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Phytochemical and Therapeutic Potential of *Alstonia scholaris* R. Br.- A Magical Traditional Plant

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Alstonia scholaris R.Br. commonly known as devil tree is a potential medicinal plant belongs to the family Apocynaceae. Endemic to the geographical areas like India, China and Bangladesh. From the ancient times it is an important medicinal plant containing medicinal potential viabilities to treat number of health condition such as stomach ache, diarrhea, abdominal disorders etc. using various preparations like decoctions, powders etc. Its parts can be administered for the treatment of various diseases. The morphological, organoleptic and microscopic characteristics are also established. It is reported to be rich source of alkaloids. Also, it contains chemical constituents like irioids, coumarins, sugars, oils, phenolics etc. The phytochemical constituents contained in each part are described in the present review. The plant was investigated by the scientists, researchers while performing the experiments on animals they concluded that the plant have pharmacological properties such as antimicrobial, antidiarreal, antitussive, antiasthmatic, immunostimulatory, antidiabetic etc. which are discussed in the article.

Keywords: Alstoniascholaris; assaptaparni; morphological phytochemical antidiarreal antimicrobial antiasthmatic; immunostimulatory; antidiabetic.

1. INTRODUCTION

Plants are beneficial to human beings in number of things such as food, vitamins, shelter and traditional medicine. Traditional / alternative medicines can also be obtained from plants leaves as well roots [1]. Various parts of the plants can be utilized in treatment of diseases; these plants are known as medicinal plants. Medicines which are derived from the plants are

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known for their safety, less side effects, lower costs etc [2-5]. The parts of the plant therapeutically active can be roots, seeds, flowers, barks, rhizomes etc [6]. Medicinal value of the plants is in the phytochemical constituents, that produce biological effects on the physical body of animals. The active chemical constituents are the flavanoids, alkaloids, tannins, terpenoids, aromatic oils and many more [7]. Number of plants are reported to have medicinal effect. From a count of 24,800 identified species of higher plants almost 12,000 are known to have therapeutic properties. As per the recent advancements, variety of plants, not only in Ayurveda but also in modern sciences, remains the active ingredient of many efficacious drugs. The traditional systems of medicines merged ancient believes, and passed on from one generation to the other. Currently, the effort is to review and gather the updated information on the plant *Alstonia scholaris*. *Alstonia scholaris*, Blackboard tree, devil tree, saptaparni, was used previously to cure various ailments like malaria, dyspepsia, laxative etc. It is an evergreen topical tree growing up to the height of 6-10 meters, belonging to the family apocynaeceae. Generally, is found in India, China, Nepal, Sri lanka, Bangladesh, Philippines etc. The tree is even native to Indian subcontinent and some parts of Malaysia, Indonesia and Australia. In India, the plant grows in humid regions, especially in the coastal areas of the southern India [8]. It's planks when polished were used by the students in drawing the alphabets [9-11]. The plant is mainly used for treating gastrointestinal conditions and work as febrifuge. It treats abdominal pains, irregular menstruation, chronic diarrhea and advanced stages of dysentery [12,13]. This review is centralised to the botanical aspect, traditional use, scientific (phytoconstituents and pharmacological) use of *Alstonia scholaris.*

2. BOTANY AND ANATOMY OF *Alstonia scholaris*

Alstonia scholaris a traditional plant raised with the help of seed grown in the soil containing alluvia, yellow earth, red earth with sandy grey earth and is planted in the garden for ornamental purposes (Bhattacherji *et al.,* 2019). Seeds are flattened with brownish hair at any of the end, oblonged and 6-8mm in length. Fruits are two lobed, containing number of brown seeds, glabrous, winged on one suture, spindle shaped [14] 20-50cm long, grows generally in the month of May to July. Flowers are greenish white in colour, small in size, umbellate in arrangement, 7-8 mm in length, fragrant, flowering month are December to march. The bark of the tree is corky grayish white in colour, rough, tessellated, ejects apex of yellow colour used for healing injuries [15]. Leaves are dark green in colour on the above and pale in the beneath,4-7 in number arranged in whorls, tip of the leaves is shortly pointed and somewhat rounded, narrow at the base [16], obovate to oblanceolate, rounded apex, petioles are 6-12 mm long [15]. In microscopic studies of fruit of the plant, the transverse section of fruits contains pericarp, testa, endosperm. In pericarp there is presence of single layer of polygonal cells of epicarp containing the covering of thick cuticles. Mesocarp is made of multilayers consisting of parenchymatous cells further showing the presence of latex cells of orange colour and vascular bundles. Endocarp is double layered [17-19]. Testa contains elongated cells. Endosperm consists of polygonal parenchymatous cells containing latex cells of orange colour [20]. The transverse section of petiole of leaf shows the presence of collenchymas, sclerenchyma, marginal bundles. Transverse section of leaf shows the presence of barrel shaped cells on the epidermis covered with thick cuticles [21]. The stomatas are sunken, and are at lower surface. Mesophyll consists of the palisade and spongy tissues. Xylem is arc shaped surrounding phloem from both sides [22].

3. TRADITIONAL USES OF *Alstonia scholaris*

Alstonia scholaris have been in use from the ancient times in treating certain health problems. As per ayurveda, different segments of the plant namely fruit, leaves, roots, bark are used in treating different ailments [1]. The bark has astringent and bitter taste, acts as stomachic, cardiotonic, antipyretic, laxative, antihelmintic. Also, is useful in the treatment of dyspepsia, abdominal disorders, malarial fevers [23]. Bark extract is reported to be effective as antispasmodic, anticancer, hepatoprotective, immunostimulant [24]. When the bark is kept in water overnight, it helps in reducing the blood glucose levels [25]. Ripen fruit of the plant is effective in epilepsy and certain sexually transmitted disease such as syphilis. Also, acts as antiperiodic, tonic, antihelmintic. Traditionally leaves were used as folk remedies, for the treatment of malaria, snakebites, dysentery. Extract of the leaf acts as powerful galactogogue [26].

4. SCIENTIFIC REPORTS

4.1 Phytochemical Contents

Alstonia scholaris contains various chemical constituents such as alkaloids, tannins, flavanoids, coumarins, iridoids, reducing sugars, phenolics, steroids, leucoanthocyanins, carbohydrates, fats, fixed oils and many other [27]. The bark of *Alstonia scholaris* is useful in malarial fevers, abdominal disorders, dyspepsia and abdominal disorders, dyspepsia. The ripen fruits are used in various diseases like syphilis and epilepsy also used as tonic and anthelmintic. *Alstonia scholaris* has been used from the ancient times to treat many health problems. As per ayurveda it's various parts like fruit, bark, flowers, leaves are used in curing the diseases [28]. The bark is bitter and astringent in taste acts as stomachic, laxative, antihelminthes, antipyretic,cures certain skin and digestion related problems. Also, is useful in abdominal disorders, dyspepsia, malarial fevers. In ayurveda it is believed that the bark when soaked in water overnight, helps in reduction of blood glucose level. The exract of bark is reported to be effective as hepatoprotective, immunostimulant, anticancer, antispasmodic [29]. Ripen fruits treats syphilis, epilepsy. The fruit also acts as antiperiodic, antihelmintic Leaves of the plant were traditionally used as folk remedies for the treatment of diseases like diarrhea, dysentery, malaria Extract of the leaves act as powerful galactogogue [30]. But, the plant is exclusively investigated to be rich source of alkaloids [31] and there is interest among the scientists to use this for therapeutic purposes. Amongst the chemical classes present in medicinal plant species, alkaloids stand as a class of major importance in developing new drugs because alkaloids own a great variety of chemical structures and have been identified as being responsible for the pharmacological properties of medicinal plants. Almost all the parts of plant (bark, root) are found to contain active principle. The plant is investigated to be exclusively ample source of alkaloids [31] such as echitamine, indole alkaloids, 2,3 secofernaneterpenoids, alstonic acid A and B, 3 beta acetate-24-nor-urs-4, 12-diene ester triterpene, 3 beta- hydroxyl-24-nor-urs-4,12, 28-tripene, triterpene, 3, 28,- beta- diacetoxy-5-olea-triterpene, alpha-amyrin acetate [32]. ursolic acid, lupeol acetate, monoterpenes, triterpene, megastigmane-3beta,4alpha, 9 triol, 7-megastigmane-3,6,9-triol, C13-norisoprenoid [33]. The essential oils in flowers of the plant contains 2-dodecyloxrane, 1,2-dimethoxy-4-(2-propenyl)benzene, spinacene, 1,54-dibromotetrapentacontane, 2,6,10,15-tetramethylheptadecane, tripenyl acetate, linalool, tritetracontane, 2-(3-methyl-1,3 butadienyl)-1,3,3 trimethyl-1-cyclohexanol, 9-methyl,5-methylene-8-decen-2-one [34]. Ethanolic extract of flower consists ofalstoprenyol, 3-beta-hydroxy-28-beta-acetoxy-5-olea, alpha-amyrin acetate, lupeol acetate, alstoprenylene,3beta-acetate-24-nor-urs-4,12,2-triene ester, 3beta hydroxyl-24-nor-urs-4,12,28-triene [35]. 12-diene ester triterpene,3,28 beta-acetoxy-5-olea-triterpene [36]. 5beta-methoxyaspidophylline, 5-methoxystrictamine [37]. Leaf has losbanine,6,7-seco-angustilobine B ,19-epischolaricine, N-methyl,19-scholaricine, N-methyl scholaricine, N-methyl burnamine,vallesamine N-oxide [38]. Some of the n- alkanes like C31, C33,C29,C32,C25,C17,C22 in minor quantities [39]. Leaf extract consists of various elements like Cu, Zn, Fe, Ca, Cr, Mn and Cd [40]. 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 [39]. cycloeucalenol, 7,3,4-trimethoxy-5-hydroxy flavones, 3,5,7,4-tetrahydroxy-flavone-3-O-beta-D-glucoside. The leaves contain cycloeucalenol, cycloartanol, lupeol, betulin, lupeol acetate, picralinal, nareline, alstonamine, sitsirikine, rhazmanine [41]. Some of the chemical constituents in both stem, roots, bark are tubotaiwine, akuammicine, echitamidine, ditamine, echitenine. Leaves, roots, bark contains pseudo the chief-o-akuammidine, picrinine, picralinal, nareline, strictamine. N-hxacosane, lupeolt beta- amyrin, ursolic, palmitic acid is some of the non-alkaloids in the flower of the plant [42,43]. Alpha-amyrin acetatelupeol, beta-sitosterol (, indole alkaloids are present in the root barks [44] Stem bark contains indole alkaloids, akuammigi, echitamidine N-oxide-19-O-none, beta-D-glucoside, echitaminic acid, echitaminidine N-oxide, N-demethylalstogustine [45] scholarisines beta-G together with analogues Feng et al. [43], 11-noriridoids, scholereins A-D, isoboonein,alyxial -acetone, loganin),17-O-acetylechitamine, echitamine scholarisines-I, II. Alpha-amyrin acetate, beta-ayrin acetate, lupeol acetate, alpha-amyrin fatty acid esters, beta-amyrin fatty acid esters, lueol fatty acid esters, phytyl fatty acid esters mixtures of these

chemical constituents are also present in flower [46]. Miscellaneous constituents are isookanine-7-O alpha-lrhamnpyranside, a new flavanone glycoside, alstonoside, secoiridoids glycoside, agr-amyrin, lupeol acetate, linalool, cis trans linalool oxide, alpha-terpineol, 2-phenyethyl acetate, terpinen-4-ol,steroids.

5. PHARMACOLOGICAL REPORTS

5.1 Anti-bacterial Activity

The antibacterial activity of the plant constituents of *A. scholaris* were the methanolic andacetonic extracts of the plant [47]. The leaves, roots, stems, bark, contains the crude methanolic extract [48]. Powder of leaf is extracted with the help of ether, chloroform, ethyl acetate, methanol. The in vitro studies of antibacterial activity reports that the total alkaloidal, methanolic and aqueous extract of the trunk bark was effective against two gram positive bacteria which are Streptococcus pyrogen and Bacillus subtilis, also against four negative bacteria's which are *E. coli*, *Pneumonia*, *Pseudomonas aerugenosa*, *Proteus mirabilis*. Different extracts shows varying degrees of inhibitory activities, against the bacterias. As compared to the other extracts aqueous extracts was found to be very active against all types of bacteria whether gram positive or gram negative. The entire alkaloids were active against gram negative bacteria (Swafiya *et al.,* 2010). Various bacterial strains were used to test the antibacterial activity such as *Streptococcus aureus, Micrococcus luteus*, In the study bacteria used were associated with different infections such as typhoid, cough, fever like *Salmonella typhi, Salmonella paratyphi*. Microorganisms like *Aspergillus niger, Candida tupicallis, Pencillium notatum, Trychophyton tronsrum*. Antibacterial activity against test bacterias demonstrated the possibility of utilizing other antibiotic component in the plant [49].

5.2 Anti-tuberculosis

Antituberculosis activity of ethanolic extract of leaf, stem, bark, root of the plant also reported [50].

5.3 Anti-Asthmatic, Anti-tussive, Expectorant

The ethanolic extract of the leaves of the plant shows anti-asthmatic, anti-tussive, expectorant activity. During the investigation of the anti-asthnatic property a guinea pig was taken as a study model, histamine was injected into the animal resulting into bronchial contraction. While, studying the anti-tussive behavior of the plant, three different models were considered such as sulphurdioxide, ammonia, citric acid. Ammonia or sulphur dioxide, caused coughing in mice, citric acid induction resulted to coughing in guinea pig. During the study of expectorant activity, phenol red was introduced into trachea of mice. Fraction of alkaloids resulted in inhibiting certain frequency of coughing in mice, induced by the sulphur dioxide, and increase the latent coughing period in guinea pig. Along with these activities, sudden disappearance in the symptoms of convulsions were also seen in guinea pig during the anti-asthmatic tests. Picrinine, the main alkaloidal constituents of the plants is reported to be effective in anti-tussive, anti-asthmatic activity [51].

5.4 Bronchovasodilatory Activity

The leaves of the plant A.scholaris containing ethanol extract possess the bronchodilatory action. The study model was anesthetic rat [51]. The vasodilation activity was reported to be through endothelial from which relaxing factor, nitric oxide is obtained. The study observed that the ethanolic extract resulted into inhibition of contractile effects of histamine, acetylcholine, on ileum of guinea pig, and the inhibition of movements in jejunum of rabbit. Also, there was reduction observed in contraction in ileum and pulmonary artery of guinea pig caused by injecting barium chloride, potassium chloride, calcium chloride. There was influx of calcium ion into the cells. So, the overall studies of broncho vasodilator activity showed by the plant is mechanized by prostaglandins, calcium antagonism and the endothelium derived relaxing factor [52].

6. ANTILEISHMANIAL

Antileishmanial property was obtained from the extract of the plant *A.scholaris*. The property was evaluated by study in hamster which was infected by *Leishmania donovan* [53].

6.1 Antiplasmodial and Antimalarial

The various parts of the plant *A.scholaris* consisting the methanolic extract were tested against multidrug resistant K1 strain of the specie *P. falciparum* which was cultured in human 73

red blood cells. Also from the active extract of the plant, indole alkaloids were extracted out and were tested against the K1 strain of Plasmodium falciparum, that resulted in anti plasmodial action mostly amoung various chemical constituents such as villalstonine, macro carpamine and bis-indole alkaloids [54]. The plant's methanolic and petroleum ether extract lacked the antimalarial activity when was studied by injecting the *Plasmodium berghei* in mice. Methanolic extract when received by the animal showed the dose dependent improvements and delayed mortality in animals [55]. Final result came out to be that *A. scholaris* do not show antimalarial effect in humans and monkey like species. Some of the constituents were recommended such as quinine and some of the cinchona alkaloids..

6.2 Anti-Inflammatory Activity and Analgesic

Various experimental studies on the anti-inflammatory and analgesic property of the plant were conducted such as inhibition of the enzyme cycloxygenase-1,2 and 5-lipoxygenase , ear edema induced by xylene, air pouch induced by carrageenan in mice. The alkaloidal fractions decreased writhing response in mice induced by injecting acetic acid (Arulmozhi, *et al.,* 2007). During the experimentations in hot plate test in mice there was no increase in latency periods by the alkaloids. Even in the formalin test there was no inhibition in licking time during the first phase, though it resulted in inhibition during the second phase. The alkaloidal extract inhibited the ear edema induced by xylene. Also it resulted in decreasing the levels of prostaglandins, malondialdehyde in the air pouch test method. The mechanism of anti-inflammatory is also beneficial in the anti-cancer property (Protein kinase A was inhibited by some compounds lupane triterpenoids, ursane triterpenoids alpha amyrin, they also possess anti-inflammatory property [56]. The conclusion came out to be that the leaf constituents like 16-formyl5α-methoxystrictamine, picralinal, and tubotaiwinepicrinine, vallesamine, scholaricine of the plant *A.scholaris* are beneficial in inhibiting the cycloxygenase enzymes COX-1,COX-2, 5-LOX. thus it has anti-inflammatory properties and analgesic properties confirmed by performing various in-vivo assays [57].

6.3 Ameliorating effect

The aqueous extract shows the ameliorating effect of the plant. As it is reported that A.scholaris reduces the injury in organs like liver and kidney. Injury is reduced histopathologically compared to the viper venom that may associate with the complexation of polyphenols with some venom enzymes [58].

7. ANTIFERTILITY PROPERTY

Antifertility effect was studied in the male Wister rats developed in the laboratory. Bark extract was given to the rat for 60 days, there were some significant changes in the reproductive organs such as reduction in the weights of epididymes, seminal vesicle, ventral prostate, testes [59]. The spermatids were reduced in the experimented rats. The number of pachytene and preleptotene spermatocytes reduced. The population of sertoli cells and spermatogonia was also affected. A significant decrease in the sperm count, motility, sialic acid content, leydig cells, seminiferous tubules [60]. Thus *A.scholaris* was reported to be effective in its anti-fertility activity. The lupeol acetate when isolated from benzene extract of *Alstonia scholaris* also showed anti-fertility activity when injected in albino rats [60].

7.1 Antiulcer Property

During the experimentation of pyloric ligation method, the ethanolic extract of the plant showed the anti-ulcer property. Extract when injected into the animal showed no ulcers, while the score of ulcers was found to be high with the diclofenac sodium in rats (Arulmozhi, *et al.,* 2007).

7.2 Antihypertensive

Hypertensive activity of the plant is shown by the decoction of bark. The property was studied in the patients suffering from hypertension or high blood pressure [61].

7.3 Antidepressant Activity

Leaves containing ethanol extract of *A.scholaris* appears to be beneficial as anti-depression, anti-anxiety. The ethyl acetate fragment of the extract is reported to be effective against the various models which are open field, elevated plus maze, hole board, mirror chamber, foot shock, light dark box (Arulmozhi, *et al.,* 2008). Estimation of change in monoamines was studied. 5-hydroxy tryptophan was induced to test serotonergic effects during experimentation in wet dog shake, tail suspension, modified forced swim test. In open field test, foot shock, mirror chamber anxiety models, the ethyl acetate was found to

be active. Although there was no activity found in the elevated, plus maze, light dark box, hole board test models. Increase in the levels of 5-hydroxy tryptamine, enhance HTP 5-hydroxy tryptophan, decreased motor activity proved the serotonergic effect of ethyl acetate in brain. Reserpine inhibited the immobility time during tail suspension test. In forced swim test the swimming behavior was increased hence proved the inhibition of selective serotonin reuptake. Therefore, the ethyl acetate in the plant worked on the mechanism of selective serotonin reuptake inhibition, Concluding the plant to be effective as antidepressant, antianxiety (Arulmozhi, *et al.,* 2012)

8. WOUND HEALING PROPERTY

Both the ethanolic as well as methanolic extracts of the plant was tested for the wound healing activity by testing against the dead space wound, excision, incision models [62]. The mechanism was studied by the effects on skin breaking strength, granulation strength, period of epithelialization, rate of wound contraction, hydroxyproline, dry granulation tissue weight, collagen and the histological pathology of granulation tissue. Estimation of malondialdehyde levels were performed to evaluate the lipid peroxidation. Wound healing was promoted by the extract in every experimental models. Resulting in increased rate in wound contraction, strength of skin breaking and granulation, dry granulation tissue weight, collagen and the hydroxyproline, reduction in the rate of epithelialisation, increase in process of collagenation in histopathological sections. There were also decrease in levels of lipid peroxidation observed.

8.1 Hepatoprotective Activity

Liver sufferings caused due to the acetaminophen, Carbontetrachloride, beta-D galactosamine and ethanol were studied with the help of histopathological and serum biochemical studies [63]. Treatment with *A.scholaris* caused certain results such as elevatation of serum transaminases levels were reduced, changes in inflammation f cell infilteration, cell necrosis by injecting acetaminophen in mice. Beta-D galatosamine induced increase in levels of serum transaminases were lowered by A.scholaris, durng serum biochemical analysis in rats. Therefore, methanolic extract of the bark was effective in improving hepatocytes, decreased the parameters like serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, Thymidine Phosphorylase, Alkaline phosphatase [54].

8.2 Antidiabetic and Antihyperlipidemic

Streptozotocin diabetic rats shows reduced elevation in blood glucose level by injecting the aqueous extract of *A.scholaris*. The more usage of glucose by the peripheral tissue can be the main reason for the anti-diabetic effect, serum triglyceride level was decreased in streptozotocin diabetic rats, normalized lipid metabolism, which further prevent cardiovascular disorders (Arulmozhi, *et al.,* 2010). Thus, blood sugar level was reduced by glebenclamide and ethanolic extract, many significant effects were increased body weight, liver, muscle glycogen, antioxidant values, but the beta cells of pancreas were not reversed. In diabeties mellitus, antiantherogenic potential is beneficial and also during chronic diabeties mellitus it is also beneficial (Arulmozhi, *et al.,* 2007)

8.3 Antidiarrheal and Spasmolytic Activity

Alkaloids present in the plant *A. scholaris* were effective in providing protection during the experiment of diarrhea induced by castor oil in mice, it worked similar to the drug loperamide hydrochloride. *A. scholaris* inhibited high potassium induced contraction, during rabbit jejunum preparation test. Thus, worked by showing spasmolytic property blocking calcium channel. Further studies of the tissue with extract gave right ward shift curve of calcium concentration response, same as virapamil which is a standard calcium channel blocker. Result concluded *A. scholaris* to be having medicinal use through the mechanism presence of calcium channel blocker like constituents. Hence, beneficial in the case of colic, diarrhea.

8.4 Antioxidant

Extracts of A.sholaris were evaluated by conducting various tests that are free radical scavenging, hydrogen peroxide scavenging, superoxide anion radical scavenging, 1,1-diphenyl-2-picryl-hydrazil, ferric thiocyanate reducing ability test [65]. The compound such as dichloromethane and ethyl acetate have properties like free radical scavenging and metal ion chelation. But petroleum ether and n-butanol fractions did not possess anti oxident property. Butylated hydroxyanisole (BHA) and l-ascorbic

acid which are known to be standard antioxidant were compared with various antioxidant activities. It was concluded that the dichloromethane and ethyl acetate were proved to possess powerful antioxidant reducing agent, metal chelator etc. Also, the ethanolic extract of the plant worked as oxidant-induced lipid peroxidation and radical chain reactions.

8.5 Anticancer

In earlier days, herbal healers of India, thailand and admiralty islands used to treat cancer with the decoction of *A. scholaris* (Graham *et al.,* 2000), which is also experimentally or pharmacologically proven nowadays [66,67]. Human sarcoma type of cancer in embryonated egg has been reported to be treated with bark's alcholic extract of *A .scholaris* (CHEMEXCIL, 1992). Methanolic extract of bark (root bark) of *A. macrophylla*, *A. scholaris* and *A .glaucescens* has been reported to treat human lung cancer, COR-L23 (large cell carcinoma) and MOR-P (adenocarcinoma) by its cytotoxic activity, this study was done by, thus proving that *A .scholaris* and its related species have some anticancer or antineoplastic effects [68]. The activity of this plant biologically are known to change ever season, for that an experiment was done with *A. scholaris* (it's hydroalcholic extract) of same tree with human cervix cells which are neoplastic and cultured in laboratory in vitro. The results of study determined that killing of cells was totally dependent on the season during the harvestation of the same plant bark.In summer effect of extract was (IC50 of 30 µg/mL) highest followed by (IC50 of 45 µg/mL) winter, and (IC50 of 55 µg/mL)monsoon. As per the polarity the fractionating hydro alcoholic extract was assayed and solvents like petroleum ether, ethyl acetate, n-butanol, diethyl ether etc. were used and their cytotoxic effect on cells (HeLa cells) were investigated and in postive control echitamine was taken, which is the prime alkaloid of the *A .scholaris*. After the study cytotoxicity was found to be in decreasing order:(IC50 = 8 µg/mL) etract residue fratcion> (IC50 = 30 µg/mL) whole extract > (IC50 = 35 µg/mL) chloroform fraction > (IC50 = 47 µg/mL) echitamine> (IC50 = 73 µg/mL) ethyl acetate fraction > (IC50 = 76 µg/mL) diethyl ether fraction > (IC50 = 78 µg/mL) petroleum ether fraction > (IC50 = 96 µg/mL) n-butanol fraction > (IC50 = 96 µg/mL) aqueous fraction [69].

In an another study, after preliminary investigation it was found that chloroform extract, whole extract and extract residue fraction (was found to be effective for antitumoral effects in mice bearing tumor, results were extended from in vitro to in vivo. were dense with alkaloids and some of those alkaloids few were responsible for antineoplastic or anticancer effects. It was also found that echitamine was cytotoxic to HeLa, KB, HepG2, MCF-7 cells, HL-60, fibrosarcoma, Vero cells, and was effective in treating fibrosarcoma in rats, Regression in growth of tumor of fibrosarcoma in rats which was induced by methylcholanthrene (in vivo) was seen to be treated with echitamine. Echitamine was found to regulate as well as normalize the levels of liver and plasma transaminases, lipid peroxidation and activities of superoxide dismutase, glutathione peroxidase, and catalases. Echitamine also regulates the level of liver glutathione to normal [69].

Alstonine an indole alkaloid found in A scholaris, it was found to have anticancer effects for pathological condition YC 8 lymphoma ascites in mice and ehlrichascite in Swiss mice. Alstonine inhibits synthesis of DNA by formation of a complex (alkaloid-DNA complex), it has selective cytotoxic effect on tumor cells and it was partially effective in solid tumors [70]. Some reports have shown that the presence of triterpenoid lupeol in *A. scholaris* and plants like mango and olive, have antiproliferative action on cancerous cells of different origin in humans, like melanoma cells WM35, B162 and 451Lu [71]. Epidermoid carcinoma cells A431; AsPC-134 in pancreatic adenocarcinoma; hepatocellular carcinoma cells SMMC7721; [72]. and cells of prostate carcinoma LNCaP PC-3, [71] and CWR22Rγ1.37 Lupeol was also found that it was not cytotoxic for normal cells, which shows the selective cytotoxic action on cancerous cells by lupeol. The growth of CWR22Rnu1 and 451Lu tumor was reduced by giving lupeol to athymic nude mice [72]. Lupeol causes arrest of G1-S phase in cell cycle and reduced the expression of cyclins like D1 and D2, and cdk2 with increased expression of protein p21 in PC-3 cells [73]. Expression of Rasoncoprotein was reduced and modulation of expression of signaling molecules like MAPKs, PI3/Akt, PKCα/ODC, and NFκB in signalling pathway of AsPC-1 [73]. The expression of the death receptor-3 was redcued and elevation of expression of FADDmRNA in SMMC7721 cells [74]. Expression of metalooproteinases-3, ERBB2, MMP-2 genes, and cyclin D-1 (are modulated by lupeol) which are involved in survival and growth of LNCap cells [75]. Lupeol inhibits cyclin B, plk1, and

cdc25C expression, but it induces the expression of the 14-3-3 sigma genes in PC-3 cells. Some reports suggested that lupeol induces the apoptis by downregulating Bcl2, activating caspase-3, upregulating Bax and activating caspase-9, -3 and PC-3 cells with are cancerous. Treatment of lupeol is found to increase ROS and loss of mitochondrial membrane potential and DNA fragentation is induced in PC-3 cells Lupeol decreases phosphocofilin and inhibits haptotaxis of B16 2F2 canceros cells to fibronectin.

9. CONCLUSION

Alstonia scholaris, plant has been utilized traditionally in several health related problems. The study reveals the pharmacognostic and pharmacological activities of the compounds existing in *Alstonia scholaris*. It is reported to be exclusively rich in bioactive compounds. Examinational studies performed by the researchers concluded the medicinal potential existing in the segments of the plant. The results of the studies conducted is explained briefly in the article.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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