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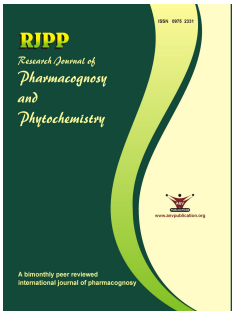

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A Pharmacological Review : *Amaranthus spinosus*

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ABSTRACT
In this paper traditional, clinical potential, ethanopharmacology, phytoconstituent studies and safety profile of *Amaranthus spinosus* are presented. Through this review auther wish to attract the attention of nature product researchers throughout the world to explore this potential plant systemically. Perliminary work has been reported on Antiprotozoal activity, Anti-inflammatory activity, Antioxidant properties, Anti-malarial activity, Analgesic properties, Immuno-modulatory properties, Haematology Properties, Antifertility activity, Anti-diabetic, anti-hyperlipidemic and spermatogenic effects. Therefore *A. spinosus* hold a great potential for in depth biological evaluation. Even, no work has ever been carried out for standaridizing this potentially useful plant.

Keywords: *Amaranthus spinosus,* ethanopharmacology, clinical study.

INTRODUCTION
Amaranthus spinosus Linn. (Family: Amaranthaceae) is commonly known as ‘‘Kate Wali Chaulai (Kanatabhajii)” in ‘Hindi”, also used as vegetable and cultivated throughout in India, Sri Lanka and many tropical countries [(1)]. The juice of *A. spinosus* is used by tribal of Kerala, India to prevent swelling around stomach while the leaves are boiled without salt and consumed for 2–3 days to cure jaundice [(2)]. Plant as one of the vegetable have high concentration of antioxidant components [(3)] and high nutritive values due to presence of fibre, proteins and high concentration of essential amino acids, especially lysine [(4)].

The liver regulates several important metabolic functions and the hepatic injury is associated with distortion of these metabolic functions [(5)]. Thus, liver diseases remain one of the serious health problems. In spite of tremendous strides in the modern medicine, there are not much drugs available for the treatment of liver diseases. There are a number of medicinal preparations recommended in the Indian traditional system of medicine ‘‘Ayurveda” for the treatment of liver diseases. There are scientific claims to offer significant relief as hepatoprotective [(6)]. *A. spinosus* is used as antiinflammatory, antimalarial, antibacterial, antimicrobial, antidiuretic, antiviral and in hepatic disorders [(7,8,9)]. Water extract of plant showed significant immunostimulating activity [(10)] and stem extract showed antimalarial activities [(11)]. *A. spinosus* have several active constituents like alkaloids, flavonoids, glycosides, phenolic acids, steroids, amino acids, terpenoids, lipids, saponins, betalains, b-sitosterol, stigmasterol, linoleic acid, rutin, catechuic tannins and carotenoids. The betalains in stem bark of A. spinosus were identified as amaranthine, isoamaranthine, hydroxycinnamates, quercetin and kaempferol glycosides [(12,13,14)]. It also contains amaranthoside, a lignan glycoside, amaricin, a coumaroyl adenosine along with stigmasterol glycoside, betaine such as glycinebetaine and trigonelline [(15,16)]. Betalains are well known for their antioxidant, anticancer, antiviral and antiparasitosis properties [(17)]. Many betalain containing species are used as popular medicinal plants to treat various kinds of ailments such as hepatic disorders, malaria, jaundice and scanty urine or to cure wounds [(18)].

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PHARMACOLOGICAL ACTIVITY:

Antiprotozoal activity [19]:

The dichloromethane extract of *A. spinosus (*2 mg/mL) was moderately inhibited to Blastocystis hominis, a common human protozoan. The reference anti-protozoan agent, metronidazole (40 µg/mL) killed 97% of the protozoan and inhibited all protozoan samples at concentrations of 1.25-20 µg/mL .

Anti-inflammatory activity [13]:

The anti-inflammatory property of methanolic extract of *A. spinosus* leaves was studied in different animal models. *A.* spinosus extract (25-100 mg/kg) significantly inhibited carrageenan-induced rat paw edema and produced significant inhibition of acetic acid-induced increase in vascular permeability indicating that the extract has anti-inflammatory activity. In the cotton pellet granuloma test, rats were treated orally with the extract for 4 consecutive days after the subcutaneous implantation of a sterile pellet. The highest dose of the extract (100 mg/kg) was able to significantly reduce the post-implantation weight of cotton pellets compared to controls indicating its effectiveness against acute inflammation.

Severe gastric erosion was seen in rats given the extract (50 and 100 mg/kg) repeatedly for 4 days, which may reflect its ability to inhibit prostaglandin synthesis. This was not seen in the controls or with a lower dose of the extract (25 mg/kg). The extract (25-100 mg/kg) also delayed castor oil-induced diarrhea in rats, which was postulated to reflect its prostaglandin synthesis inhibitory activity.

Antioxidant properties [20]:

The antioxidant capacity of *A. spinosus* was studied in roadside plants which were postulated to be continuously exposed to the high levels of nitrogen oxides and sulphur dioxide from automobile emissions. *A. spinosus* was shown to possess a very good free radical scavenging system for combating air pollution through analysis of the enzymes superoxide dismutase, catalase, ascorbate peroxidase, glutathione reductase and phenolic peroxidase activities. *Amaranthaceae* plants contain betalain pigments which showed strong antioxidant activities by the DPPH assay. Their EC50 values range from 3.4 to 8.4 µM. The antioxidant activity of *A. spinosus* extract may be due to its betalain content.

Anti-malarial activity:

1. The aqueous extract *of A. spinosus* bark obtained from mature stems was screened for antimalarial properties in mice inoculated with erythrocytes parasitized with *Plasmodium berghei.* The bark extract showed a dose-dependent antimalarial activity in a 4-day suppressive antimalarial assay using chloroquine as the reference antimalarial drug. ED50 values for the antimalarial activities of the extract and chloroquine were 789.4 and 14.6 mg/kg, respectively [19].

2. Extracts obtained from two Burkinabe folk medicine plants, spiny amaranth (*Amaranthus spinosus* L., Amaranthaceae) was screened for antimalarial properties with the aim of testing the validity of their traditional uses. The plant extracts showed significant antimalarial activities in the 4-day suppressive antimalarial assay in mice inoculated with red blood cells parasitized with *Plasmodium berghei berghei.* ED_{50} value was found 789 and 564 mg/kg for *Amaranthus spinosus*. Moreover the tested vegetal material showed only low toxicity 1450 mg/kg as LD_{50} for *Amaranthus spinosus* [11].

Analgesic properties [13]:

Methanolic extract of *A. spinosus* leaves (25-100 mg/kg) produced a dose-dependent decrease in acetic acid-induced writhing with the highest dose producing an effect (56.2% inhibition of writhing) which was comparable to that of 5 mg/kg indomethacin (58.4% inhibition of writhing) . These doses of the extract also reduced the licking time at the late phase (20 minutes post formalin), not the early phase of the formalin-induced paw licking assay in mice. These results indicate that *A. spinosus* extract has analgesic activity. Positive results in the late phase of the formalin test indicate that the extract inhibited pain which was associated with inflammation.

Immuno-modulatory properties[21].:

The aqueous extract of *A. spinosus* leaves showed immuno-modulatory effects by significantly stimulating splenocyte proliferation in primary splenocytes from female BALB/c mice. The extract stimulated isolated B lymphocytes, not T lymphocytes, in a dose response manner. The water extract (1250 µg/mL) elicited a much higher proliferation rate in bulk splenocytes than in isolated purified B and T cells, suggesting some sort of interaction between these cells. Thus, the immuno-stimulating effects of the water extract may lead to B lymphocyte activation which will subsequently, through secondary signaling, lead to T lymphocyte proliferation. A novel immuno-stimulatory protein (GF1) with a molecular weight of 313 kDa was obtained after sequential purification of the water extract. GF1, which was assumed to be a glycoprotein and was heat labile, had an immuno-stimulatory activity which was 309 times higher than that of the water extract.

Haematology Properties [22]:

Ethanol extract of *Amaranthus spinosus* leaf (EEAL) was administered orally to growing pigs to determine its effects on the haematological characteristics-packed cell volume (PCV) red blood cell (RBC) and white blood cell (WBC) counts, and haemoglobin (HB) concentration. Eighteen growing pigs were randomly allotted to two treatments with each treatment replicated thrice. Pigs in treatment 1 were administered with EEAL. Treatment 2 served as control receiving no treatment. Results showed that there were significant ($P<0.05$) reduction in the PCV, RBC and Hb of the pigs administered with EEAL seven days post treatment and their weight gains significantly ($P<0.05$) improved. *Amaranthus spinosus*, although an active vermifuge should be used in animals with adequate precaution to avoid any probable toxic effects.

Hepatoprotective activity [23]:

The hepatoprotective and antioxidant activity of 50% ethanolic extract of whole plant of *Amaranthus spinosus* (ASE) was evaluated against carbon tetrachloride (CCl4) induced hepatic damage in rats. The ASE at dose of 100, 200 and 400 mg/kg were administered orally once daily for fourteen days. The substantially elevated serum enzymatic levels of serum glutamate oxaloacetate transaminase (AST), serum glutamate pyruvate transaminase (ALT), serum alkaline phosphatase (SALP) and total bilirubin were restored towards normalization

significantly by the ASE in a dose dependent manner. Higher dose exhibited significant hepatoprotective activity against carbon tetrachloride induced hepatotoxicity in rats. The biochemical observations were supplemented with histopathological examination of rat liver sections. Meanwhile, in vivo antioxidant activities as malondialdehyde (MDA), hydroperoxides, reduced glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) were also screened which were also found significantly positive in a dose dependent manner. The results of this study strongly indicate that whole plants of *A. spinosus* have potent hepatoprotective activity against carbon tetrachloride induced hepatic damage in experimental animals. This study suggests that possible mechanism of this activity may be due to the presence of flavonoids and phenolics compound in the ASE which may be responsible to hepatoprotective activity.

Antifertility activity [24]:

The Anti-fertility screening after ingestion of aqueous and ethanolic extracts of *Amaranthus spinosus* Linn roots have been investigated in pregnant rats. The ingestion of 125, 150 and 175 mg/kg body weight of alcoholic extracts of the plant from day one to day five of pregnancy by female rats did cause significant pregnancy interception. On other hand the ingestion of 125mg/kg body weight of aqueous and alcoholic extracts of plant from day 11 to day 15 of pregnancy did not cause significant pregnancy interception. However, the ingestion of 150 and 175 mg/kg body weight of alcoholic extracts of plant drugs exhibited significant pregnancy interceptory affect. The alcoholic extracts of selected ethno medicinal plants possessing more pregnancy interception than aqueous extracts.

Anti-diabetic, anti-hyperlipidemic and spermatogenic effects [25]

Anti-diabetic, anti-hyperlipidemic and spermatogenic effects were studies with methanolic extract of stem of *Amaranthus spinosus* Linn (Family: Amaranthaceae) in diabetic rats. In streptozotocin (STZ)-induced diabetic rats, it was observed that both the standard drug (Glibenclamide) and methanolic extract of *Amaranthus spinosus* Linn. Significantly exhibited control of blood glucose level on a 15day model. Further, the methanolic extract also showed significant anti hyperlipidemic and spermatogenic effects in STZ-induced diabetic rats. The methanolic extract has also accelerated the process of spermatogenesis by increasing the sperm count and accessory sex organ weights. The present investigation of the plant established some pharmacological evidence to support the folklore claim that it is used as an anti-diabetic.

Toxicities [26-29]:

The aqueous extract of the bark of *A. spinosus* has a relatively low toxicity LD50 value of 1450 mg/k *A. spinosus* was reportedly the culprit in cases of spontaneous poisoning of cattle in Brazil during a severe drought. Clinical signals appeared after 30 days in 11 out of 35 adult cows and 8 out of 20 yearling calves which were introduced into a 15 ha maize plantation heavily infested with *A. spinosus***.** However, only one calf died within 3-7 days. The clinical signs were depression, anorexia, marked weight loss, foul-smelling diarrhea occasionally tinged with blood, and subcutaneous oedema. Sub acute cases showed distended abdomens, the animals were reluctant to stand and walked with difficulty. Sloughing of the hooves occurred in some animals. The main post-mortem findings in 5 animals were moderately pale and swollen kidneys, perirenal oedema and varying degrees of oedema in several tissues and cavities. In some cases petechiae and suffusions were associated with the subcutaneous oedema. The mucosa of the digestive system showed necrotic glossitis, oesophagitis and pharyngitis, abomasal hemorrhages and button-like ulcerations in the large intestine. The contents of ileum, colon and rectum were blood stained. Hemorrhagic diathesis was apparent by the presence of intra-abdominal hematomas. Histologically, there was marked tubular nephrosis associated with epithelial regeneration and hyaline intra-tubular casts. The mucosal lesions consisted of large necrotic areas in the epithelium which extended into the lamina propria and were associated with inflammatory reaction with massive infiltrations of mastocytes. The omasal mucosa had selective necrosis of the basal layer cells. Renal failure was suggested as the primary lesion which triggered the other changes.

A. spinosus also caused an outbreak of acute poisoning in ewes in southern Brazil. The clinical signs were uremic halitosis, loss of ruminal motility**,** dispnoea and abortion. The kidneys showed pale red spots, white streaks extending from the cortex to medulla and congestion. Histologically, there was severe acute tubular nephrosis, dispersed foci of coagulative necrosis in the liver, areas of coagulative necrosis in the myocardium and acute incipient interstitial pneumonia and secondary bronchopneumonia. Hyperkalemia secondary to renal insufficiency was the underlying cause of myocardial coagulative necrosis observed in seven sheep.

CONCLUSION:

Literature reveled that *Amaranthus spinosus* Scintifically roported for Antiprotozoal activity, Anti-inflammatory activity, Antioxidant properties, Anti-malarial activity, Analgesic properties, Immuno-modulatory properties, Haematology Properties, Antifertility activity, Anti-diabetic, anti-hyperlipidemic and spermatogenic effects, and traditionally it is used to prevent swelling around stomach, jaundice, cure wounds. A. spinosus have several active constituents like alkaloids, flavonoids, glycosides, phenolic acids, steroids, amino acids, terpenoids, lipids, saponins, betalains, b-sitosterol, stigmasterol, linoleic acid, rutin, catechuic tannins and carotenoids.

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