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A Comprehensive Review of the Pharmacological Actions of *Asparagus Racemosus*

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ABSTRACT

Plants have been an important source for developing drugs since time immemorial. Various medicinal herbs are indigenous to the Indian subcontinent and Asparagus is one such plant. *Asparagus racemosus* Willd., more commonly known as Shatavari, has been traditionally used in many systems of medicine such as Ayurveda, Unani and Siddha. It has been used for decades as a galactogogue, uterine tonic, adaptogen, and rejuvenator. Also it has been used to mitigate symptoms of peptic ulcer, as an immunostimulant, hepatoprotective, and aphrodisiac. In addition, several other health benefits of this wonder plant, such as antidepressant, antiamnesic, antianxiety, hypolipidemic, antidiabetic, and anticonvulsant effects have been discovered in the recent years. In this article, an effort has been made to comprehensively enumerate all the health benefits of A. racemosus, known so far.

Keywords: *Asparagus racemosus*, Shatavari, Galactogogue, Immunostimulant, Hepatoprotective, Uterine relaxant.

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INTRODUCTION

Plants and plant products form an important source of drugs. According to the estimation of world health organization (WHO), about 80% of people in the world depend on plant-based remedies. [1] Asparagus is one such herb, used for decades in various forms of therapy. *Asparagus racemosus* Willd., (Figure 1) also known as satavar, shatavari, or shatamull is an important medicinal herb, commonly seen in Asia and Africa. [2] In the literal sense, the word 'Shatavari' means 'one who possesses a hundred husbands or acceptable to many'. It has been used in the traditional systems of medicine like Ayurveda, Siddha and Unani, as a general health tonic. The word Asparagus is derived from Greek and it denotes 'stalk' or 'shoot'. [3, 4]

Figure 1: Leaves and roots of *Asparagus racemosus* Willd.

Asparagus racemosus has been playing a vital role in traditional medicine in India. The roots of this plant are used in Ayurvedic medicine, generally as a uterine tonic, as a galactogogue, in hyperacidity, and as a rejuvenator. It is described in Ayurvedic texts as useful in the prevention and treatment of gastric ulcers and dyspepsia. Moreover, it has also been employed for the treatment of some neuronal disorders. In addition, a few recent reports demonstrated some additional beneficial effects of this herb including hepatoprotective, immunostimulant, aphrodisiac and antilithiatic effects. [5, 6]

MORPHOLOGICAL CHARACTERISTICS

Scientific classification

Kingdom: Plantae

Clade: Angiosperms

Clade: Monocots

Order: Asparagales

Family: Asparagaceae

Subfamily: Asparagoideae

Genus: Asparagus

Species: racemosus

Vernacular names

Asparagus racemosus Willd. is an indigenous plant in India and hence its vernacular names are as diverse as the languages of our country. The different vernacular names of this plant are described in Table 1.

Table 1: Different vernacular names of *Asparagus racemosus* Willd.

Language/ Region	Vernacular name
Sanskrit	Satavari
Hindi	Satavari, Satawar or Satmuli
Assamese	Satomul
Bengali	Shatamuli
Marathi	Shatavari or Shatmuli
Gujarati	Satawari
Oriya	Vari
Telugu	Toala-gaddalu or Pilli-gaddalu
Tamil	Shimaishadavari or Thanner Vittan Kizhangu or Inli-chedi
Malayalam	Chatavali
Kannada	Majjigegadde or Aheruballi
Kumaoni	Kairuwa
Madhya Pradesh	Narbodh or Satmooli
Rajasthani	Norkanto or Satawar
Manipuri	Nunggarei
Urdu	Satawar
Nepali	Kurilo

Habitat

Asparagus racemosus is a plant indigenous to India, Nepal, Sri Lanka, Australia, and also Africa and East Europe. [4] Botanically described in 1799, this woody climbing plant grows upto one to two metres height, and prefers to take root in gravelly, rocky soils, at 1,300 - 1,400 metres elevation. [5] Due to the various described health benefits of A. racemosus, there is a constant increase in demand for this plant, though the supply is rather unpredictable and insufficient. Injudicious, destructive harvesting, along with deforestation has further worsened the scenario. The plant is now designated to be ‘endangered’ in its natural habitat, and the need for conservation of this plant is crucial. [7]

PLANT CHARACTERISTICS

Leaves, flowers and fruits

A. racemosus is well-known by its characteristic appearance of small, uniform, pine needle-like phylloclades (photosynthetic branches), that are a glossy green. It produces small, white flowers on short, spiky stems in the month of July, and in September, it produces deep purple, globular berries.

Roots

The plant possesses an adventitious root system with tuberous roots, measuring about one metre in length, tapering at both ends, with more than a hundred on each plant.

Chemical constituents

Numerous phytochemical constituents have been isolated from various parts of A. racemosus, which have been depicted in Table 2. The most important among these are the steroidal saponins, which are named as Shatavarin, ranging from I-VI, which are collectively termed as saponins. [8, 9] A sulphur-containing 5-membered heterocyclic compound called asparagusic acid (1,2-dithiolane-4-carboxylic acid) has been isolated, which seems to be unique to *Asparagus*. Though this compound is presumably harmless to humans, it has been thought to be responsible for the strange odor imparted to urine following asparagus ingestion. [10]

Table 2: Phytochemical constituents of *Asparagus racemosus* Willd.

Chemical class	Phytochemical constituent
Steroidal saponins	Shatavarin I-VI
Oligospirostanoside	
Carboxylic acid	Asparagusic acid
Polycyclic alkaloid	Asparagamine A
Isoflavones	8-methoxy-5, 6, 4-trihydroxy isoflavone-7-0-beta-D-glucopyranoside
Cyclic hydrocarbons	Racemosol, Dihydrophenantherene
Furan compound	Racemofuran
Carbohydrates	Polysaccharides, Mucilage
Flavonoids	Glycosides of quercitin, rutin and hyperoside
Sterols	Sitosterol, 4, 6-dihydroxy-2-O (-2-hydroxy isobutyl) benzaldehyde, Undecanyl cetanoate
Kaempferol	
Trace minerals	Zinc, Manganese, Copper, Cobalt, Magnesium, Calcium, Potassium, Selenium, Iron
Miscellaneous constituents	Gamma linolenic acid, Vitamins A, B1, B2, C and E, Folic acid, Diosgenin, Arginine, tyrosine, Resin, Tannin

PHARMACOLOGICAL ACTIONS OF A. RACEMOSUS

Galactogogue action

The effect of asparagus on milk production and secretion has been studied and established in humans and other animals. It is one of the herbal drugs used extensively in ancient systems of

medicine like Ayurveda and other folk medicine as a galactogogue. [11] It was seen that A. racemosus significantly increased plasma prolactin levels in buffaloes, thereby increasing milk production. [12] In rats, the galactogogue effect of two different preparations of A. racemosus were studied, namely the milk and aqueous decoctions. Both the preparations were seen to produce a significant increase in milk production and also increase the pup weight gain. [13] Even in humans, A. racemosus was found to increase the plasma prolactin levels and increase mother and baby body weight, thereby indicating galactogogue effect. [14] However, in a previous study conducted by Sharma et al., no such effects were seen. [15]

Effects on the uterus

The ethanolic extract of A. racemosus roots were found to produce significant uterine muscle relaxation, more so in pregnant rats than non-pregnant ones. Mechanisms involved were both calcium-dependent and -independent pathways. [16] A polyherbal formulation containing A. racemosus, similarly showed decreased spasmogen-induced contraction, and also increased uterine weight. [17] The effects of this plant on the uterus have been shown to mimic that of estrogen. [18] Moreover, it has also been shown to be effective in the treatment of dysmenorrhoea and abnormal uterine bleeding. [19]

Aphrodisiac activity

A. racemosus powder was seen to produce a significant increase in mounting behavior of male Wistar rats, which was comparable to action produced by standard drug, sildenafil citrate. [20, 21] In another study, an increase in body weight of male albino rats was observed with aqueous extract of A. racemosus, suggesting anabolic action. Also, it produced a significant reduction of mount latency, ejaculation latency, post-ejaculatory latency, intromission latency, hesitation time, and an increase of mount frequency, along with enhanced penile erection. Observed effects were similar to that produced by testosterone. [22] The lyophilized aqueous extract was also seen to increase pendiculatory activity in male Wistar rats and *in vitro* sperm count, thereby providing further evidence for aphrodisiac activity of A. racemosus. [23]

Adaptogenic activity

The ethanolic extracts of A. racemosus roots were found to improve stress tolerance in chemical writhing and swimming endurance tests. Moreover, stress induced increases in blood glucose, triglycerides and cholesterol levels were all significantly lowered by the extract. [24] In another study, methanolic and aqueous extracts of the roots were seen to reduce the serum corticosterone levels, indicating beneficial effect in management of stress. [25] These findings were further

supported by reports of the ability of methanolic extract of A. racemosus to decrease plasma corticosterone and norepinephrine levels, and thereby act as an adaptogen. [26]

Antidepressant activity

The methanolic extract of A. racemosus seeds demonstrated a decrease in immobility time in forced swim test (FST) and tail suspension test (TST) in mice, which was comparable to imipramine, and increased the levels of dopamine *in vitro*. [27, 28] Furthermore, it was found to significantly reduce brain monoamine oxidase (MAO-A and MAO-B) levels as compared to control. [28] In a study focusing on finding the underlying mechanism of action, it was seen that methanolic extract significantly inhibited cholinesterase and MAO activities. [29] In another study, antidepressant-like activity was seen with methanolic root extract in FST and learned helplessness models. [30]

Antiamnesic activity

Ethanolic root extract of A. racemosus was observed to produce a significant dose dependent enhancement of memory in the elevated plus maze (EPM) model in mice, the effect being significantly higher than that produced by piracetam. Also, there was an increase in the acetylcholinesterase levels in hippocampal areas associated with learning and memory. [31] In another study, methanolic root extract was found to reverse amnesia produced by scopolamine and sodium nitrite in the EPM and Morris water maze models in mice. [32]

Antianxiety effect

Methanolic extract of root of A. racemosus demonstrated significant antianxiety effect in open-field test (OFT), hole-board, and (EPM) tests in rats, the activity being comparable to that of standard drug, diazepam. The levels of serotonin and norepinephrine were seen to be elevated in the amygdala, along with an increase in the expression of 5-HT_{2A} receptors. Moreover, the anxiolytic effect of A. racemosus in OFT, hole-board, and EPM tests, was found to be attenuated by flumazenil, indicating $GABA_A$ -mediated action. However, it did not show sedative-like effect in OFT and EPM tests as compared to diazepam. Thus, the anxiolytic response of A. racemosus are believed to be mediated by GABA-ergic and serotonergic mechanisms. [33]

Anticonvulsant effect

Ethanolic extract of A. racemosus roots showed significant anticonvulsant effect in both maximal electroshock seizures (MES) and pentylenetetrazole (PTZ) induced seizure models in albino mice. [34] Similarly, in another study the methanolic and ethanolic extracts demonstrated antiepileptic activity in Swiss albino mice in MES, picrotoxin and strychnine induced seizures models. [35]

Anti-secretory and antiulcer activity

Traditional systems of medicine have been using A. racemosus for the treatment of acid peptic disease and ulcers since many centuries. [36] Various studies have proved the efficacy of A. racemosus in treatment of peptic ulcers. In a study done by Sairam et al., methanolic root extracts of A. racemosus were used in different models of gastroduodenal ulcers like pyloric ligation, cold stress and cysteamine induced ulcers, and it was seen that A. racemosus significantly healed the peptic ulcers and increased mucosal defensive factors like mucus secretion, cellular mucus and life span of cells. [37] In another similar study, aqueous extract of A. racemosus roots was found to display a cytoprotective effect by preventing and healing gastric ulcers and erosions. [38] In yet another study, the crude extract of A. racemosus was found to reduce the gastric acid secretion and heal the gastric ulcers, at a rate comparable to ranitidine. [39]

Hepatoprotective action

Hydroalcoholic extracts of A. racemosus demonstrated a hepatoprotective effect by inhibiting CCl_4 induced formation of lipid peroxides in liver of rats. [40] Also, ethanolic root extract of the plant was found to produce hepatoprotective action in isoniazid induced hepatotoxicity in rats. [41] In another analogous study, A. racemosus powder was found to significantly reduce the elevated serum hepatic marker enzymes, namely aspartate amino transferase (AST), alanine amino transferase (ALT) and alkaline phosphatase (ALP). [42] Similarly, it was found that aqueous extract of A. racemosus attenuated the hepatotoxic effects caused by lead in Swiss albino mice. [43]

Neuroprotective effect

A. racemosus root extract was observed to decrease the neuronal loss in hippocampus and medial prefrontal cortex in ovariectomized rats, thereby demonstrating a neuroprotective action. [44] In another study, root extract of A. racemosus was seen to significantly increase the normal cell count in various regions of hippocampus in mice, with no significant change in behavioral test results. In the same study, memory retention and recall test was administered in humans treated with A. racemosus and significantly higher test scores were seen in this group as compared to the control group. This again demonstrates neuroprotective action of A. racemosus. [45] In yet another study it was found that ethanolic extract of A. racemosus provided neuroprotection by reversing cognitive impairment and oxidative stress produced by ethanol on rat brain. [46]

Nephroprotective action

Methanolic and hydromethanolic extracts of A. racemosus were found to attenuate uremia induced by acetaminophen in rats, thereby exhibiting a nephroprotective effect. [47]

Antineoplastic activity

Aqueous extract of A. racemosus roots were seen to prevent incidence of hepatocarcinogenesis in diethylnitrosamine treated rats. [48] Shatavarins (containing shatavarin IV) extracted from roots of A. racemosus were found to exhibit significant anticancer activity in both *in vitro* and *in vivo* experimental models. [49]

Immunomodulatory action

Oral administration of milk fortified with A. racemosus in mice was observed to produce a significant increase in percent phagocytosis and proliferation of lymphocytes, thereby demonstrating its immunostimulant action. [50] A steroidal sapogenin extracted from A. racemosus roots was also found to produce an immunostimulant effect in experimental animal models. [51]

Immunoadjuvant effect

In experimental animals immunized with diphtheria, pertussis, and tetanus (DPT) vaccine and then challenged with intracerebral administration of Bordetella pertussis, administration of A. racemosus aqueous root extract showed significant decrease in mortality and morbidity. The antibody titers were also found to be significantly higher in these animals as compared to control group. [52] Moreover the aqueous root extract of A. racemosus was seen to significantly increase CD3(+) and CD4/CD8(+) percentages, suggesting T-cell activation in experimental animals. Also these animals showed significant up-regulation of Th1 (IL-2, IFN-g) and Th2 (IL-4) cytokines, suggesting mixed Th1/Th2 adjuvant activity of A. racemosus. [53]

Antioxidant effects

Crude extract of A. racemosus was found to exhibit an antioxidant effect in rat liver mitochondria, where oxidative damage was done by gamma radiation of 450 Gray. This action was comparable to that of glutathione and ascorbic acid. [54] Also, the aqueous and ethanolic root extracts were found to suppress lipid peroxidation. [55] In another study, CCl_4 induced formation of lipid peroxides in rat liver was inhibited by root extracts of A. racemosus and levels of antioxidant enzymes like superoxide dismutase, glutathione and catalase were elevated. [40] Antioxidant and antiapoptotic activities were demonstrated by A. racemosus root extracts in human lung epithelial H460 cells. [56]

Anti-inflammatory effects

In one study, the ethanolic root extracts of A. racemosus showed anti-inflammatory action in carrageenan induced paw edema in Wistar rats. It further showed antiarthritic activity by significantly reducing paw volume and decreasing arthritic score in Freund's adjuvant induced arthritis in rats. [57] In another study, liposomes prepared from A. racemosus root extracts displayed significant anti-inflammatory activity in vitro, which was comparable to the action of

dexamethasone. [58] Ethanolic leaf extract of the plant also showed significant anti-inflammatory activity. [59]

Analgesic action

Aqueous and alcoholic root extracts of A. racemosus were found to produce significant analgesic action in Eddy's hot plate and heat conduction models in Swiss albino mice. [60] In another study, ethanolic extract of A. racemosus was found to inhibit writhing reflex in acetic acid induced writhing model in mice. [61]

Antipyretic action

The ethanolic extract of A. racemosus showed significantly higher antipyretic activity as compared to the aqueous extract in brewer's yeast induced pyrexia model in Wistar albino rats, the effect being comparable to the standard antipyretic, paracetamol. [62]

Antibacterial activity

Antibacterial efficacy was seen *in vitro* with methanolic extract of A. racemosus roots against various pathogens such as Escherichia coli, Shigella dysenteriae, Shigella sonnei, Shigella flexneri, Vibrio cholera, Salmonella typhi, Salmonella typhimurium, Pseudomonas putida, Bacillus subtilis and Staphylococcus aureus, and this effect was compared with chloramphenicol. [63] These findings were further supported by other studies where various extracts of root and leaf of the plant exhibited antibacterial activity. [64, 65] In yet another study, nor-lignans and steroidal triterpenes isolated from A. racemosus displayed antibacterial effect against Escherichia coli and Staphylococcus aureus, but not Salmonella typhi. [66]

Antiprotozoal activity

Inhibitory effect on the growth of Entamoeba histolytica was observed *in vitro* with crude alcoholic extract of the roots of A. racemosus. [5]

Antifungal activity

Methanolic extract of A. racemosus was found to inhibit the growth of several Candida species isolated from vaginal thrush patients and this effect was comparable to that produced by fluconazole. [67]

Antitussive effect

Methanolic extract of A. racemosus roots, administered orally, was observed to produce a significant antitussive activity on sulphur dioxide-induced cough in mice. The inhibition of cough produced by this drug was seen to be comparable to that produced by codeine phosphate. [68]

Antiurolithiatic effect

It was observed that the ethanolic extract of A. racemosus significantly reduced the elevated level of calcium, oxalate and phosphate ions in urine, induced by ethylene glycol in male albino Wistar rats. Also, it was found to elevate urinary concentration of magnesium, which is believed to be an inhibitor of crystallization. [69] In another study it was found that ethanolic extract significantly reduced the serum concentrations of calcium, phosphorus, urea and creatinine, and also protected against ethylene glycol and ammonium chloride induced renal tissue damage. [70]

Hypolipidemic activity

In a study done by Visavadiya et al., A. racemosus root powder was administered orally along with diet in hypercholesteremic rats and it was found that there was a dose-dependant reduction in plasma and hepatic lipid profiles, increased fecal excretion of cholesterol, neutral sterol and bile acid along with increase in hepatic HMG-CoA reductase activity and bile acid content. [71]

Diuretic activity

Significant diuretic activity was seen with aqueous root extract of A. racemosus in rats at the dose of 3200 mg/kg, and it was comparable to standard drug, furosemide. [72]

Antidiabetic action

Ethanolic extract and five different partition fractions of A. racemosus roots, were found to stimulate insulin secretion in isolated perfused rat pancreas, isolated rat islet cells and clonal β-cells. This stimulatory action was enhanced by glucose, 3-isobutyl-1-methyl xanthine, tolbutamide and depolarizing concentration of potassium chloride, and was inhibited by diazoxide and verapamil. Moreover, they increased intracellular levels of calcium ions. [73] In another study it was observed that, A. racemosus extract, when administered orally together with glucose, improved glucose tolerance in normal as well as in diabetic rats. Postprandial hyperglycaemia after sucrose ingestion was significantly suppressed by the extract, and reversibly increased unabsorbed sucrose content throughout the gut. Furthermore, glucose transport and insulin action in 3T3-L1 adipocytes were enhanced by the extract. Decreased serum glucose, increased pancreatic insulin, plasma insulin, liver glycogen and total oxidant status were observed on daily administration of the extract in diabetic rats. The antihyperglycemic activity of A. racemosus thus observed is believed to be partly mediated by inhibition of carbohydrate digestion and absorption, together with enhancement of insulin secretion and action in the peripheral tissue. [74]

Effect on wound healing

The aqueous root extract of A. racemosus was seen to produce significant improvement in the epithelialisation period, remarkable enhancement of wound contraction rate and an increased skin

breaking strength in incision and excision wound models in rats, thereby enhancing wound healing. [75]

Effect on benign prostatic hypertrophy

Efficacy and safety of A. racemosus as a part of a polyherbal preparation, Himplasia, in the management of benign prostatic hypertrophy (BPH) was studied. It was observed that Himplasia produced significant reduction in the mean American Urological Association (AUA) symptom score, prostate volume, post-void residual volume, latent period and urinary flow time, and a significant increase in peak flow rate and voided urinary volume at the end of six months treatment period. There were no reported adverse effects of Himplasia. [76]

Effects on cardiovascular system

Alcoholic root extract of A. racemosus was found to produce positive ionotropic and chronotropic effects on frog heart with lower doses and cardiac arrest with higher doses. It was also seen that the extract produced hypotension in cats, which was blocked by atropine, signifying cholinergic mechanism of action. Furthermore, the extract was seen to cause congestion and complete stasis of blood flow in mesenteric vessels of mice and rat, slight increase in the bleeding time, without affecting the clotting time. [47]

Antidiarrhoeal effect

Ethanolic extract of whole plant of A. racemosus was found to produce an antidiarrhoeal effect in castor oil induced diarrhoea model in mice. It increased the mean latent period and decreased the stool frequency, the action being comparable to the standard drug used, loperamide. [61]

Antianemic and antithrombocytopenic effect

It was seen that the methanolic extract of A. racemosus significantly increased the number of red blood corpuscles (RBC) and haemoglobin percentage. Also it was found to significantly decrease bleeding time and clotting time as compared to heparin. [77]

Miscellaneous effects

The functionality of bread was found to be enhanced by incorporating A. racemosus and yeast at permissible levels of 3.5 % and 4.96 % respectively. [78] The addition of freeze dried aqueous extract of A. racemosus at a concentration of 1g/100 ml of milk showed a decrease in pH, rennet coagulation time and an increase in acidity, viscosity and heat stability at maximum. Proteins in milk were modified and a brown colour was imparted to the milk by the extract. [79] Supplementation of A. racemosus during lactation was found to reduce estrus interval and enhance reproductive performance in Karan Fries crossbred cows. [80]

Teratogenic effects

In spite of being considered a relatively safe drug in traditional systems of medicine and numerous beneficial effects, one study showed teratogenic effects of A. racemosus. The methanolic root extract at the dose of 100 mg/kg/day for 60 days, showed increased resorption of fetuses, gross malformations like swelling in legs and intrauterine growth retardation with a small placenta size in Charles Foster rats. Pups of mother rats exposed to the drug throughout gestation, showed higher rates of resorption and hence smaller litter size. The live pup showed significant decrease in body weight and length, and delay of various development parameters when compared to control group. [81]

CONCLUSION

Various studies conducted on A. racemosus have concluded that it has numerous medicinal and beneficial properties in both experimental animals and humans. However, due to the concerns raised by the teratogenic effects reported, cautious use of the drug, after an extensive and exhaustive screening is recommended.

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