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ANDROGRAPHIS PANICULATA (ACANTHACEAE) - AN OVERVIEW

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ABSTRACT

Andrographis paniculata (Burm. f.) Wall. Ex Nees is an erect annual herb family Acanthaceae, commonly native of Southern Asia. It is bitter in taste. As an Ayurveda herb is also known as *Kalmegh* or *Kalamegha*, meaning "dark cloud" The present review is an attempt to provide the detailed survey of Antimicrobial activity, Antioxidant activity, Antifungal activity, Antihyperglycemic and hypoglycemic effects, hepatoprotective activity, antibacterial activity, anticancer activity, apoptosis inducing effect, cardioprotective action, immuno-modulatory activity, anti-inflammatory activity, and effects on reproductive systems, traditional uses as well as Phytochemical based screening.

KEY WORDS: *Andrographis paniculata*, Anti hyperglycaemic, hepatoprotective actitity, carioprotective, immune-modulatory activity

INTRODUCTION

Fig 1: ***Andrographis paniculata***

Andrographis paniculata is a plant that has been effectively used in traditional Asian medicines for centuries. It's perceived "blood purifying" property results in its use in diseases where blood "abnormalities" are considered causes of disease, such as skin eruptions, boils, scabies, and chronic undetermined fevers. *A. paniculata* has been reported as having antibacterial, antifungal, antiviral, choleretic, hypoglycemic, hypocholesterolemic, and adaptogenic effects. In the Unani system of medicine, it is considered aperients, anti-inflammatory, emollient, astringent, diuretic, emmenagogue, gastric and liver tonic, carminative, antihelmintic, and antipyretic. Due to its "blood purifying" activity it is recommended for use in cases of leprosy, gonorrhea, scabies, boils, skin eruptions, and chronic and seasonal fevers. Juice or an infusion of fresh leaves is given to infants to relieve griping, irregular bowel habits, and loss of appetite. It appears to have antithrombotic actions, suggesting a possible benefit in cardiovascular disease. Pharmacological and clinical studies suggest the potential for beneficial effects in diseases like cancer and HIV infections. *A. paniculata* contains diterpenes, lactones, and flavonoids. Flavonoids mainly exist in the root, but have also been isolated from the leaves. The aerial parts contain alkanes, ketones, and aldehydes. Although it was initially thought that the bitter substance in the leaves was the lactone andrographolide, later investigations showed that the leaves contained two bitter principles – andrographolide and a compound named kalmeghin. Four lactones – chuanxinlian A (deoxyandrographolide), B (andrographolide), C (neoandrographolide) and D (14-deoxy-11, 12-didehydroandrographolide) – were isolated from the aerial parts in China.

Pharmacological evidence of *Andrographis paniculata*

Antimicrobial activity

R.Radha *et al* was designed with the objective to examine the petroleum ether, acetone, chloroform and methanol extracts of *Andrographis paniculata* leaves and stems, in order to evaluate the chemical composition, investigate it's *in vitro* antimicrobial potential against strains of *Enterococcus faecalis, Streptococcus pyogenes, Klebsiella pneumonia, Proteus vulgaris, Candida albicans and Aspergillus flavus*. Phytochemical analysis revealed the presence of flavonoids, alkaloids, glycosides, steroids, phenols, tannins and saponins. The antibacterial activity is more significant against Gram positive bacterium *Enterococcus faecalis* whereas the antifungal activity is more significant against *Aspergillus flavus*. These results may justify the popular use of this species as it has antimicrobial activity. However, in order to evaluate possible clinical application in therapy of infectious diseases, further clinical trials are required.[1]

Antioxidant and gastro productive Activity

S Q Wasman *et al* was screened aqueous and ethanolic extract of *Andrographis paniculata* leaves in rats have been reported. Sprague Dawley rats, 6 per group were used and rats in groups 1 to 6 were pretreated with (0.25% w/v) carboxymethyl cellulose (negative control, 5 ml/kg), 20 mg/kg omeprazole (positive control), (250 mg/kg and 500 mg/kg) of aqueous leaf extracts (APLAE) and (250 and 500 mg/kg) of ethanol leaf extracts (APLEE) respectively. Animals were orally administered with 95% ethanol (5 ml/kg) 60 min after their pretreatments. Rats were sacrificed 1 h after treatment and gastric contents were collected to measure *p*H and mucous weight. Stomach was analyzed for gross and histological changes. Ulcer control group showed extensive lesions of gastric mucosal layer, whereas rats pretreated with omeprazole, 250 and 500 mg/kg of APLAE showed significant and dose dependent reduction in gastric lesions with increased *p*H and mucus content of stomach. Rats pretreated with 250 or 500 mg/kg of APLEE showed significantly better inhibition of gastric mucosal lesions. Further, the *in vitro* antioxidant studies using 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay showed that ethanol extracts have superior free radical scavenging activity with IC_{50} value = 10.9 than aqueous extracts with IC_{50} value = 24.65. Results of this study showed that pretreatment with ethonolic extract of *A. paniculata* ethanolic provided significant protection against gastric ulcer by regulating of *p*H, mucous production and antioxidant property.[2]

Antifungal Activity

The aerial parts of the plant (leaves and stems) are used to extract the active hytochemicals. The leaves contain the highest amount of andrographolide (2.39%), the medically most active phytochemical in the plant, while the seeds contain the lowest amount. The plant pathogenic microorganism *F. oxysporum* (MTCC 7678) was procured from the Microbial Type Culture Collection (MTCC), in Chandigarh. The fungal culture was grown and maintained on a Potato Dextrose Agar medium. The antifungal activity of Andrographolide solution was investigated by using the method of zone of inhibition. Pure culture of microorganisms that form discrete colonies on solid media, e.g., yeasts, most bacteria, many other micro fungi, and unicellular microalgae, may be most commonly obtained by plating methods such as streak plate method, pour plate method and spread plate method.[3]

Antidiabetic and antihiperlipidemic effect: Agung Endro Nugroho *et al* was investigated the purified extract of the plant and its active compound andrographolide for antidiabetic and

antihyperlipidemic effects in high-fructose-fat-fed rats, a model of type 2 DM rats. Antidiabetic activity was measured by estimating mainly the pre– and postprandial blood glucose levels and other parameters such as cholesterol, LDL, triglyceride, and body weight. The purified extract and andrographolide significantly ($P<0.05$) decreased the levels of blood glucose, triglyceride, and LDL compared to controls. However, no changes were observed in serum cholesterol and rat body weight. Metformin also showed similar effects on these parameters. *Andrographis paniculata* (Burm. f.) Nees or its active compound andrographolide showed hypoglycemic and hypolipidemic effects in high-fat-fructose-fed rat.[4]

Hepatoprotective activity

The leaf extract of *Andrographis paniculata* (Ap) against ethanol induced liver toxicity in male albino rats. The liver toxicity was induced by the administration of ethanol to the animals at the optimum dosage of 7.9g/kg body wt., orally for 45 days. After induction of liver toxicity the aqueous plant extract of A.p was administered to the animal 250 mg/kg body wt., for 45 days. The liver toxicity and protective effect of the plant extract was assessed by the estimation of liver marker enzymes, antioxidant enzymes and liver histopathological studies. The ethanol induced animals the liver marker enzymes like ALT, AST, ALP and Bilirubin were significantly elevated ($P<0.001$) when compared to the normal animals. After administration of aqueous extract of A.p the elevated levels of marker enzymes were significantly decreased ($P<0.001$). The antioxidant enzymes were decreased significantly in ethanol induced animals after administration of plant extract the decreased levels were increased significantly ($P<0.001$). The aqueous leaf extract of *A.paniculata* could protect the liver against ethanol induced liver toxicity by possibly reducing the rate of lipid peroxidation and increasing the antioxidant defense mechanism in rats.[5]

Antibacterial activity: Aniel Kumar O *et al* were studied for their antibacterial activity by Agar-well diffusion method against different gram-positive (Staphylococcus aureus and Bacillus subtilis) and gramnegative (Escherichia coli, Klebsiella pneumoniae and Proteus vulgaris) bacteria. It was observed that, methanol extracts of whole plant and leaves showed the significant antibacterial activity against Gram-positive bacteria. No bacterial activity was recorded with aqueous extracts of stem and root.[6]

Anticancer Activity: Sukardiman *et al* was isolated the Andrographolide from Andrographis paniculata Ness (Acanthaceae) at 0.35 mM , 0.70 mM and 1.40 mM induced

DNA fragmentation and increased the percentage of apoptotic cells when TD-47 human breast cancer cell line was treated for 24 , 48 and 72 h. The results demonstrated that andrographolide can induce apoptosis in TD-47 human breast cancer cell line in a time and concentration-dependent manner by increase expression of p53, bax, caspase-3 and decrease expression of bcl-2 determined by immunohistochemical analysis.[7]

APOPTOSIS INDUCING EFFECT

Andrographolide isolated from *Andrographis paniculata* Ness (Acanthaceae) at 0.35 mM , 0.70 mM and 1.40 mM induced DNA fragmentation and increased the percentage of apoptotic cells when TD-47 human breast cancer cell line was treated for 24 , 48 and 72 h. The results demonstrated that andrographolide can induce apoptosis in TD-47 human breast cancer cell line in a time and concentration-dependent manner by increase expression of p53, bax, caspase-3 and decrease expression of bcl-2 determined by immunohistochemical analysis.[8]

Cardioprotective action

Shreesh Kumar Ojha *et al* was studied the cardioprotective potential of hydroalcoholic extract of *Andrographis paniculata* was evaluated against left anterior descending coronary artery (LADCA) ligation-induced I-R injury of myocardium in rats. MI was induced in rats by LADCA ligation for 45 min followed by reperfusion for 60 min. The rats were divided into five experimental groups viz., sham (saline treated, but LADCA was not ligated), I-R control (saline treated + I-R), benazepril (30 mg/kg + I-R), A. paniculata (200 mg/kg per se) and A. paniculata (200 mg/kg + I-R). A. paniculata was administered orally for 31 days. On day 31, rats were subjected to the I-R and cardiac function parameters were recorded. Further, rats were sacrificed and heart was excised for biochemical and histo pathological studies. In I-R control group, LADCA ligation resulted in significant cardiac dysfunction evidenced by reduced haemodynamic parameters; mean arterial pressure (MAP) and heart rate (HR). The left ventricular contractile function was also altered. In I-R control group, I-R caused decline in superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and reduced glutathione (GSH) as well as leakage of myocytes injury marker enzymes, creatine phosphokinase-MB (CK-MB) isoenzyme and lactate dehydrogenase (LDH), and enhanced lipid peroxidation product, malonaldialdehyde (MDA). However, rats pretreated with A. paniculata 200 mg/kg showed favourable modulation of haemodynamic and left ventricular contractile function parameters, restoration of the myocardial antioxidants and prevention of

depletion of myocytes injury marker enzymes along with inhibition of lipid peroxidation. Histopathological observations confirmed the protective effects of A. paniculata. The cardioprotective effects of A. paniculata were found comparable to that of benazepril treatment. The results showed the cardioprotective effects of *A. paniculata* against I-R injury likely result from the suppression of oxidative stress and preserved histoarchitecture of myofibrils along with improved haemodynamic and ventricular functions.[9]

Immunostimulant, cerebroprotective & nootropic activity

P. Radhika *et al* was studied the the effect of chronic administration (7 days) of methanolic extract of A. paniculata leaves was studied in rats with experimentally induced diabetes, nootropic and immunostimulant activities were evaluated. The effect of acute administration of methanolic extract of A. paniculata leaves was also studied for cerebroprotective activity. Type 2 diabetes was induced in rats by streptozotocin (STZ) (65 mg/kg) + nicotinamide (150 mg/kg). Various biochemical parameters were estimated using standard methods. A significant ($P<0.05$) increase in cognitive function was observed in both normal and type 2 diabetic rats. Nootropic activity in terms of per cent reduction in latency period was more in type 2 diabetic rats. A significant increase in blood lymphocyte count, splenic lymphocyte count and peritoneal macrophage count was observed in both normal and type 2 diabetic rats. Immunostimulant activity was observed more in type 2 diabetic rats. The per cent decrease in cerebral infarction was more in type 2 diabetic rats when compared to normal rats. The per cent increase in superoxide dismutase (SOD) levels was more in type 2 diabetic rats. The antioxidant activity of the methanolic extract of A. paniculata leaves was evident by decreased tissue malondialdehyde (MDA) levels and increased SOD levels. These properties may be responsible for the observed cerebroprotective activity. The methanolic leaf extract of A. paniculata showed significant immunostimulant, cerebroprotective and nootropic activities in normal and type 2 diabetic rats.[10]

Anti-inflammatory activity

Vasu Kandat *et al* were study was aimed to evaluate the analgesic and anti-inflammatory activity (by both in-vitro and in-vivo) of both chloroform and methanol root extracts of Andrographis serpyllifolia (Rottl. Ex Vahl.) Wt. Methods used for the studies were In-vitro 5-Lipoxygenase inhibition assay and In-vivo measurement of rat paw edema and ear edema in rats, acetic acid induced writhing response and hot plate method in albino mice. Chloroform and methanolic extracts of A. serpyllifolia root have shown moderate potency in inhibiting 5-

LOX and shown significant anti-inflammatory activity. Despite the IC50 values are little higher, anti-inflammatory efficacy of these extracts possibly due to other mechanisms apart of 5-LOX inhibition. However, In-vivo anti-inflammatory studies revealed that A. serpyllifolia methanolic extract has shown higher degree of efficacy when compared to the chloroform extract. In terms of analgesic activity in writhing test, methanolic extract has shown more efficacy than chloroform extract. Hence, it is important to isolate the active principles for further testing the anti-inflammatory efficacy.[11]

Effects on reproductive systems

Jintana Sattayasai *et al* was studied the effect of andrographolide from *Andrographis paniculata* on sexual functions; vascular reactivity and serum testosterone level in experimental animals were observed. The suspension of andrographolide in 5% DMSO was administered orally at the dose of 50 mg/kg to male ICR mice. The female mice involved in mating were made receptive by hormonal treatment. The mating behaviors, mounting latency and mounting frequency, were determined and compared with the standard reference drug sildenafil citrate. Administration of andrographolide significantly decreased the mounting latency at 120 and 180 min and increased mounting frequency at 180 min after treatment. In endothelium-intact rat aortic strips, norepineprine-induced contraction was reduced by preincubation with andrographolide. Administration of 50 mg/kg andrographolide orally to male mice once daily for 2, 4, 6 or 8 weeks had no significant effects on sperm morphology and motility. Interestingly, at week 4, serum testosterone level in mice treated with andrographolide was significantly increased when compared to the control. Thus, the effects of andrographolide on vascular response to nor epinephrine and testosterone level observed in this study might be contributed to the sexual enhancing properties observed.[12]

Effect of *Andrographis paniculata* Leaves extract on ovary

J. Roopavathy *et al* was studied an attempt was made to investigate the reproductive disturbance of the medicinal plant Andrographis paniculata leaves extract on ornamental fish black molly (Mollienisia latipinna). Since, immemorial time the A. paniculata commonly used for various ailments in humans. The experimental adult black molly fishes were treated with the leaves extract of A. paniculata 100mg / lit of water for a period of 24 days. At end of the experiment, the animals were sacrificed and dissected out the ovaries for histopathological observations. The histopathology of ovary reveals that there was no change in the structure of oogonia, yolk, and tunica albugenea of control animals, but in 11 and 24

days treated animal's ovaries shown remarkable changes in the structure of oogonia, the content of yolk substances, structure of oozyte wall, arrangement of columnar cells and tunica albugenea. Therefore, it concludes that the aqueous extract of leaves of Andrographis paniculata has considerable impact on the reproductive organ of block molly.[13]

Contraceptive action

Palaniyandi Krishnamoorthy *et al* was studied the fractions (F) 3 and 4 derived from the root extract of *Andrographis paniculata* Wall. ex Nees were used in the present investigation to study the contraceptive action of the plant on albino rats. Rats were treated with 500 mg/kg body weight/day of fraction 3 and 4 of the extract for a period of 48 days. The total body and ovary weight, levels of hormones, such as estrogen, LH, FSH and progesterone, histological changes in the ovary and uterus were observed. There was no remarkable change in total body weight of *A. paniculata* treated rats, whereas the size of the ovary was reduced in treated rats as compared to control. The levels of LH, FSH, estrogen and progesterone were found to be raised in treated groups when compared with control and there were remarkable changes noted in the histology of ovary and uterus of experimental rats. The obtained results suggest that the presence of active principle in the fractions 3 and 4 of *A. paniculata* might be responsible for the contraceptive efficacy of the plant extract. These alterations are possibly due to the interference of secondary metabolites of the plant on the physiology of the sexual cycle of female rats.[14]

CONCLUSIONS

The demand of *Andrographis paniculata* is greatly increased in the past few years for its therapeutic potentials. *Andrographis paniculata* also clearly expresses a broad spectrum of pharmacological properties of this plant. Verification of the efficacy of other biological activities of *Andrographis paniculata* including antidiabetic, anticancer, anti-inflammatory, and hepatoprotective activities, on human study subjects would bring a lot of benefits for the largest population of the globe. To fulfill this dream, the researchers might focus on multiplication of this plant to meet commercial demand besides the pharmacology study.

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