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Complete Aspects Of Alstonia Scholaris

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Abstract: Herbal remedies have been employed in various medical systems for the treatment and management of different diseases. The plant Alstonia scholaris has been used in different system of traditional medication for the treatment of diseases and ailments of human beings. It is reported to contain various alkaloids, flavonoids and phenolic acids. It has been reported as bronchodilatory, antimicrobial, antiamoebic, antidiarrhoeal, antiplasmodial, hepatoprotective, immunomodulatory, anti-cancer, antiasthmatic, free radical scavenging, antioxidant, analgesic, anti-inflammatory, anti-ulcer, anti-fertility and wound healing activities. There are also reports available for the traditional use of this plant for its cardiotonic, anti-diabetic and anti-arthritic properties.
Keywords: Alstonia scholaris; ailments, bronchodilatory.

INTRODUCTION

Plants plays a vital role in maintaining human health and improving the quality of human life from thousands of years and serves to human the valuable components of medicines, seasonings, beverages, cosmetics and dyes. Herbal medicine contains natural substances that can promote health and reduce illness. Now days researchers gives main focus on plant research has increased all over the world and a large body of evidence has been collected to show immense potential of medicinal plants used in various traditional systems. Furthermore many western drugs had their origin in plant extract. There are many herbs, which are used to treat cardiovascular problems, liver disorders, central nervous system, digestive and metabolic disorders. They give their potential to produce significant therapeutic effect and can be used as drug or supplement in the treatment, management of various diseases. Herbal drugs or medicinal plants, their extracts and their isolated compounds have exhibits spectrum of biological activities. The plant, Alstonia scholaris, invites attention of the researchers worldwide for its pharmacological activities ranging from antimalarial to anticancer activities. Alstonia scholaris Linn. R.Br. belongs to family Apocynaceae, grows throughout India, in deciduous and evergreen forests and also in plains. The plant is found in India in the sub Himalayan region from the Yamuna eastward ascending to 3000 feet above sea level, abundantly found in West Bengal and South India . It has wide occurrence also in the Asia-Pacific region from India, Sri Lanka through mainland South-East Asia and Southern China, throughout Malaysia to northern Australia and Solomon Islands. The timber is a non-durable hardwood, suitable for light indoor construction purposes, pulp and paper production. The wood has been used for school blackboards, hence the name ‘scholaris’. The bark is official in the Indian, British and French Pharmacopoeias. The plant is a large evergreen tree up to 17 to 20 m in height with a straight often fluted and buttressed bole, about 110 cm in diameter. Bark is grayish brown, rough, lenticellate abounding in bitter, white milky latex; leaves 4-7 in a whorl, coriaceous, elliptic-oblong, pale beneath; flowers small, greenish white, numerous in umbellate panicles, corolla tube short, very strongly scented; fruits follicles, 30 – 60 cm long; seeds papillose with brownish hair at each end . The synonyms of the Alstonia Scholaris include Echites scholaris L. Echites pala Ham., Tabernaemontana alternifolia Burm. The plant is

also known as Alipauen, Andarayan, Bita, Dalipauen, Dirita, Dita, Ditaa, Dilupaon, Lava, Lipauen, Oplai, Pasuit, Pulai, Tanitan, Tangitang, Milky pine, White chesse wood, Devil tree, Shaitan wood, Saittan ka jat, Hale, Satween, Elilappalai, Saptaparna, Phalagaruda throughout the world. In the literature this plant is reported as a stimulant, carminative, stomachic, expectorant and febrifuge . The decoction of the dried bark is used extensively to treat asthma, hypertension, lung cancer and pneumonia, whereas an infusion of the leaves is used to cure fever , no systemic pharmacological studies regarding broncho-vasodilatory activity have been carried out. The present investigation was, therefore, undertaken to test this possibility on ethanol extract from leaves of Alstonia scholaris, and it comprised two parts. The first series of experiments was performed on anaesthetized rats (in vivo) to examine the effects of the extract on carbachol-induced respiratory and cardiovascular changes. The second series was performed in vitro using vascular, tracheal and gut tissues from rabbit and guinea-pig to assess the potential bronchodilatory and other antagonistic effects of the extract on carbachol-induced hypotension and bradycardia. In Ayurveda, it is reported that the bark of the plant when soaked in water overnight, can reduce the 9 blood glucose level after oral administration however no much characterization of this activity has been done on scientific basis. We therefore subjected the aqueous extract of bark of Alstonia scholaris L. to preliminary photochemical investigation which showed presence of alkaloids, tannins, flavonoids, saponins, glycosides and triterpenoids. The photochemical are indicative of its potential in the treatment of diabetes mellitus hence we undertook the present work to study the chronic antidiabetic effect and antihyperlipidemic effect of the bark extract in healthy and streptozotocin diabetic rats with the objective to focus on mechanism underlying the activity.

PROFILE

Local Names

Bengali (satiani,chattin,chatium); Burmese (lettok); English (white cheesewood,birrba,milkwood pine,milk wood,milky pine,black board tree,devil's tree,dita bark); Filipino (dita,dalipoen); Gujarati (satuparni); Hindi (chatian,satni,satwin,saitan-ki-jhad); Indonesian (rite,pulai,pule); Javanese (pule); Lao (Sino-Tibetan) (tinpet); Malay (pulai,pulai linlin); Nepali (chhatiwan,chhataun); Sanskrit (saptaparna); Tamil (elalaipalai,palegaruda,pala); Thai (sattaban,teenpet,teenpethasaban); Trade name (pulai,shaitan wood,chatiyan wood,white cheese wood); Urdu (chatiana); Vietnamese (caay suwxa,caay mof cua).

BOTANIC DESCRIPTION

Alstonia scholaris is a medium to large tree, to about 40 m high with a somewhat tessellated corky grey to grey-white bark. The boles of larger trees are strongly fluted to 10 m. The outer blaze is cream to yellowish in colour with abundant, milky latex that flows rapidly when cut. Leaves in whorls of 4-8 in the upper axils; leaf stalks 1-1.5 cm long, the lamina obovate to elliptical or elliptical-lanceolate, glabrous or sparsely hairy, tapering towards the base, 11.5-23 x 4-7.5 cm. Upper surface is dark green, the lower green-white with 25-40 pairs of lateral veins on each side of the midrib and 2-6 mm apart. The tip of the leaf is rounded or shortly pointed, tapering towards the base. The inflorescence is a much-branched terminal panicle, up to 120 cm long; flowers 7-10 mm long white, cream or green; the tube hairy; lobes sparsely or densely pubescent, 1.5-4 mm long, the left margins overlapping; strongly perfumed. Fruit a pendulous, two-lobed, dehiscent follicle, brown or green, dry or woody, spindle-shaped, 15-32 cm long, 4-6 mm in diameter, containing numerous flat, oblong, brown seeds, 4-5 x 0.9-1.2 mm, with a tuft of hairs 7-13 mm long at each end. The seed does not taper to a point at either end. Alstonia is named after Dr C. Alston (1685-1760), a professor of botany at Edinburgh University. The specific name scholaris is derived from the use of the wood for school boards in Myanmar.

Biology

The trees are often deciduous at irregular intervals. They do not flower at every leaf-change, but only after marked periods of dry weather. The large branches provide favourable nesting sites for wild bees. Pollination is by insects; when flowering, butterflies and bees often surround trees. The fruits open on the tree and the seeds, which have a tuft of silky hairs at each end, are dispersed by wind.

Ecology

In its natural range in Australia, it is a dominant canopy species found in coastal mesophyll vine forest with a canopy height of 35-42 m, in palm-dominated forests and in notophyll vine forests, associated with Argyrodendron peralatum, Castanospermum australe and Cerapetalum sucirubrum.

Biophysical Limits Altitude: 0-900 m, Mean annual temperature: 12-32 deg. C, Mean annual rainfall: 1200-1400 mm Soil type: Favourable soils include alluvia, basaltic red earth, yellow earth with grey-brown topsoil, stony red earth on basic volcanic soils, sandy grey earth, brown earth from a volcanic mixture of rocks and soils derived from metamorphic rocks.

Documented Species Distribution

Native-Australia, Bangladesh, Brunei, Cambodia, China, India, Indonesia, Laos, Malaysia, Myanmar, Nepal, Papua New Guinea, Philippines, Solomon Islands, Sri Lanka, Thailand, Vietnam

Exotic-Taiwan, Province of China, USA.

Products

Food: The latex provides a good quality chewing gum.

Fuel: A. scholaris has been recommended as a fuelwood species for the patana lands of Sri Lanka.

Fibre: Bark yields a fibre, and the wood is regarded as suitable for pulp and paper production.

Timber: A. scholaris is the most important source of pulai timber. The density of the wood is 270-490 kg/cubic m at 15% mc. Heartwood cream to pale yellow, sapwood wide and visually indistinct from the heartwood. Often has strong odour and a bitter taste. It is used for pattern making, corestock, plywood, carving and mouldings. The wood is also used for making coffins in Sri Lanka and school boards in Myanmar.

Essential oil: Flowers of A. scholaris yield an essential oil.

Medicine: Australian aborigines used the bark for treatment of abdominal pains and fevers, the latex for neuralgia and toothache. In India, the bark is used to treat bowel complaints and has proved a valuable remedy for chronic diarrhea and the advanced stages of dysentery. Leaves used for treating beriberi, dropsy and congested liver.

Other products: Wood charcoal is used as gun powder.

Services

Ornamental: The tree is sometimes planted as an ornamental.

Other services: In a study of the ethnobotany of the Nagas of Nagaland in northeast India, A. scholaris was amongst the native plants used in magico-religious beliefs.

Tree Management

Regular dry season watering is essential for good growth, and deep mulch has proved beneficial to young trees. It has been managed as a fuelwood species in Sri Lanka under a short coppice rotation of 6-8 years. In a social forestry planting in India, the species reached 3.6 m height and 10 cm diameter at 3.5 years in mixed species. In plantations in Taiwan, it reached an average of 23.5 m in height and 51 cm dbh in 18 years. A maximum of 35 m in height and 109 cm dbh was attained at 41 years of age.

Germplasm Management

Seeds can be stored in closed tins for 2 months, maintaining a germination rate of 90%. Based on the seed size, this species may show orthodox seed storage behaviour. There are approximately 357 000 seeds/kg.

Pests And Diseases

A leaf skeletonizer, Parotis marginata, causes significant damage to nursery stock and young plantations. The timber is liable to termites, pinhole and marine borers, while the sapwood is highly susceptible to lyctid borers.

PHYTOCHEMISTRY

Alstonia scholaris Linn. is known to be a rich source of alkaloids and there is interest among the scientist to use this for therapeutic purposes. Amongst the chemical classes present in medicinal plant species, alkaloids stand as a class of major importance in the development of newer drugs because alkaloids possess a great variety of chemical structures and have been identified as responsible for pharmacological properties of medicinal plants. However, of the large variety of the alkaloids (about 180 alkaloids) isolated, so far only few have been assessed for biological activities (4). Almost all the parts of plant (bark, flower, root) are found to contain active principles. The species A.scholaris is used in commercial formulation Ayush (3). The bark of this plant contains alkaloid ditamine and echitamine, echitenine, echicaoutchin, an amorphous yellow mass, echicerin in acicular crystals, echitin in crystallized scales, echitein in rhombic prisms (a crystallisable acid) and echiretin an amorphous substance, resembling an alkaloid, a fatty acid and fatty resinous substances. An uncrystallisable bitter principle called ditain was isolated and ascribed the febrifuge properties of the drug (2). Dung et al extracted the fresh plant material with hexane, hydrodistilled the combined extracts in slight and wet residue and analyzed by a high-resolution GC and GC/MS. The principal constituents were reported to be linalool (35.7 %), cis and trans linalool oxides, alpha-terpineol and terpinen-4- ol (5). Atta-ur-Rahman et al reported the isolation of an anilinoacrylate alkaloid, scholaricine, from the leaves of Alstonia scholaris to which structure 2-(demethylschoarine) has been suggested (6, 7). They also reported the isolation of 19, 20-dihydrocondylocarpine alkaloid from the leaves of Alstonia scholaris (8). Atta-ur-Rahman et al also isolated 19, 20-Z- Vallesamine and 19, 20-E-Vallesamine from Alstonia scholaris (9). Lagunamine (19-hydroxytubotaiwine), angustilobine B acid and losbanine (6,7-seco-6-norangustilobine

B) were obtained from the leaves of Philippine A.scholaris, together with tubotaiwine, its oxide and 6,7- seco-angustilobine B by Tatsuo Yamauchi et al (10). 17-OAcetylechitamine was isolated from the bark of the plant along with echitamine (10). Macabeo et al reported the isolation and structural elucidation (MS and NMR) of first seco-uleine alkaloids, manilamine (18-hydroxy-19,20-dehydro-7,21-seco-uleine) and N4-methyl angustilobine B) from the (pH 5) alkaloid extract of Philippine Alstonia scholaris leaves together with the known indole alkaloids 19,20-(E) vallesamine, angustilobine B N4- oxide, 20(S)-tubotaiwine and 6,7-seco-angustilobine B (11). Tatsuo Yamauchi et al isolated several alkaloids from the leaves of A. scholaris. 19-epischolaricine, Nb-methyl scholaricine, Na-methylburnamine and vallesamine Nb oxide were isolated and their structures were determined by spectral and chemical methods. They reported that the leaves of plants from Taiwan and Thailand showed similar alkaloid patterns, with picrinine, nareline and alschomine as the major alkaloids (12). Indole alkaloids, nareline ethyl ether, 5-epi-nareline ethyl ether and scholarine-N4-ioxide, in addition to nareline methyl ether, picrinine and scholaricine were isolated form the leaf extract of A. scholaris by Toh-Seok Kam et al (13).Another indole alkaloid, alstonamine and a sitsrikine type indole alkaloid, rhazimanine, were also isolated from the leaves of scholaris by Atta-ur-Rahman et al (14).

PHARMACOLOGY

Traditional the bark is bitter, astringent, acrid, thermogenic, digestive, laxative, anthelmintic, febrifuge, antipyretic, depurative, galactogogue, stomachic, cardiotonic and tonic. It is useful in fever, malarial fever, abdominal disorders, diarrhoea, dysentery, dyspepsia, leprosy, skin diseases, pruritus, tumours, chronic and foul ulcers, asthma, bronchitis, cardiopathy, helminthiasis, agalactia and debility. The milky exudate is bitter and is good for ulcers, vitiated conditions of vata and otalgia (47,48). The preparation infusion, 1 to 2 ozs., of tincture, 1 to 2 drachms diluted in water and of ditanin 5 to 10 grains given two or three times a day and an extract is prepared from the fresh bark and given in milk in cases of leprosy. It is also used as an anthelmintic (48). Milky juice is applied to ulcers and to rheumatic pains; mixed with oil and dropped into ear it relieves earache. Tincture of the bark acts in certain cases as a powerful galactogogue. Juice of the leaves with that of fresh ginger-root or zedoary is administered to women after confinement. The drug is also used in cases of snake-bite (48). The active constituents of the plant include antimalarials, CNS depressants, anticancers, antituberculosis, antidysentrics and galactopoietics (47-49).

SCIENTIFICALLY VALIDATED USES

Antimicrobial activity

Goyal et al (15) reported the antimicrobial property of the plant constituents of A. scholaris (alkanes, alkanols and sterols). Khan et al (16) evaluated the antibacterial activity of the petrol, dichloromethane, ethyl acetate, butanol fractions of crude methanolic extracts of the leaves, stem and root barks of Alstonia scholaris and reported that butanol fraction exhibited broader spectrum of antibacterial activity.

Antidiarrhoeal activity

The antidiarrhoeal effects of the aqueous and the alcoholic bark extracts of A. scholaris in mice were reported by Patil et al (17).

Antiplasmodial activity

Keawpradub et al evaluated the antiplasmodial activity of the methanolic extracts of various parts of A. scholaris which was tested against multidrug-resistant K1 strain of Plasmodium falciparum cultured in 73 human erythrocytes. Pronounced antiplasmodial activity was exhibited. The indole alkaloids were isolated from the active extract and were subsequently tested against the K1 strain of P. falciparum. They reported pronounced antiplasmodial activity mainly among the bisindole alkaloids, particularly villalstonine and macrocarpamine with IC50 values of 0.27 and 0.36 μM, respectively (18). Ironically Gandhi and Vinayak have reported that the petroleum ether extract and methanol extract of the bark of Alstonia scholaris were found to be devoid of antiamalarial activity in mice infected with Plasmodium berghei. However, they have noticed a dose-dependent improvement of conditions and delayed mortality amongst animals receiving methanol extract of A. scholaris (19). Reports state that A. scholaris has little or no demonstrable action in malaria induced in monkeys and naturally occurring in human patients. It cannot, therefore, be recommended as a substitute for quinine and other cinchona alkaloids (2).

Hepatoprotective activity The hepatoprotective effect of Alstonia scholaris R. Br. On liver injuries induced by carbon tetrachloride (CCl_4), H-Dgalactosamine, acetaminophen and ethanol was investigated by Lin et al by serum-biochemical and histopathological examinations. All serological and histopathological effects of A. scholaris were comparative with those of Bupleurum chinense, which has been reported previously as treatment criteria of hepatitis. A tendency was also shown to inhibit cell necrosis and inflammatory cell

infiltration caused by H-Dgalactosamine in histopathological examination (20).

Anticancer activity

Methanol extracts of root barks of Alstonia macrophylla, A. glaucescens, and A. scholaris, collected from Thailand, have been assessed for cytotoxic activity against two human lung cancer cell lines, MOR-P (adenocarcinoma) and COR-L23 (large cell carcinoma), using the SRB assay. Pleiocarpamine, O-methylmacralstonine and macralstonine were all considerably less active than villalstonine (21).

Antimutagenic activity

Lim et al reported the antimutagenic effect of Alstonia scholaris in micronucleus test in mice. Methylmethanesulfonate, mitomycin C and dimethylnitrosamine are genotoxic to bone marrow cells, since they fragment the chromatin material leading to the formation of micronucleated polychromatic erythrocytes in bone marrow cells of experimental mice. Expressions from Alstonia scholaris L. reduced the induction of micronucleated polychromatic erythrocytes by methylmethanesulfonate, mitomycin C and dimethylnitrosamine indicating that the plant has antimutagenic effect (22). The ASERS pretreatment increased the effect of radiation which was evidenced by enhanced cell killing when compared with the concurrent phosphate-buffered saline (PBS) treated irradiation group. Their study demonstrated that ASERS treatment enhanced the effect of radiation and disease-free survival of the mice (23). They have also observed the alterations in the neoplastic activity of cyclophosphamide (CPA) by the extract of Alstonia scholaris (ASE) in mice transplanted with Ehrlich ascites carcinoma (EAC). Administration of Alstonia scholaris (120 mg/kg) 6 h before the administration of 25 mg/kg of CPA resulted in a greater tumor remission, drastic decline in the glutathione levels and increased the lipid peroxidation considerably when compared with drug alone (24). Jagetia et al studied the chemopreventive effect of various doses of hydroalcoholic extract of Alstonia scholaris (ASE) on the benzo(a)pyrene (BaP) induced fore stomach carcinoma in female mice. The pre or post-treatment of mice with 4 mg/ml ASE also significantly reduced the frequency of BaP-induced MN in the splenocytes of treated animals (25). Jagetia et al (26) also reported the seasonal variation as well as cytotoxicity of different fractions of Alstonia scholaris R. Br. (ASE) against HeLa cells. The exposure of HeLa cells to different extracts prepared from the stem bark collected in monsoon, winter and summer seasons resulted in a dose dependent increase in the cell killing effect of ASE and they observed the highest cell killing effect for the extract prepared from the summer collections.Their study demonstrated that the extract prepared from the summer collection and the fractions containing the alkaloids were highly effective in cell killing.

Teratogenicity: The teratogenic effect of hydroalcoholic extract of Alstonia scholaris (ASE) was studied in the pregnant Swiss albino mice by Jagetia et al (27) on Day 11 of gestation. The litters were monitored regularly for mortality, growth retardation, congenital malformations, and appearance of physiological markers up to 7 weeks post-parturition (p.p.). The administration of 60, 120, 180, and 240 mg/kg ASE to the pregnant mice on day 11 did not induce mortality, congenital malformations, or alter the normal growth patterns. A further increase in the herbal extract dose up to 360 or 480 mg/kg resulted in a dose dependent increase in the mortality, growth retardation, and congenital malformations, characterized mainly by bent tails and syndactyly. The administration of higher doses (360 or 480 mg) of ASE also caused a significant delay in the morphological parameters such as fur development, eye opening, pinna detachment, and vaginal opening. The incisor eruption and testes descend were found to be delayed in litters born to the mothers treated with 240-480 mg/kg ASE. The study indicated clearly that ASE treatment caused teratogenic effect only at doses above 240 mg/kg. Lower doses had no developmental toxicity.

Immunomodulatory activity

The immunostimulating effect of Alstonia scholaris bark extracts was studied in BALB/c mouse by Iwo et al (28). The aqueous extract at 100 mg/kg b.w. increased lytic activity of peritoneal exudate cells against Escherichia coli. At the doses of 50 and 100 mg/kg b.w., the aqueous extract had no effect on primary antibody level. The aqueous extract at 50 mg/kg b.w. induced the cellular immune response while at 100 mg/kg b.w. inhibited the delayed type of hypersensitivity reaction (28).

Antiasthmatic activity

Bronchodilatory activity of the ethanol extract of Alstonia scholaris leaves in anaesthetized rats was reported by Channa et al (29). In vitro preparations of guinea pig trachea did not confirm this property, indicating that bronchodilation is not due to the direct tracheal smooth muscle relaxation. The vasodilatory activity of the extract was reported to be independent of adrenergic or muscarinic receptors or prostaglandins but was mainly via endothelial-derived relaxing factor, nitric oxide. The extract inhibited the spontaneous movements of rabbit jejunum and contractile effects of

acetylcholine and histamine on guinea-pig ileum. Additionally, the extract caused marked reduction of barium chloride-, potassium chloride- and calcium chloride-induced contraction on guinea-pig ileum and pulmonary artery, implying a direct interference of plant extract with the influx of calcium ions into cells. However, the extract had no detectable effect on mobilization of intracellular calcium. These results coupled with the in vivo effects of ethanol extract reveal that the Alstonia scholaris leaves possess broncho-vasodilatory activity mediated presumably by prostaglandins, calcium antagonism and endothelium-derived relaxing factor(s).

Anti-fertility activity

The antifertility effect of Alstonia scholaris bark extract in male rats was evaluated by Gupta et al (30). Male Wistar rats were given with oral (200 mg/kg) bark extract of Alstonia scholaris 60 days. This did not cause body weight loss, while the weights of testes, epididymes, seminal vesicle and ventral prostate were significantly reduced. The production of step- 19 spermatids was reduced by 79.6% in treated rats. The population of preleptotene and pachytene spermatocytes was decreased by 61.9% and 60.1%, respectively. Spermatogonia and Sertoli cell population were also affected. There was a decrease in seminiferous tubule and Leydig cell nuclear area, sperm count, motility, protein and sialic acid content of the testes, epididymes, seminal vesicle and ventral prostate. Alstonia scholaris bark extract had a significant antifertility effect in male rats. Gupta et al reported the antifertility effect of lupeol acetate isolated from benzene extract of Alstonia scholaris in male albino rats, which further augmented their findings (31). Free Radical Scavenging Activity Jagetia et al evaluated the plant extracts of 17 commonly used Indian medicinal plants for their possible regulatory effect on nitric oxide (NO) levels using sodium nitroprusside as a NO donor in vitro. The potency of scavenging activity was reported to be as follows: Alstonia scholaris > Cynodon dactylon > Morinda citrifolia > Tylophora indica > Tectona grandis > Aegle marmelos (leaf) > Momordica charantia > Phyllanthus niruri > Ocimum sanctum > Tinospora cordifolia (hexane extract) = Coleus ambonicus > Vitex negundo (alcoholic) > T. cordifolia (dichloromethane extract) > T. cordifolia (methanol extract) > Ipomoea digitata > V. negundo (aqueous) > Boerhaavia diffusa > Eugenia jambolana (seed) > T. cordifolia (aqueous extract) > V. negundo (dichloromethane/methanol extract) > Gingko biloba > Picrorrhiza kurroa > A. marmelos (fruit) > Santalum album > E. jambolana (leaf). All the extracts evaluated exhibited a dose-dependent NO scavenging activity. The A. scholaris bark showed its greatest NO scavenging effect of 81.86% at 250 microg/mL, as compared with G. biloba, where 54.9% scavenging was observed at a similar concentration (32).

Wound healing activity

Wound healing activity of the ethanol and aqueous extracts of Alstonia scholaris was tested against excision, incision and dead space wound models (33). The wound healing was assessed by the rate of wound contraction, period of epithelialisation, skin breaking strength, granulation strength, dry granulation tissue weight, hydroxyproline, collagen and histopathology of granulation tissue. Malondialdehyde level was also estimated to evaluate the extent of lipid peroxidation. The extracts promoted wound healing significantly in all the wound models studied. Increased rate of wound contraction, skin breaking strength, granulation strength, dry granulation tissue weight, hydroxyproline and collagen, decrease in the period for epithelialisation and increased collagenation in histopathological section were observed with extracts treated groups. The extracts also significantly decreased the levels of lipid peroxidation.

Analgesic and anti-inflammatory activities

The effect of ethanolic extract of leaves of alstonia scholaris was evaluated in experimental models of pain and inflammation (34). the leaf extract at 200 and 400 mg/kg showed significant decrease in acetic acid induced writhings in mice with a maximum of 65.76 % at 400 mg/kg. in hot plate method, the percentage of pain inhibition was found to be 73.90 % and 79.56 % with 200, 400 mg/kg of extract. There was a significant inhibition in carrageenan induced paw edema with 200 and 400 mg/kg of the extract.

Anti-ulcer activity The ethanolic extract of leaves of Alstonia scholaris was evaluated for anti-ulcer activity (34) by pyloric ligation method. The animals treated with the extract did not show ulcer, whereas the ulcer score was found to be significantly high ($p<0.01$) in rats administered diclofenac sodium.

Anthelmintic activity

Anthelmintic activity of the alcoholic extract of Alstonia scholaris was investigated using Ascardia galli. Glucose uptake, glycogen content, lactic acid production, gross motility and acetylcholine esterase (AchE) activity of the worms were estimated after the incubation. There was a significant inhibition of glucose uptake and decrease in glycogen content of the worms with Alstonia scholaris. There was a significant increase in lactic acid content and decrease in gross motility which indicates that the extract affects the energy generating mechanism of the parasite. The significant increase in lactic acid

content suggests the inhibition of ATP production or accumulation of lactic acid. The extract had significant anthelmintic activity and the possible mechanism of action may be by inhibition of energy metabolism (unpublished data of the author).

Antioxidant activity

The effect of ethanolic extract of Alstonia scholaris Linn. (Apocynaceae) on various in vitro antioxidant parameters was evaluated. Ethanolic extract of Alstonia scholaris had significant (DPPH.) free radical scavenging, metal ion chelating, hydrogen peroxide scavenging, superoxide anion radical scavenging and ferric thiocyanate reducing activities. Ethanolic extract of Alstonia scholaris Linn. was found to prevents lipid peroxidation and radicalic chain reactions. The results observed were comparable to that of BHA, BHT, lascorbic acid and tocopherol .

PHARMACOLOGICAL ACTIVITIES OF ISOLATED CONSTITUENTS

Echitamine Chloride: Saraswathi et al reported that echitamine chloride (EC), an indole alkaloid, extracted from the bark of Alstonia scholaris has got highly promising anticancer effect. The effect of this drug on the microsomal drug detoxifying system was studied in sarcoma-180 induced mice. When given subcutaneously at a dosage of 5 mg/kg body weight, it was able to alter the impaired drug detoxifying system which was observed in the sarcoma-180 bearing mice (35). Further, echitamine chloride was also found to affect both cellular and mitochondrial respiration, leading to reduction of the cellular energy pool and thereby resulting in the loss of viability of S-180 cells (36). They have also reported the enhancement of the cytotoxic effects of echitamine chloride by vitamin A on in vitro Ehrlich ascites carcinoma cell culture. They report a tumoricidal action by a free radical dependent mechanism similar to that of adiramycin, mitomycin – C and bleomycin (37). Saraswathi et al (38) screened for the anticancer effects of echitamine chloride on methylcholanthrene-induced fibro sarcoma, which exhibited significant regression in tumor growth. The altered activities of plasma and liver transaminases and gamma-glutamyl transpeptidase and lipid peroxidation in fibrosarcoma have been corrected to near normal after echitamine chloride treatment. The decreased liver glutathione content and the lowered activities of glutathione peroxidase, superoxide dismutase and catalase have also been reversed to near normals after echitamine chloride treatment.

Alstonine:

The indole alkaloid alstonine has been identified as the major component of a plant-based remedy. In a preliminary evaluation done by Wright et al, alstonine demonstrated in vivo antimalarial activity (39). It is used in Nigeria to treat mental illnesses by traditional psychiatrists. Although it is certainly difficult to compare the very concept of mental disorders in different cultures, the traditional use of alstonine is remarkably compatible with its profile in experimental animals. Even though alstonine in mice models shows a psychopharmacological profile closer to the newer atypical antipsychotic agents, it also shows important differences. Meldrum and Ozawa et al reported that alstonine possesses clear anxiolytic activity (40), mediated by 5-HT2A/2C serotonin receptors, suggesting effectiveness against negative symptoms of schizophrenia; It interferes with the glutamate system in a manner consistent with resulting beneficial effects for schizophrenia (41 – 43). According to the study of Costa-Campos et al, alstonine lacks the pro-convulsant property (44) common to many antipsychotics, a considerable advantage for chronic use in general and epileptic schizophrenic patients in particular. The lack of direct effects on dopaminergic system suggests lack of significant extra pyramidal effects, the major drawback of many antipsychotic agents. Beljanski and Beljanski reported about the anticancer activity (45) of alstonine which successfully treated a relatively important proportion of BALB/C mice inoculated with transplantable YC8 lymphoma ascites cells as well as Swiss mice bearing Ehrlich ascites carcinoma cells. Development of some solid tumours was only partially prevented by alstonine. Beljanski also reported the capacity of alstonine to distinguish cancer DNA from the healthy tissue DNA (46). It inhibits DNA in vitro synthesis when DNA from different cancerous tissues or cells is used as template. The reported inhibitory effect of alstonine is due to its capacity to form an alkaloid-cancer DNA complex.

CONCLUSION

An official Publication of Phcog.Net Plants, which are used in traditional medicine, require detailed investigation with ethnopharmacological approach. The recently developed isolation, characterization techniques and pharmacological testing have led to interest in plants as a source of new drugs. The plant Alstonia scholaris has a wide array of pharmacological activities as it causes Inhibitory effect of extract on carbachol-induced changes, Effect of extract on rabbit blood vessels and jejunum, Effect of extract on acetylcholine and histamine-induced contraction of guinea-pig ileum, Effect of extract on guinea-pig pulmonary artery and

trachea, Acute toxicity test and many isolated compounds of Alstonia scholaris lack study on their pharmacological activity and therefore seems worthwhile to scientifically validate the pharmacological properties of constituents of Alstonia scholaris, which will substantiate the use of this plant over centuries for medicinal purposes by tribal people.

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