using the micronucleus test in mice. Philippine Journal of Science 117(3): 231-235 (1990).

E.Elisabetsky and L. Costa-Campos. The Alkaloid Alstonine: A Review of Its Pharmacological properties. eCAM 3(1): 39 – 48 (2006).

G.C. Jagetia and M.S. Baliga. Induction of developmental toxicity in mice treated with Alstonia scholaris (Sapthaparna) in utero. Birth Defects Res. B. Dev. Reprod. Toxicol. 68(6): 472 – 478 (2003).

G.C. Jagetia and M.S. Baliga. Modulation of antineoplastic activity of cyclophosphamide by Alstonia scholaris in the Ehrlich ascites carcinoma-bearing mice. J. Exp. Ther. Oncol. 3(5): 272-82 (2003).

G.C. Jagetia and M.S. Baliga. The effect of seasonal variation on the antineoplastic activity of Alstonia scholaris R.Br., in HeLa cells. J. Ethnopharmacol. 96(1-2): 37 – 42 (2005).

G.C. Jagetia and M.S. Baliga. The evaluation of nitric oxide scavenging activity of certain Indian medicinal plants in vitro: a preliminary study. J. Med. Food. 7(3): 343 48 (2004).

G.C. Jagetia and M.S. Baliga. Treatment with Alstonia scholaris enhances radiosensitivity in vitro and in vivo. Cancer Biother. Radiopharm. 18(6): 917-29 (2003).

G.C. Jagetia, M.S. Baliga and P. Venkatesh. Effect of Sapthaparna (Alstonia scholaris Linn.) in modulating the benzo(a)pyrene-induced forestomach carcinogenesis in mice. Toxicol. Lett. 144(2): 183-93 (2003).

K.R. Kirtikar and B.D. Basu, Indian Medicinal Plants, Vol. II, Bhushen Singh and Mahendra Pal Singh, Dehradun, 111-14 (1980).

L. Costa-Campos, M. Iwu and E. Elisabetsky. Lack of pro-convulsant activity of the antipsychotic alkaloid alstonine. J. Ethnopharmacol. 93: 307 – 10 (2004).

M. Beljanski and M.S. Beljanski. Selective inhibition of in vitro synthesis of cancer DNA by alkaloids of beta-carboline class. Exp. Cell. Biol. 50: 79 – 87 (1982).

M. Beljanski and M.S. Beljanski. Three alkaloids as selective destroyers of cancer cells in mice. Synergy with classic anticancer drugs. Oncology 43: 198 – 203 (1986).

M. Gandhi and V.K. Vinayak. Preliminary evaluation of extracts of Alstonia scholaris bark for in vivo antimalarial activity in mice. J. Ethnopharmacol. 29(1): 51

M.I. Iwo, A.A. Soemardji, D.S. Retnoningrum and U.M. Sukrasno. Immunostimulating effect of pule (Alstonia scholaris L. R.Br., Apocynaceae) bark extracts. Clin Hemorheol Microcirc. 23(2-4): 177-83 (2000).

M.M. Goyal and A. Varshney. Effects of natural products isolated from three species of Alstonia on some gram-positive and gram-negative bacteria. Indian Drugs 32(2): 69-72 (1995).

M.R. Khan, A.D. Omoloso and M. Kihara. Antibacterial activity of Alstonia scholaris and Leea tetramera. Fitoterpia 74(7-8): 736-40 (2003).

N. Keawpradub, G.C. Kirby, J.C.P. Steele and P.J. Houghton. Antiplasmodial activity of extracts and alkaloids of three Alstonia species from Thailand. Planta Medica 65(8): 690-94 (1999).

N. Keawpradub, P.J. Houghton, E. Eno-Amooquaye and P.J. Burke. Activity of extracts and alkaloids of thai Alstonia species against human lung cancer cell lines. Planta Med. 63(2): 97-101 (1997).

N.X. Dung, P.H. Ngoc, D.D. Rang, N.T. Nhan, N. Klinkb and P. Leclercq. Chemical composition of the volatile concentrate from the flowers of Vietnamese Alstonia scholaris (L.) R.Br. Apocynaceae. Journal of Essential Oil Research 13(6): 424-26 (2001).

P. Kamarajan, N. Sekar, V. Mathuram and S. Govindasamy. Antitumor effect of echitamine chloride on methylcholonthrene induced fibrosarcoma in rats. Biochem Int. 25(3): 491 – 498 (1991).

P. Versha, B. Ghosh, B. Anroop and M. Ramanjit. Antimicrobial activity of Alstonia scholaris leaf extracts. Indian drugs 40(7): 412-13 (2003).

R.S. Gupta, A.K. Bhatnager, Y.C. Joshi, M.C. Sharma, V. Khushalani and J.B. Kacchawa. Induction of antifertility with lupeol acetate in male albino rats. Pharmacology 75(2): 57 – 62

(2005).

R.S. Gupta, R. Sharma, A. Sharma, A.K. Bhatnager, M.P. Dobhal, Y.C. Joshi and M.C. Sharma. Effect of Alstonia scholaris bark extract on testicular function of Wistar rats. Asian J. Androl. 4(3):175-78 (2002).

R.S. Patil, A.R. Juvekar, S.N. Joglekar, P.B. Shamkuwar and S.R. Nimbkar. Study of antidiarrhoeal activity of Alstonia scholaris bark. Indian Drugs 36(7): 463-65 (1999).

S. Arulmozhi, Papiya Mitra Mazumder, Purnima Ashok and L. Sathiya Narayanan. Anti-nociceptive and anti-inflammatory activities of Alstonia scholaris Linn. R.Br., Pharmacognosy Magazine 3(10) in press article (2007).

S. Arulmozhi, V.P. Rasal, L. Sathiya Narayanan and Purnima Ashok. Screening of Alstonia scholaris Linn. R.Br., for wound healing activity. Oriental Pharmacy and Experimental Medicine 7(3) in press article (2007).

S. Channa, A. Dar, S. Ahmed S and Atta-ur-Rahman. Evaluation of Alstonia scholaris leaves for broncho-vasodilatory activity. J. Ethnopharmacol. 97(3): 469–76 (2005).

S. Ozawa, H. Kamiya and K. Tsuzuki. Glutamate receptors in the mammalian central nervous system. Prog. Neurobiol. 54: 581 – 618 (1998).

S.C. Lin, C.C. Lin, Y.H. Lin, S. Supriyatna S and S.L. Pan. The protective effect of Alstonia scholaris R.Br. on hepatotoxin-induced acute liver damage. Am. J. Clin. Med. 24(2): 153-64 (1996).

Saraswathi Viswanathan, Nalini Ramamurthy, S.Subramanian, V. Mathuram and S.Govindasamy. Enhancement of the cytotoxic effects of echitamine chloride by Vitamin A: An in vitro study on ehrlich ascites carcinoma cell culture. Indian Journal of Pharmacology 29: 244 – 249 (1997).

Tatsuo Yamauchi, Fumiko Abe, Rong-Fu Chen, Gen-Ichiro Nonaka, Thawatchai Santisuk and William G. Padolina. Alkaloids from leaves of Alstonia scholaris in Taiwan, Thailand, Indonesia and the Philippines. Phytochemistry 29(11): 3547-52 (1990).

Tatsuo Yamauchi, Fumiko Abe, William G. Padolina and Fabian M. Dayrit. Alkaloids from leaves and bark of Alstonia scholaris in the Philippines. Phytochemistry 29(10): 3321-25 (1990).

The Wealth of India, Raw Materials, Vol. I, CSIR, New Delhi, 50 – 51 (2004).

Toh-Seok Kam, Kok-Tih Nyeoh, Kooi-Mow Sim and K. Yoganathan. Alkaloids from Alstonia scholaris. Phytochemistry 45(6): 1303-05 (1997).

V. Saraswathi, N. Ramamoorthy, S. Subramaniam, V. Mathuram, P. Gunasekaran and S. Govindasamy. Inhibition of glycolysis and respiration of sarcoma-180 cells by echitamine chloride. Chemotherapy 44(3): 198-205 (1998).

V. Saraswathi, V. Mathuram, S. Subramanian and S. Govindasamy. Modulation of the impaired drug metabolism in sarcoma-180-bearing mice by echitamine chloride. Cancer Biochem Biophys. 17(1-2): 79-88 (1999).