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REVIEW ARTICLE **OPEN ACCESS**

Pharmacological Potentials of *Alstonia scholaris* and *Enhydra flactuans*: A Comprehensive Review

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ABSTRACT
This study is based on chemical profiling and medicinal importance of Alstonia scholaris and Enhydra flactuans. Many Pharmacological investigations with animal models and clinical platforms has suggested that the different parts of both the plants are evidenced to have potency towards the ailment of some diseases. It has been reported as antiamoebic, antimicrobial, antidiarrhoeal, immunomodulatory, antiplasmodial, hepatoprotective, anti-cancer, anti-inflammatory, antiasthmatic, antioxidant, free radical scavenging activity, analgesic, anti-ulcer, fertility enhancing and wound healing potentials. The evidence also reports available for the traditional use of this plant for cardiotonic, anti-arthritic and anti-diabetic properties. The bioactive components of Alstonia scholaris and Enhydra flactuans like Carbohydrates, phenolic compounds, carotenoids, flavonoids, biogenic sterols, amines, which imparts into multiple healthcare procurement. Present study will be helpful to explore and focused on identification, isolation and purification of various compounds to empower its modern medicinal properties.
Keywords: *Alstonia scholaris, Enhydra flactuans, bioactive compounds, ethno medicine, therapeutic potentials*

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INTRODUCTION

The significant role of plants in control and management of diseases in human health thus providing a quality life for thousands of years and imparted valuable components such as beverages, medicines, seasonings, dyes and cosmetics. In current researches, the focus of plant research has been considered across the glove with a huge value of evidence suggested with tremendous medicinal plants purposed for medication in the ethno-medicinal systems. Recent days, it is witnessing with the interest of public towards the herbal remedies. Moreover, many of the developing countries where the plants extract are considered to be as origin of drugs. Many clinical conditions such as cardiovascular problems, central nervous system, liver disorders, metabolic and digestive disorders where herbs are used predominantly. Herbal medicines and plants extract or the isolated compound obtained from them are with spectrum of biological activities demonstrated, which are followed to be a purpose of medication in folklore as nutritional supplement and disease treatment. The research investigators enhanced with more interest by Ethnopharmacological findings towards the studies on such herbs/medicine worldwide.

Alstonia scholaris plant seeks attention of the investigators with its diverse chemical components and respective potency across the world by the different pharmacological properties ranging from anticancer to antimalarial activities. *Alstonia scholaris* Linn. R.Br. belongs to the family Apocynaceae [1], it grows in plains, evergreen forests and deciduous region. The plants are widely available in India Bangladesh and some other countries of Asia, southern china, Solomon Islands, Northern Australia and Malaysia. In India it is distributed in abundantly in South India, West Bengal and North-eastern states [2]. This plant is a height about 17 to 20 m having straight buttressed bole mostly fluted with a diameter of around 110. The bark is grayish brown, lenticellate abounding in bitter, rough latex are milky; leaves are elliptic-oblong coriaceous and 4-7 in a whorl with pale beneath; small flowers with multiple umbellate panicles, colours are greenish white, short corolla tube strongly scented fruits follicle 30-60 cm long, brownish colour seeds papillose with hair at each end [1, 2].

Table 1: Phytoconstituents, ethnoedicainal uses of various parts of *Alstonia scholaris* Linn. [1–6]

	Parts of plants	**Leaves**	**Bark**	**Roots**	**Flowers**
***Alstonia scholaris* [1-3]**	**Phyto-constituents**	Alschomine, flavonoids, phenolic acids, isoalschomine, tubotaiwine, picrinine, nareline Nb-oxide, lagunamine, Nb-methyl scholaricine, Nb oxide, akuammidine, β - sitosterol, scholarine. picraline, picrinine, picrarinal, ursolic acid, vallesamine, picralinal, akuammigine, akuammidine, vallesamine, areline, angustilobine B acid, 6, 7 seco angustilobine B, losbanine and betulin,	ditamine, picraline deacetyl, losbanine, Ditamine, β sitosterol. echiretin, echitamine, angustilobine B, echitenine, echicaoutchin, echicerin, echitin, echitein, ditain, 6,7-seco Nb-demethyl 17-Oacetyl echitamine and lupeol.	Picraline diacetyl	β-amyrin, ursolic acid tetrahydroalstonine, Picrinine, n-hexacosane, strictamine, lupeol, and palmitic acid,
	Medicinal uses	Anti–ulcer, asthma. Anti – rheumatic, anti-diabetic snake – bite and scorpion bite, stimulant to unhealthy ulcers. Also used in women after confinement,	aphrodisiac, gastrointestinal sedative, astringent, expectorant, stomachic, fever, dysentery carminative, bitter tonic, stimulants febrifuge, febrifuge, alterative, tonic, leprosy, dyspepsia, valuable in debility, after effects of fever, chronic diarrhoea,. Malaria, plaudism with enlargement of spleen and liver Malarial fever, anaemia and indigestion,	Hepatoprotective and pain in liver with large size	Respiratory difficulties, Asthma,
***Enhydra flactuans* [4-6]**	Parts of plants	Aerial Parts			
	Phytoconstituents	β-carotene, saponins, Enhydra fluctuanskaurol, sesquiterpene, germacranolide, enhydrin, fluctuanin and fluctuandin, myricyl alcohol, cholesterol, sitosterol, stigmasterol, glycoside, other steroids			

	Medicinal uses	Antimicrobial, skin diseases, liver disorders, acidity, neurological disorders, sleeplessness, obesity, burning stool symptoms, antioxidant, antidiarrhoeal, antidiabetic, prevent retina damage, ovarian and lung cancer, osteoarthritis, chronic obstructive pulmonary disease (COPD) anti-inflammatory, central nervous system (CNS) depressant and anti-anxiety.

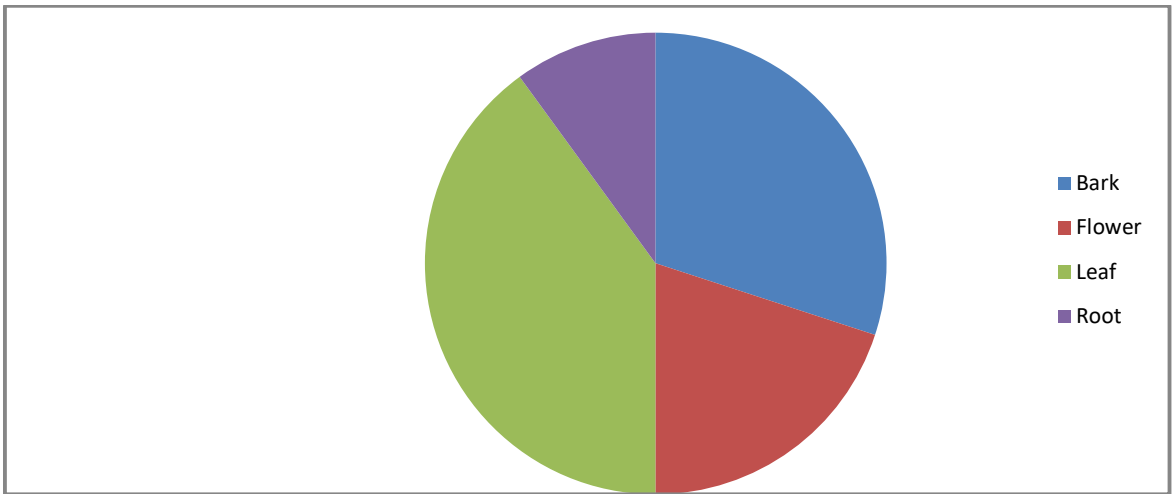

Figure 1: Parts used for *Alstoniascholaris*

Figure 2: *Enhydra flactuans*

Figure 3:*Alstoniascholaris*

Pharmacological Potential: The use of plants in the healthcare had been a trend since ancient time through the ethnic knowledge in generation after generation. Various parts of both the plants attributes to the potential activity of antioxidant, anticancer, anti- ulcerogenic, ant diarrheal, anti-diabetic; wound healing, antimicrobial and anti-diarrheal.

Antimicrobial activity:

The alkanols, alkanes, and sterols constituents of *Alstonia scholaris* are reported to possess antimicrobial property [7]. The various solvents such as butanol, dichloromethane, ethyl acetate, and methanol are used and the extracts of the root barks, leaves, and stem of *Alstonia scholaris* are evaluated and report suggesed that butanol extract fraction posses antibacterial activity i.e; broader spectrum [8].

Antidiarrhoeal activity:

The alcoholic and aqueous extracts of bark of *Alstonia scholaris* were evaluated in mice and evidenced to exhibited antidiarrhoeal effects [9].

Antiplasmodial activity

The methanolic extracts of different parts of *Alstonia scholaris* investigated against *Plasmodium falciparum* K1 strain multidrug-resistant which is cultured in 73 different human erythrocytes. Pronounced to exhibits antiplasmodial activity. The isolated indole alkaloids extract was subsequently tested against the *Plasmodium falciparum* K1 strain. The report suggested antiplasmodial potentials chiefly the bisindole alkaloids, macrocarpamine and villalstonine with IC50 values of 0.36 µM and 0.27 µM respectively [10].

Hepatoprotective activity

The hepatoprotective activity was evaluated by inducing hepatotoxicity by carbon tetrachloride (CCl4), acetaminophen, ethanol and β-Dgalactosamine by histopathological and serum-biochemical findings. The histopathological and serological activity of *Alstonia scholaris* were compared with *Bupleurum chinense*, which earlier reported to be used for the treatment of hepatitis. In β-Dgalactosamine induced hepatotoxicity it was shown to inhibit inflammatory cell infiltration and cell necrosis examined in

histopathological observation [11].

Anticancer activity

Methanolic extracts from root barks of *Alstonia scholaris*, *Alstonia glaucescens* and *Alstonia macrophylla* collected from Thailand, were evaluated for cytotoxic effect against COR-L23 (large cell carcinoma) and MOR-P (adenocarcinoma), two lung cancer cell lines of human, with SRB assay. Pleiocarpamine, macralstonine, O-methylmacralstonine found comparatively less active than the villalstonine [12].

Immunomodulatory activity:

The bark extracts of *Alstonia scholaris* immunostimulating activity was evaluated in BALB/c mouse. The aqueous found to increase lytic activity against *Escherichia coli*. at a concentration of 100 mg/kg body weight. At the doses extract at 50 mg/kg body weight a cellular immune response reported to be induced while at 100 mg/kg body weight found to inhibit the hypersensitivity reaction in delayed type [13].

Antiasthmatic activity:

Ethanolic extract of leaves of *Alstonia scholaris* were evaluated and reported in anaesthetized rats [14]. The plant extract does not confirm bronchodilator effects with guinea pig trachea in *in-vitro* study, reflecting the bronchodilation is not related to the direct relaxation of tracheal smooth muscle. The extract was possessed adrenergic, prostaglandins or muscarinic receptors independently but mostly imparted via relaxing factor derived from endothelial, nitric oxide. The extract also reported to inhibit the subsequent movements of jejunum part of rabbit and also a decrease contractile activity by histamine and acetylcholine guinea-pig ileum. The coupled determination of vivo effects of ethanolic extract suggest that the leaves of *Alstonia scholaris* possess broncho-vasodilatory potentials presumably mediated relaxing factors from endothelium, prostaglandins, and calcium antagonism [14].

Antioxidant (Free Radical Scavenging Activity):

An evaluation has made with extracts of 17 different plants commonly used Indian medicinal plants among these *Alstonia scholaris* bark was reported to possess maximum scavenging of free radical NO it effect at a concentration of 250 µg/mL with a inhibition concentration of 81.86%, whereas *Gingko biloba* reported with a inhibition concentration of 54.9% the scavenging identified at the same concentration [15].

Wound healing activity:

Wound healing activity was investigated by considering the wound contraction rate, epithelialisation duration, strength of breaking of skin, strength of granulation, weight of tissue, collagen and histopathological findings from tissue granulation. To estimate the extent of lipid peroxidation the level of Malondialdehyde was also estimated. The plants extract found to possess an increment in the wound healing significantly observed in studied models. The extract was found to reduce lipid peroxidation with an increased wound contraction rate, breaking strength of skin, strength of granulation, dry granulation weight of tissue, and collagen, a reduced duration in epithelialisation and prolonged collagenation were observed in histopathological section of extract treated groups of animals [16].

Analgesic and anti-inflammatory activities:

The investigation of ethanolic extract of *Alstonia scholaris* leaves was reported with animal experimental models which suggest to possess anti-inflammatory and pain-relieving potentials. The leaf extract were evaluated for writhings test by acetic acid induced model in mice 65.67% decrease of pain was identified at a concentration 400 mg/kg, in hot plate method, at 200 and 400 mg/kg concentration of the extract the inhibition of pain was found to be 73.90 % and 79.56 % respectively. A significant reduction was also in paw edema induced by carrageenan [17].

Anti-ulcer activity:

The anti-ulcer property of ethanolic extract of *Alstonia scholaris* leaves was determined by pylorus ligation method. The treated groups of animals were observed absence of ulceration, whereas in the diclofenac sodium treated group of animals the ulcer score was reported significantly higher ($p<0.01$) in rats [18].

Anthelmintic activity:

Alcoholic extract of *Alstonia scholaris* leaves was evaluated for Anthelmintic activity on *Ascardia galli*. The production of lactic acid, uptake of glucose glycogen content, gross motility and acetylcholine esterase (AchE) activity of *Ascardia galli* were incubated and estimated. *Alstonia scholaris* possess a significant decrease in glycogen content, uptake of glucose in the worms. The increase of lactic acid contents with a certain decrease in gross motility was observed suggesting that the extract also affecting the energy processing mechanism in parasite [18].

Enhydra flactuans

Antimicrobial Assay The primary screening of antimicrobial activity was done by the disc diffusion technique. *Staphylococcus aureus* ATCC 25923 and *Bacillus megaterium* ATCC 13578 the two strains of Gram Positive bacteria and *Pseudomonas aeruginosa* ATCC 27833 and *Escherichia coli* ATCC 25922 two strains of Gram Negative bacteria and *Aspergillus flavus* and *Aspergillus niger* are two strains of fungus, the bacteria were cultured with nutrient agar media and fungi

were cultured with potato dextrose agar media the different fractions of extracts by using dichloromethane or methanol were separately dissolved in a definite volume of solvents based on the solubility. The dissolved and diluted extract samples at a concentration of 500µg/disc were applied and standard antibacterial Kanamycin (30µg/disc) and anti-fungal ketoconazole (30µg/disc) were used and evaluated. Vehicle treated groups are used as negative control. After the incubation of 18 hrs at 37°C and 48 hrs at 28°C for bacteria and fungus respectively, the test agents were evaluated and reported as moderate antibacterial activity but the extract fraction shows negative results on fungus [19].

Thrombolytic Activity

The extract of *Enhydra flactuans* may act as activators for plasminogens forming plasmin leading to the lysis of blood clots. The test sample shows a significant clot lysis of about 46.91% when compared with a negative control (water) the mean percentage for the lysis of clots was significant with a p-value < 0.001. However, the thrombolytic potential was nearly same as that of standard thrombolytic agents may confirmed further through the specific test [20].

Membrane Stabilizing Activity

The ethyl acetate extract of *Enhydra flactuans* contains Flavonoid which was tested for anti-inflammatory activity in histamine and carrageenan inducing paw edema for rats [21].

Antioxidants activity

Previous report of *E. fluctuans* collected from West Bengal, India suggested significant antioxidant property of ethyl acetate extract.

Also there has been report of isolation of antioxidative carbohydrate polymer from aqueous extract of *E fluctuans* which is most consistent with our finding [22].

Anxiolytic activity

Hydroalcoholic extract of *Enhydra fluctuans* were tested with the Elevated Plus Maze and Rota Rod for evaluation of anxiolytic activity using clonazepam a standard drug. The obtained results were elicited by the standard drug clonazepam as (4 mg/kg, i.p.) showing the potential anxiolytic activity as concentration variable manner [23].

CONCLUSION

The study elucidated the rich knowledge on *Enhydra fluctuans's* and *Alstonia scholaris* content diverse bioactive chemical components such as flavonoids, phenolic compound, β-carotene, saponins, terpenoids, glycoside, steroids etc. which chiefly involved in the various pharmacological potentials. The various pharmacological screening of both the plants through *in-vivo* or *in-vitro* studies has reported the potentials towards cytotoxicity, anti-microbial, anti-diarrhoeal, anti-ulcer, thrombolytic, anti-inflammatory, anxiolytic, hepatoprotective etc. A further study with the molecular mechanism can be helpful by providing the new avenues in future pharmacological evaluation and the natural drug discovery.

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