Rebuttal in red and blue fonts

Red = correct, blue =delete

Alstoniascholaris: A magical traditional drug used in healthcare system

SMART Topic: Roles of Alstonicaris, Magical Drug as the Alternative Medicine for Gastrointestinal Infections.

ABSTRACT

Alstoniascholaris, often called (assaptaparni), devil tree etc as well, is a medicinal plant, easily accessible, and belongs to family theapocynaceae. Endemic to the geographical areas like India, China, and Bangadesh etc. Since, from the ancient times it is an important medicinal plant containing medicinal potential viabilities to treat number of health conditions issues such as stomachic ache, diarrhea, abdominal disorders etc. By various preparation as de concoctions, powders and so on. Its part can be administered for the treatment. The morphological, organoleptic and microscopic characteristics are written in detail as SOPs. 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 listed in SOPs. The plant was investigated by the scientists, researchers while performing the experiments method used sample size calculation, study design and sampling design??? Brief results??? On animals they concluded that the plant have pharmacological properties such as antimicrobial, antidiarreal, antitussive, antiasthmatic, immunostimulatory, antidiabetic etc discussed in the article.

Introduction

Plants are beneficial to human beings in number of things such as food, vitamins, shelter and traditional medicine etc. Tradinal / alternative Medicines can also be obtained from plants leaves as well roots (Bainsal, et.al 2021). 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 known for their safety, less side effects, lower costs etc. The parts of the plant therapeutically active can be roots, seeds, flowers, barks, rhizomes etc (Sharma, Rana.*et.al*, 2011).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 (Zahoor, Ullah.et.al, 2014). 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 Alstoniascholaris. Alstoniascholaris,also named as called Blackboard tree, devil tree, saptaparni, was used previously to cure various ailments name them . It is an evergreen topical tree growing up to the height of 6-10metres, belonging to the family apocynaeceae (Bhattacharji, Not theapocynaceae?? Harunaker.et.al, 2019). 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 (Tomar, 2016). In India, the plant grows in humid regions, especially in the coastal areas of the southern India (Dey, 2011). Its planks when polished were used by the students in drawing the alphabets. The plant is mainly used for treating skin allergies?? Is not gastrointestinal condition, and work as febrifuge. It treats abdominal pains, irregular menstruation, chronic diarrhea and advanced stages of dysentery (Tomar, 2016). This review is centralized to the botanical aspect, traditional use, scientific (phytoconstituents and pharmacological) use of *Alstoniascholaris.*

Botanical Aspect Botany and anatomy of *Alstoniascholaris*

Alstoniascholarisis 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, Harunaker.et.al, 2019). Seeds are flattened with brownish hair at any of the end, obliged and 6-8mm in length. Fruits are two lobed, containing number of brown seeds, glabrous, winged on one suture, spindle shaped (Nadkarni, 1976), 20-50cm long, grows generally in the month of May to July. Flowers are greenish white in color, small in size, umbellate in arrangement, 7-8mm in length, fragrant, flowering month are December to march. The bark of the tree is corky grayish white in color, rough, tessellated, and ejects atex of yellow color used for healing injuries (Nitika, Meena.*et.al*, 2001). 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 (Chakraborty, Kalakari.et.al, 2012),obovate to oblanceolate, rounded apex, petioles are 6-12 mm long (Dey, 2011). 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 (Agarwal and Paridhav, 2007).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. Testa contains elongated cells. Endosperm consists of polygonal parenchymatous cells containing latex cells of orange colour(Mukherjee, 2002). The transverse section of petiole of leaf shows the presence of collenchymas, sclerenchyma, marginal bundles(khyade and Vaikos, 2009). Transverse section of leaf shows the presence of barrel shaped cells on the epidermis covered with thick cuticles (Chopra, Nayer.et.al, 1956). 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 (Joshi, 2000).

Traditional Medicinal Uses of *Alstoniascholaris*

Alstoniascholaris have been in use from the ancient times in treating certain health problems. As per Ayurveda: (meaning in English), different segments of the plant namely fruit, leaves, roots, bark are used in treating different ailments (Bainsal, Goyal.et.al, 2020). The bark has astringent and bitter taste, acts as stomachic, cardiotonic, antipyretic, laxative, antihelmintic (Nadkarni, 1976). Also, is useful in the treatment of dyspepsia, abdominal disorders, malarial fevers (Kirtikar and Basu, 1999). Bark extract is reported to be effective as antispasmodic, anticancer, hepatoprotective, immunostimulant (Supriyatna, Pal.et.al, 1996). When the bark is kept in water overnight, it helps in reducing the blood glucose levels (Deepti, Archana.et.al, 2011). Ripen fruit of the plant is effective in epilepsy and certain sexually transmitted disease such as syphilis. Also, acts as antiperiodic, tonic, antihelmintic (Pawan, dhirender.et.al, 2011) .Traditionally leaves were used as folk remedies, for the treatment of malaria, snakebites, dysentery. Extract of the leaf acts as powerful galactogogue(Arulmozhi, Mozumder.et.al, 2010).

Scientific Reports

Phytochemical reports contents.

Alstoniascholaris contains various chemical constituents such as alkaloids, tannins, flavanoids, coumarins, iridoids, reducing sugars, phenolics, steroids, leucoanthocyanins, carbohydrates, fats, fixed oils and many other (Chakraborty, Kalakari.et.al, 2012), (Vaidyanatha, Joel.*et.al*, 2011). The bark of Alstoniascholaris is useful in malarial fevers, abdominal disorders, dyspepsia and abdominal disorders, dyspepsia. And. The ripen fruits are used in various diseases like syphilis and epilepsy also used as tonic and anthelmintic (Pawan.et.al, 2011). Alstoniascholaris 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 (Bainsal, Goyal.*et.al*,2020). The bark is bitter and astringent in taste acts as stomachic, laxative, antihelminthes, antipyretic,cures certain skin and digestion related problems (Nadkarni, 1976). Also, is useful in abdominal disorders, dyspepsia, malarial fevers (Kirtikar and Basu, 1999). In ayurveda it is beleived that thebark when soaked in water overnight, helps in reduction of blood glucose level (Deepti, Archana.et.al, 2011). The exract of bark is reported to be effective as hepatoprotective, immunostimulant, anticancer, antispasmodic (Supriyatna, Pal.et.al, 1996). Ripen fruits treats syphilis, epilepsy. The fruit also acts as antiperiodic, antihelmintic (Pawan, Dhirender.et.al, 2011). Leaves of the plant were traditionally used as folk remedies for the treatment of diseases like diarrhea, dysentery, malaria (Kirtikar and Basu, 1999). Extract of the leaves act as powerful galactogogue (Arulmozhi, Mazumder.et.al, 2010). But, the plant is exclusively investigated to be rich source of alkaloids (Chakraborty, Kalakari.et.al, 2012) 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, □ower, root) are found to contain active principle. The plant is investigated to be exclusively ample source of alkaloids(Chakraborty, Kalakari.et.al, 2012) 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(Quattrocchi, 2012), ursolic acid, lupeol acetate, monoterpenes, triterpene, megastigmane-3beta,4alpha, 9 triol, 7-megastigmane-3,6,9-triol, C13-norisoprenoid (Dung, Ngoc.et.al, 2001).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 (Shang, Fang.et.al, 2010). 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(Hirasawa, Miyama, 2009).12-diene ester triterpene,3,28 beta-acetoxy-5-olea-triterpene (Sultana, Saleem, 2010). 5beta-methoxyaspidophylline, 5-methoxystrictamine (Cai, Liu.et.al,

2008). Leaf has losbanine,6,7-seco-angustilobine B ,19-epischolaricine,N-methyl,19-scholaricine, N-methyl scholaricine, N-methyl burnamine,vallesamine N-oxide (Yamauchi, Abe.et.al, 1990). Some of the n- alkanes like C31,C33,C29,C32,C25,C17,C22 in minor quantities (Dutta, Laskar, 2009).Leaf extract consists of various elements like Cu, Zn, Fe, Ca, Cr, Mn and Cd (Zhang, Gao. Et. al, 2009), 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 (Yamauchi, Abe.et.al, 1990), cycloeucalenol, 7,3,4-trimethoxy-5-hydroxy flavones, 3,5,7,4-tetrahydroxy-flavone-3-O-beta-D-glucoside (Deepthi, Remya, 2008). The leaves contains cycloeucalenol, cycloartanol, lupeol, betulin, lupeol acetate, picralinal, nareline, alstonamine, sitsirikine, rhazmanine(Macabeo, Krohn.et.al, 2005, Quattrocchi, 2012). 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 (Feng, Cai, 2008). N-hxacosane, lupeolt beta- amyrin, ursolic, palmitic acid is some of the non-alkaloids in the flower of the plant (Feng, Cai, 2008). Alpha-amyrin acetatelupeol, beta-sitosterol(Hirasawa, Miyama, 2009), indole alkaloids are present in the root barks (Wongseripipatana S, Chaisri.et.al, 2004). Stem bark contains indole alkaloids, akuammigi, echitamidine N-oxide-19-O-none, beta-D-glucoside, echitaminic acid, echitaminidine N-oxide, N-demethylalstogustine (Salim, Garson.et.al, 2004), scholarisines beta-G together with analogues (Feng, Cai, 2009), 11-noriridoids, scholereins A-D, isoboonein,alyxial -acetone, loganin (Feng, luo, 2008),17-O-acetylechitamine, echitamine (Yamauchi, Abe.et.al, 1990),scholarisines-I, II (Cai, Shang.et.al, 2010). 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 (Kam, Sim.et.al, 1997). Miscallanous constituents are isookanine-7-O alpha-lrhamnpyranside,a new flavanone glycoside,alstonoside,secoiridoidsglycoside,agr-amyrin,bgr-amyrin,lupeolacetate,linalool,cis trans linalool oxide, alpha-terpineol, 2-phenyethyl acetate,terpinen-4-ol,steroids (Salim, Garson.et.al, 2004).

Pharmacological reports **Potency and viability**

ANTI-BACTERIAL ACTVITY

The antibacterial activity of the plant constituents of A. scholaris were the methanolic andacetonic extracts of the plant (Gami, Parabia.et.al,2011). The leaves, roots, stems, bark, contains the crude methanolicextract(Khan, Omoloso.et.al, 2003). Powder of leaf is extracted with the help of ether, chloroform, ethyl acetate, methanol (Khyade, Vaikos.et.al, 2009). The invitro 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 bacterias 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 bacterias whether gram positive or gram negative. The entire alkaloids were active against gram negative bacteria (Swafiya, Ranu.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 etc. Salmonella typhi, Salmonella paratyphi. Microorganisms like Aspergillus niger, Candida tupicallis, Pencilliumnotatum, Trychophytontronsrum. Antibacterial activity against test bacterias demonstrated the possibility of utilizing other antibiotic component in the plant(Gami, Parabia.et.al,2011).

ANTI-TUBERCULOSIS

Antituberculosis activity was found inside themethanolic extract of leaf, stem, bark, root of the plant(Macabeo, Krohn.et.al, 2008).

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 (Shang, Cai.et.al, 2010).

BRONCHOVASODILATORY ACTIVTY

The leaves of the plant A.scholaris containing ethanol extract possess the bronchodilatory action. The study model was anesthetic rat(Channa, Der.et.al, 2005). The vasodilating activity was reported to be through endothelial from which relaxing factor, nitric oxideare 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 bronchovasodilatiory activity showed by the plant is mechanized by prostaglandins, calcium antagonism and the endothelium derived relaxing factor(Arumozhi, Mazumder.et.al, 2007).

ANTILEISHMANIAL

Antileishmanial property was obtained from the extract of the plant A.scholaris. The property was evaluated by studyingantileishmanial property in hamster which was infected by LeishmaniaDonovan(Singh, Guru.et.al, 1992).

ANTIPLASMODIAL AND ANTIMALARIAL

The various parts of the plant A.scholarisconsisting themethanolic 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 antiplasmodial action mostly amoung various chemical constituents such as villalstonine, macrocarpamine and bis-indole alkaloids(Keawpradub, Kirby.et.al, 1999). 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(Gandhi, Vinayak, 1990). Final result came out o 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(Nadkarni, Nadkarni, 1976).

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, Mazumder.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 (Rajic, Kweifio-Okai.et.al, 2000). 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 antiinflammatory properties and analgesic properties confirmed by performing various invivoassays(Shang, Cai.et.al, 2010).

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(Ghosh, Mana.et.al, 2018).

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 vescicle, ventral prostate, testes(Gupta, Bhatnager.et.al, 2005). The spermatids were reduced in the experimented rats. The number of pachytene and preleptotenespermatocytes 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(Gupta, Sharma.et.al, 2002). Thus A.scholaris was reported to be effective in its anti-fertility activity. The lupeol acetate when isolated from benzene extract of Alstoniascholaris also showed anti-fertility activity when injected in albino rats(Gupta, Bhatnager.et.al, 2005).

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, Mazumder.et.al, 2007).

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 (Bhogayata, Sharma.et.al, 2009).

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, Mazumder.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, and 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 behaviour 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, Papiya.et.al, 2012)

WOUND HEALING PROPERTY

Elevated plus maze, open □eld, hole board, light dark, mirror chamber and foot shock induced aggression model

Elevated plus maze, open □eld, hole board, light dark, mirror chamber and foot shock induced aggression model of 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 (Saraswathi, Mathuram.et.al, 1999). The mechanism was studied by the effects on skin breaking strength, granulation strength, and 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 (Arulmozhi, Rasal.et.al, 2007).

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 (Lin, Lin.et.al, 1996). 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 (Kumar, Khan.et.al, 2012).

ANTIDIABETIC AND ANTIHYPERLIPIDEMIC

Streptozotocin diabetic rats shows reduced elevation in blood glucose level by injecting the aqueous extract of A.scholaris(Deepti, Archana.et.al, 2011). The more usage of glucose by the peripheral tissue can be the main reason for the anti-diabetic effect, serum triglyceride level were decreased in streptozotocin diabetic rats, normalized lipid metabolism, which further prevent cardiovascular disorders(Arulmozhi, Mazumder.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 reversed9Deeti, Archana.et.al, 2011). In diabeties mellitus, antiantherogenic potential is beneficial and also during chronic diabeties mellitus it is also beneficial (Arulmozhi, Rasal.et.al, 2007)

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(Shah, Gowani.et.al, 2010).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 (Patil, Juvekar.et.al, 1999).

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(Arulmozhi, Mazumder.et.al, 2010), (Shanker, Ramesh.et.al, 2008). 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 chelation etc. Also, the ethanol extract of the plant worked as oxidant-induced lipid peroxidation and radical chain reactions(Arulmozhi, Mazumder.et.al, 2007).

ANTICANCER

In earlier days, herbal healers of India, thailand and admiralty islands used to treat cancer with the decoction of A scholaris (pp337-346) send to references(Graham, Quinn.et.al, 2000), which is also experimentally or pharmacologically proven nowadays. (Baliga, 2003), (Jagetia and Baliga, 2005), Human sarcoma type of cancer in embryonated egg has been reported to be treated with bark's alcholic extract of A scholaris(CHEMEXCIL, 1992) pp205-207 send to references(.Methanolic extract of bark (root bark) of A macrophylla, Ascholaris and A glaucescens has been reported to treat human lung cancer, COR-L23 (largecell 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.(Keawpradub,Houghton.et.al, 1997). 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 hydroalcoholic 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.(Jagetia and Baliga, 2005).

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 (Jagetia and Baliga, 2006). were

dense with alkaloids and some of those alkaloids few were responsible for antineoplastic or anticancer effects(Jagetia and Baliga, 2005). It was also found that echitamine was cytotoxic to HeLa, KB, HepG2, MCF-7 cells, HL-60,(Jagetia and Baliga, 2005)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 (Kamarajan, Ramamurthy.et.al, 1995).

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 (Beljanski and Beljanski, 1982). 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(Hata, Hori.et.al, 2008). Epidermoid carcinoma cells A431; AsPC-134 in pancreatic adenocarcinoma; hepatocellular carcinoma cells SMMC7721;(Zhang, hang.et.al, 2009), and cells of prostate carcinoma LNCaP(Saleem, Kweon.et.al, 2005) PC-3, (Parsad, Nigam.et.al, 2009) 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.(Saleem, Kweon.et.al, 2005). The growth of CWR22Rnu1 and 451Lu tumor was reduced by giving lupeol to athymic nude mice, (Maddodi, Saleem.et.al,2008), (Saleem, Kaur.et.al, 2005). 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. (Parsad, Nigam.et.al, 2009) 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(Saleem, Kweon.et.al, 2005) . The expression of the death receptor-3 was redcued and elevation of expression of FADDmRNA in SMMC7721 cells (Zhang, hang.et.al, 2009). 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(Saleem, Murtaza.et.al, 2009)Lupeol inhibits cyclin B, plk1, and cdc25C

expression, but it induce 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(Parsad, Nigam.et.al, 2009) Treatment of lupeol is found to increase ROS and loss of mitochondrial membrane potential and DNA fragentation is induced in PC-3 cells (Parsad, Nigam.et.al, 2009)Lupeol decreases phosphocofilin and inhibits haptotaxis of B16 2F2 canceros cells to fibronectin(Hata, Hori.et.al, 2008)

Brief Methods of extracting each Pharmacological potency drug brief of testing its viability and potency, efficacy / to human being. Not given by the author

CONCLUSION

Alstoniascholaris, plant has been utilized traditionally as the alternative medicine for many gastrointestinal diseases and conditions in several health related problems. The study reveals the pharmacognostic and pharmacological activities of the compounds existing in Alstoniascholaris. Demonstrate in scientifically via quasi experiments with controls.

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. Demonstrate in scientifically via quasi experiments with controls.

NOTE:

The study highlights the efficacy of "Ayurveda" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

REFERENCE: Use APA 6th edition of referencing: arrange in alphabetic order, Name, year. Title. Chapter volume page.) referencing mean you only list the authors cited in your text only.

1[1]. Neeraj.Bainsal ,Simranjeet.Kaur , and Sudhanshu.Mallan, *Pharmacognostical, Physicochemical and Phytochemical sStudies of DifferentVarieties of BeetrRootgGrown in Punjab* , (2020) 1689-1692).

2[2]. Neeraj.Bainsal ,Pradeep.Goyal and, Singh.JitenderSingh , and Sciences, Chandigarh University, , *India Running Title: Multi-tTherapeuticpPotential of Shorearobusta*, (2020), page no- 3313.

3[3]. Naseem.uUllah, Muhammad.zZahoor, and farhat.aAlikKhan, "shazeb khan, a review on general introduction to medicinal plants, its phytochemicals, and role of heavy metals, and inorganic constituents,",lLifesScience.journalJ.,(2014), page no- 520.

4[4]. P.KaushikP, D.KaushikD, N.SharmaN, and A. C.RanaAC, Alstoniascholaris: It'sPhytochemistry and pharmacology, Chron young sci,**2**/(2), 2011,71-78, (2011).

5[5]. Harithababu M.M* 1 ,Ananya Bhattacharjee2 , Karunakar Hegde3 , Dr. A.R Shabaraya4 Int.J. AlstoniasScholaris: A Brief Review.,Pharm. Sci. Rev. Res.,**59**/(2), Pages: 31-33;, Aarticle No.08,(November - –December2019); Article No.08, Pages: 31-33,.

6[6]. A.DeyA, AlstoniascholarisR.Br. (Apocynaceae): Phytochemistry and pharmacology: A concise review, JAPS,**01**/(06), 2011, 51-57, (2011).

7[7]. *Geographical dDistribution of AlstoniasScholarisR.Br.wWithiItsmMedicaliImportance ,aAmittTomar,2016 pPagenNo. 1-2.*

8[8]. *KalakaripPankti, gGheewalapPayal, cChakrabortymManodeep, kKamathjJagadish, a pPhytopharmacological eEview on AlstoniasScholaris: aApPanoramichHerbalmMedicine*. (2012), page no- 367-371.

9[9]. A. K.MeenaAK, G.NitikaG, N.Jaspreet N, R. P.Meena RP, and o.RaoMM. Review on ethnobotany, phytochemical and pharmacological profile on Alstoniascholaris.,Int.Res.J.Pharm. 2001;**2**/(1):, 49-54 (2001).

10[10]. Pawan K, Dhirender K, Neha S, Rana SD. Kaushik, A. Rana, P. Kaushik, N. Sharma. Alstonia scholaris: It'sPhytochemistry and pharmacology.,Chron. Young Sci. 2011;**2**/2:, 71-80 (2011). https://doi.org/10.4103/2229-5186.82970.

11[11]. A. K.Nadkarni AK. , *Indian Materia Medica. Mumbai:Bombay Popular Prakashan*, (1976), vVol.I.

12[12]. S. S.AgrawalSS, and M. ParidhaviM.;,*Herbal dDrug Technology*;,1stedition;,(2007); pg nNo.1-3 &pgnNo., Vol. 625.

13[13]. PullokPullok. K.Mukherjee; Quality Control of Herbal Drugs;,I1st- Editioned.**428**,/441, 448(2002); pg No 186-219 &pg No. **428**,441,448.

14[14]. "Quality standards of Medicinal Plants; ICMR";(2005), Vol. 3;, *pPgnNo. 49-54*.

15[15]. "Review on Indian medicinal Plants,"; **Vol. 2**(Alli-Ard); pg no;**Vol. 2**., 132-137.

16[16]. MahendraMahendra. S.Khyade*, P. NityanandP., Vaikos Department of Botany, and Dr. BabasahebAmbedkarMarathwada University, "Aurangabad"- **431** /004[MS], India.Received on:(12-09-2008); pageno- 858-860.

17[17]. S. G.JoshiSG., *Medicinal Plants, Oxford and IBH Publishing Co. Pvt.Ltd, New Delhi*, (2000), 40-41.3.

18[18]. R. N.ChopraRN, S. L.NayerSL, and I. C.ChopraIC, *Glossary of Indian MedicinalPlants*,(CSIRouncil of Scientific and Industrial Research, New Delhi, India, 1956), 1956, pp. 13-4.4.

19[19]. J. F.DasturJF, .*Medicinal Plants of India and Pakistan*,(Taraporewalaand Co., Pvt., Ltd,Bombay, 1962), 1962, p. 18.

20[20]. K. R.Kirtikar KR, and B. D.Basu BD. , *Indian Medicinal Plants. Dehradun: International Book Distributors*, (1999), vVol.II.

21[21]. B.Deepti B, and J.Archana J, Manasi J. *Antidiabetic andAntihyperlipidemic Effect of Alstonia scholaris Linn Bark in Streptozotocin Induced Diabetic Rats*., Ind.J. Pharm. Educ.Res. 2011;**45**/(2):, 114-120 (2011).

22[22]. S. C.Lin SC, C. C.Lin CC, Y. H.Linn YH, S.Supriyatna S, and S. L.Paln SL. The protective effect of AlstoniascholarisR.Br. on hepatotoxin induced acute liver damage. Am J Clin Med1996;**24**/2:,153-164 (1996). https://doi.org/10.1142/S0192415X96000207.

23[23]. S.ArulmozhiS, P. M.MazumderPM, L. S.NarayanLS, and P. A.ThakurdesaiPA. In vitro antioxidant and free radical scavenging activity of fractions from Alstoniascholaris Linn R. Br.,Int.J.Pharm.Tech. Res2010;**2**:, 18-25 (2010).

24[24]. I. T.Vaidyanatha IT, J.Joel J, T. V.Arunkumar TV, and M. S.Lipin Dev MS. Phytochemical screening and antimicrobial activity of Alstoniascholaris flowers (L)*R.Br*. Int J Pharm Res Dev2011;**3**/(4):, 172-178 (2011).

25[25]. Y. Q.YeYQ, N.WuN, L. J.YangLJ, X.NianX, D. Y.ZhangDY, and Y. T.GaoYT, Speciation analysis of eight metal elements in the leaves of Alstoniascholaris by flame atomic adsorption spectrometry, GuangPpuXxueYyuGguangPpuFfenXxi, **29**/12, 2009, 3416-3419, (2009).

26[26]. U. QuattrocchiU., *CRC World Dictionary of Medicinal and Poisonous Plants: Common Names, Scientific Names, Eponyms, Synonyms, and Etymology*,(CRC PressPress, Boca Raton, FloridaL, 2012), 2012;, pp. 210-211, 1518- 1519.

27[27]. P. K.WarrierPK, V. P. K.NambiarVPK, and C.RamankuttyC., *Indian Medicinal Plants*.(Hyderabad, India: Orient Longman Ltd:,Hyderabad, India, 1996), 1996;, Vol. 1:, pp. 75-80.

28[28]. N. Sultana, M. Saleemsultana N, Saleem M. Phytochemical studies on Alstoniascholaris.,Zeitschrift. fur Nnaturforschung. - Section B, 2010;**65**/2:,203-210, (2010). https://doi.org/10.1515/znb-2010-0218.

29[29]. N. X.DungNX, P. H.NgocPH, D. D.RangDD, N. T.NhanNT, N.KlinkbyN, and P.LeclercqP. Chemical composition of the volatile concentrate from the flowers of Vietnamese Alstoniascholaris (L.) R.Br, Apocynaceae.,J.Essent. Oil Research., 2001;**13**/6:,424-426, (2001). https://doi.org/10.1080/10412905.2001.9699714.

30[30]. X. H.CaiXH, J. H.ShangJH, T.FengT, and X. D.LuoaXD. Novel alkaloids from Alstoniascholaris.,Zeitschrift. fur Nnaturforschung. - Section B, 2010;**65**/9:,1164-1168, (2010). https://doi.org/10.1515/znb-2010-0918.

31[31]. HirasawaY, MiyamaS, KawaharaN, GodaY, RahmanA, EkasariW, et alH. Morita, Y. Hirasawa, S. Miyama, N. Kawahara, Y. Goda, A. Rahmanet al..Indole alkaloids from the leaves of Alstoniascholaris.,Heterocycles, 2009;**79**/1:,1107-1112, (2009). https://doi.org/10.3987/COM-08-S(D)65.

32[32]. A. P.MacabeoAP, K.KrohnK, D.GehleD, R. W.ReadRW, J. J.BrophyJJ, G. A.CordellGA, et al. Indole alkaloids from the leaves of PhilippineAlstoniascholaris., Phytochemistry, 2005;**66**/10:,1158-1162, (2005). https://doi.org/10.1016/j.phytochem.2005.02.018.

33[33]. T.FengT, X. H.CaiXH, Z. Z.DuZZ, and X. D.LuoXD. Iridoids from the bark of Alstoniascholaris.,Helvetica.Cchimica.Aacta, 2008;**91**/12:,2247-2251, (2008). https://doi.org/10.1002/hlca.200890244.

34[34]. S.WongseripipatanaS, L.ChaisriL, B.SritularakB, and K.LikhitwitayawuidK. Indole alkaloids from the fruits of Alstoniascholaris.,Thai Journal. of Pharmaceutical.Science., 2004;**28**:,173-180, (2004).

35[35]. A. A.SalimAA, M. J.GarsonMJ, and D. J.CraikDJ. New indole alkaloids from the bark of Alstoniascholaris.,Journal. of Natural.Products., 2004;**67**/9:,1591-1594, (2004). https://doi.org/10.1021/np0498612.

36[36]. T.YamauchiT, F.AbeF, W. G.PadolinaWG, and F. M.DayritFM. Alkaloids from leaves and bark of Alstoniascholaris in the Philippines.,Phytochemistry, 1990a;**29**/10:,3321- 3325, (1990a). https://doi.org/10.1016/0031-9422(90)80208-X.

37[37]. KamTS, NyeohKT, SimKM, YoganathanKK. Toh-Seok, N. Kok-Tih, S. Kooi-Mow, K. Yoganathan. Alkaloids from Alstoniascholaris.,Phytochemistry, 1997;**45**/6:,1303-1305, (1997). https://doi.org/10.1016/S0031-9422(97)00106-4.

38[38]. N.Sultana N, and M.Saleem M. Phytochemical studies on Alstonia scholar Zeitschri fur Naturforschung – Sec on B.,J.Chem.Sci. 2010; **65**:, 203-210 (2010).

39[39]. Du, *a M, Laskar S. Hydrocarbons in the sSurfacewWax of the lLeaves of Alstonia*.

40[40]. scholaris (Linn.) R.Br.Orient J.Chem. 2009; **25**:,437-439 (2009).

41[41]. M.DuttaM, and S.LaskarS. Hydrocarbons in the surface wax of the leaves of Alstoniascholaris (Linn.) R.Br.Orient,J.Chem. 2009; **25**:,437-439 (2009).

42[42]. X. H.CaiXH, Y.P.LiuYP, T.Feng T, and X. D.LuoXD. Picrinine-type alkaloids from the leaves of Alstoniascholaris.,Chin.J.Nat.Med. 2008; **6**/1:,20-22 (2008). https://doi.org/10.1016/S1875-5364(09)60001-7.

43[43]. S. R.Deepthi SR, R.Remya R, and V.Thankamani V. Antibacterial activity studies and phytochemical screening on the methanol extract of Alstoniascholaris R. Br.Res,J.Biotechnol. 2008; **3**:,40-3.36 (2008).

44[44]. Jian-Hua.H.Shang, Xiang-Hai.H.Cai, Tao.Feng, Yun.-Li.Zhao, and Xiao.-Dong.Luo. Pharmacological evaluation of Alstoniascholaris: Anti-inflammatory and analgesic effects., J. Ethnopharmacol. 2010;**129**/(3):, 293-298 (2010).

45[45]. A. P.MacabeoAP, K.KrohnK, D.GehleD, R. W.ReadRW, J. J.BrophyJJ, S. G.FranzblauSG, et al.AM. Activity of the extracts and indole alkaloids from Alstoniascholaris against Mycobacterium tuberculosis H37Rv., Philipp.Agric.Sci. 2008; **91**:,348-351 (2008).

46[46]. B.Gami B, and F.Parabia F. Screening of methanol and acetone extract for antimicrobial activity of some medicinal plants species of Indian folklore.,Int.J.Res.Pharm.Sci. 2011; **2**:, 69-75 (2011).

47[47]. M. R.KhanMR, A. D.OmolosoAD, and M.KiharaM. Antibacterial activity of Alstoniascholaris and Leeatetramera.,Fitoterapia2003; **74**/7-8:,736-4736-740 (2003). https://doi.org/10.1016/s0367-326x(03)00192-8.

48[48]. M. S.KhyadeMS, and N. P.VaikosNP. Phytochemical and antibacterial properties of leaves of AlstoniascholarisR. Br.Afr,J.Biotechnol. 2009; **8**:,6434-6436 (2009).

49[49]. J.Swafiya J, C.Ranu C, and G.Pradipkumar G. Anticancer Activity of an Indian Medicinal Plant, Alstonia scholaris on Skin Carcinogenesis in Mice.,Integr. Cancer Ther. 2010;**9**:,261-269 (2010).

50[50]. http://ayurveda.ygoy.comvisited on6.-12.-2011.

51[51]. S.ChannaS, A.DarA, AhmedS.Atta-Ur-RahmanS. Ahmed, Atta-ur-Rahman. Evaluation of Alstoniascholaris leaves for broncho-vasodilatory activity.,J.Ethnopharmacol. 2005; **97**/3:,469-476 (2005). https://doi.org/10.1016/j.jep.2004.12.009.

52[52]. U. K.Singha UK, P. Y.Guru PY, A. B.Sen AB, and J. S.Tandon JS. Antileishmanial activity of traditional plants against Leishmaniadonovani in golden hamsters.,Int. J.Pharm. 1992; **30**/4:,289-295 (1992). https://doi.org/10.3109/13880209209054015.

53[53]. 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):, 690-694(1999). https://doi.org/10.1055/s-1999-14043.

54[54]. M. Gandhi and V.K. Vinayak. Preliminary evaluation of extracts of Alstoniascholaris bark for in vivo antimalarial activity in mice.,J. Ethnopharmacol.**29**/(1):, 51– -57(1990). https://doi.org/10.1016/0378-8741(90)90097-d.

55[55]. A.K. Nadkarni., *K. M.Nadkarni's Indian MateriaMedica, Vol. I*,(Popular Prakashan, Bombay, (1976)), 80-83(1976), pp. 80-83.

56[56]. J. H.Shang, JH, X. H.CaiXH, T.FengT, Y. L.ZhaoYL, J. K.WangJK, L. Y.ZhangLY, et al. Pharmacological evaluation of Alstoniascholaris: Anti-inflammatory and analgesic effects.,J.Ethnopharmacol. 2010; **129**/2:,174-8174-181 (2010). https://doi.org/10.1016/j.jep.2010.02.011.

57[57]. S.Arulmozhi, PapiyaPapiya. Mitra.Mazumder, Purnima.Ashok, and L. Sathiya Narayanan., "Anti-nociceptive and anti-inflammatory activities of Alstoniascholaris Linn. R.Br.",*Pharmacognosy Magazine*, (2007), Vol. 3/(10) in press. article(2007).

58[58]. A.RajicA, G.Kweifio-OkaiG, T.MacridesT, R. M.SandemanRM, D. S.ChandlerDS, and G. M.PolyaGM. Inhibition of serine proteases by antiinflammatory triterpenoids.,Planta Med.2000; **66**/3:,206-210 (2000). https://doi.org/10.1055/s-2000-8657.

59[59]. R.GhoshR, K.ManaK, and S.SarkhelS, Ameliorating effect of Alstoniascholaris L. bark extract on histopathological changes following viper envenomation in animal models, Toxicol.Rep., 2018 5, 988-993, (2018). https://doi.org/10.1016/j.toxrep.2018.10.004.

60[60]. R. S.GuptaRS, A. K.BhatnagerAK, Y. C.JoshiYC, M. C.SharmaMC, V.KhushalaniV, and J. B.KachhawaJB. Induction of antifertility with lupeol acetate in male albino rats.,Pharmacology 2005; **75**/2:,57-657-62 (2005). https://doi.org/10.1159/000086947.

61[61]. R.S. Gupta, R. Sharma, A. Sharma, A.K. Bhatnager, M.P. Dobhal, Y.C. Joshi, and M.C. Sharma. Effect of Alstoniascholaris bark extract on testicular function of Wistar rats.,Asian J. Androl.**4**/(3):, 175-178(2002).

62[62]. K.Bhogayata K, P. P.Sharma PP, and B. R.Patel BR. A cilinical evaluation of saptaparna (Alstonia scholaris L., R. Br.) on Essential Hypertension., Ayu 2009; **30**:, 318-322 (2009).

63[63]. S.Arulmozhi S, P. M.Mazumder PM, V. A.Kangralkar VA, L. S.Narayanan LS, and P.ThakurdesaiP. Anti-Anxiety activity of Alstonia scholarislinn. R.Br., Pharmacol. Online2008; **3**:,761-767 (2008).

64[64]. S.ArulmozhiS, M.M.Papiya MM, N. P.SathiyaNP, and A.Thakurdesai A. Antianxiety and antidepressant activity of Leaves of Alstonia scholaris Linn R.,Br. Pharmacologia. 2012;**3**/(8):, 239-248 (2012).

65[65]. 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).

66[66]. S. Arulmozhi, V.P. Rasal, L. Sathiya Narayanan, and Purnima.Ashok., "Screening of Alstoniascholaris Linn. R.Br., for wound healing activity".*Oriental Pharmacy and Experimental Medicine*, (2007), Vol. 7/(3) in press. article(2007).

67[67]. S. C.LinSC, C. C.LinCC, Y. H.LinYH, S.SupriyatnaS, and S. L.PanSL. The protective effect of Alstoniascholaris R. Br. on hepatotoxin-induced acute liver damage.,Am.J.Chin.Med. 1996; **24**/2:,153-164 (1996). https://doi.org/10.1142/S0192415X96000207.

68[68]. A.KumarA, M.A.KhanM.A, A.SaxenaA, R. B.SinghRB ,K.ZamanK, and A.HusainA, Hepatoprotective Activity of Methanolic Extract of Stem Bark of Alstoniascholaris(l). R.br.,Am., J. Pharm.Tech Res,**2**/(2), 2012, 5446-5554, (2012).

69[69]. S.ArulmozhiS, V.P.RasalVP, L.SathiyanarayananL, and P.Ashok P. Screening of Alstoniascholaris Linn. R.Br. for wound healing activity.,Opem2007; **7**:,254-60.86 (2007).

70[70]. S.ArulmozhiS, P. M.Mazumder PM, S.LohidasanS, and P.ThakurdesaiP. Antidiabetic and antihyperlipidemic activity of leaves of Alstoniascholaris Linn. R.Br.,Eur. J.Integrative.Med. 2010 2/1;,23-323-32 (2010). https://doi.org/10.1016/j.eujim.2009.12.001.

72[72]. D.BandawaneD, A.JuvekarA, and M.JuvekarM, Antidiabetic and Antihyperlipidemic Effect of Alstoniascholaris Linn Bark in Streptozotocin Induced Diabetic Rats, Ind.J.Pharm.Educ.Res.,**45**/(2),2011, 114-119, (2011).

73[73]. R.S. Patil, A.R. Juvekar, S.N. Joglekar, P.B. Shamkuwar, and S.R. Nimbkar. Study of antidiarrhoeal activity of Alstoniascholaris bark.,Indian Drugs**36**/(7):, 463-465(1999).

74[74]. S.Arulmozhi S, P. M.Mazumder PM, L. S.Narayanan LS, and P. A.Thakurdesai PA. In vitro antioxidant and free radical scavenging activity of fractions from Alstoniascholaris Linn. R.Br.,Int.J.Pharm.Tech. Res2010; **2**:,18-25.94 (2010).

75[75]. K.Ravi ShankarK, K.V.RameshKV, and P.Naveena P. Free radical scavenging activity of the power and fruit extracts of Alstoniascholaris.,Biosci.Biotechnol.Res. Asia2008; **5**:,493-494 (2008).

76[76]. S.ArulmozhiS, P.Mitra-MazumderP, P.AshokP, B.HulkotiB, and L. S.NarayananLS. Antinociceptive and anti-inflammatory activities of Alstoniascholaris Linn. R.br.,PhcogMmag. 2007; **3**:,106-111 (2007).

77[77]. M. S.BaligaMS., *Evaluation of the Antineoplastic and Radiosensitizing Activities of Sapthaparna (Alstoniascholaris) IinVvivo and IinVvitro* [doctoral dissertation].(ManipalIndia: Kasturba Medical College, ManipalUniversity:,Manipal, India, 2003); 2003.

78[78]. G. C.JagetiaGC, and M. S.BaligaMS. The effect of seasonal variation on the antineoplastic activity of AlstoniascholarisR.Br, in HeLa cells.,J.Ethnopharmacol.2005; **96**/1-2:,37-42 (2005). https://doi.org/10.1016/j.jep.2004.07.024.

79[79]. G. C.JagetiaGC, and M. S.BaligaMS. Evaluation of anticancer activity of the alkaloid fraction of Alstoniascholaris (sapthaparna) in vitro and in vivo.,Phytother. Res.2006; **20**/2:,103-109 (2006). https://doi.org/10.1002/ptr.1810.

80[80]. *CHEMEXCIL, Selected Medicinal Plants of India*.(Bombay,India: Basic Book Company:, Bombay,India, 1992)Chemicals,(Pharmaceutical Press and Cosmetic Export Promotion Council, 1992); 1992.

81[81]. N.KeawpradubN, P. J.HoughtonPJ, E.Eno-AmooquayeE, and P. J. BurkePJ.Activity of extracts and alkaloids of ThaiAlstonia species against human lung cancer cell lines.,Planta Med.1997; **63**/2:, 97-101 (1997). https://doi.org/10.1055/s-2006-957621.

82[82]. G. C.JagetiaGC, M. S.BaligaMS, P.VenkateshP, et al, J. N. Ulloor, S. K. Mantena, J. Genebriera, V. Mathuram. Evaluation of the cytotoxic effect of the monoterpene indole alkaloid echitamine in-vitro and in tumour-bearing mice.,J.Pharm.Pharmacol.2005; **57**/9:,1213-1219 (2005). https://doi.org/10.1211/jpp.57.9.0017.

83[83]. P.KamarajanP, N.RamamurthyN, and S.GovindasamyS. In vitro evaluation of the anticancer effects of echitamine chloride on fibrosarcoma cells.,J.Clin.Biochem.Nutr.1995; **18**/2:,65-71 (1995). https://doi.org/10.3164/jcbn.18.65.

84[84]. M.BeljanskiM, and M. S.BeljanskiMS. Selective inhibition of in vitro synthesis of cancer DNA by alkaloids of beta-carboline class.,Exp. Cell Biol.1982; **50**/2:,79-87 (1982). https://doi.org/10.1159/000163131.

85[85]. M.BeljanskiM, and M. S.BeljanskiMS. Three alkaloids as selective destroyers of cancer cells in mice: synergy with classic anticancer drugs.,Oncology. 1986; **43**/3:,198-203. (1986). https://doi.org/10.1159/000226363.

86[86]. K.HataK, K.HoriK, J.MurataJ, and S.TakahashiS. Remodeling of actin cytoskeleton in lupeol-induced B16 2F2 cell differentiation,J.Biochem.2008; **138**/4:,467-472 (20082005). https://doi.org/10.1093/jb/mvi151.

87[87]. L.ZhangL, Y.ZhangY, L.ZhangL, X.YangX, and Z.LvZ. Lupeol, a dietary triterpene, inhibited growth, and induced apoptosis through down-regulation of DR3 in SMMC7721 cells.,Cancer Investig.2009; **27**/2:,163-170 (2009). https://doi.org/10.1080/07357900802210745.

88[88]. M.SaleemM, M. H.KweonMH, J. M.YunJM, et al, V. M. Adhami, N. Khan, D. N. Syed, H. Mukhtar. A novel dietary triterpene Lupeol induces fas-mediated apoptotic death of androgensensitive prostate cancer cells and inhibits tumor growth in a xenograft model.,Cancer Res.2005; **65**/23:,11203-11213 (2005). https://doi.org/10.1158/0008-5472.CAN-05-1965.

89[89]. M.SaleemM, I.MurtazaI, R. S.TaraporeRS, Y. Suh, V. M. Adhami, J. J. Johnson, et al. Lupeol inhibits proliferation of human prostate cancer cells by targeting beta-catenin signaling.,Carcinogenesis. 2009; **30**/5:,808-817. (2009). https://doi.org/10.1093/carcin/bgp044.

90[90]. S.PrasadS, N.NigamN, N.KalraN, and Y.ShuklaY. Regulation of signaling pathways involved in lupeol induced inhibition of proliferation and induction of apoptosis in human prostate cancer cells.,Mol.Carcinog.2008; **47**/12:,916-924 (2008). https://doi.org/10.1002/mc.20442.

91[91]. M.SaleemM, N.MaddodiN, M.Abu ZaidM, N. Khan, B. bin Hafeez, M. Asim, et al. Lupeol inhibits growth of highly aggressive human metastatic melanoma cells in vitro and in vivo by inducing apoptosis.,Clin. Cancer Res.2008; **14**/7:,2119-2127 (2008). https://doi.org/10.1158/1078-0432.CCR-07-4413.

92[92]. M.SaleemM, S.KaurS, M. H.KweonMH, V. M.AdhamiVM, F.AfaqF, and H.MukhtarH. Lupeol, a fruit and vegetable based triterpene, induces apoptotic death of human pancreatic adenocarcinoma cells via inhibition of Ras signaling pathway.,Carcinogenesis.2005; **26**/11:,1956-1964. (2005). https://doi.org/10.1093/carcin/bgi157.