

ETHNOPHARMACOLOGY, PHYTOCHEMISTRY AND BIOACTIVITY OF ASPARAGUS RACEMOSUS: AN UPDATE

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Summary

Asparagus racemosus is an herbaceous perennial plant. It is the most important rasayana herb in Ayurvedic medicine which grows in low forest areas throughout India. Their medicinal usages have been reported in indigenous systems of medicine, Indian and British Pharmacopoeias. In Ayurveda, *A. racemosus* has been used extensively as an adaptogen to increase the non-specific resistance of organisms against a variety of stress. *A. racemosus* plant contain steroidal saponins, isoflavones, asparagamine and polysaccharides, which play a major role in treatment of diarrhoea and dysentery. Roots and rhizomes of *A. racemosus* has potent antioxidant, antitussive, antidyspepsia, antiulcer and anticancer activity. *A. racemosus* is also useful as immunostimulant, galactogogue. The present article gives the detailed exploration of phytochemistry, ethnopharmacology and bioactivity of *A. racemosus*, in an attempt to give a direction for further research.

Keyword: Asparagus racemosus, Phytochemistry, Galactogogue, Steroidal saponins.

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Introduction

A. racemosus is commonly called Satavari, Satawar or Satmuli in Hindi; Satavari in Sanskrit; Shatamuli in Bengali; Shatavari or Shatmuli in Marathi; Satawari in Gujarati; Toala-gaddalu or Pilli-gaddalu in Telegu; Shimaishadavari or Inli-chedi in Tamil; Chatavali in Malayalam; Majjigegadde or Aheruballi in Kannada; Kairuwa in Kumaon; Narbodh or Satmooli in Madhya Pradesh; and Norkanto or Satawar in Rajasthan [1]. The genus *Asparagus* includes about 300 species around the world. Out of the 22 species of *Asparagus* recorded in India. *A. racemosus* Willd. (Liliaceae), is the one of the most regularly used as Rasayana in traditional system of medicine [2]. *A. racemosus* is a much-branched, spinous under shrub found growing wild in tropical and sub-tropical region of India [3]. The most well-known other species is edible i.e. *A. officinalis*, commonly referred to as just *Asparagus*. Other members of the genus are grown as ornamental plants. The most popular ornamental species are *A. plumosus*, *A. densiflorus*, and *A. sprengeri* [4]. In India, *A. racemosus* (Shatawar) translates to "she who possesses 100 husbands", referring to the herbs rejuvenating effect upon the reproductive organs of female [5]. *A. racemosus* is considered to possess many therapeutic potentials like Medhya Rasayana (Memory enhancer), Vajikaran (Aphrodisiac), Medhya (Nervine tonic), Vayasthapanav (Anti-aging), Jwar (Antipyretic), Kustha (Leprosy), Atisar (Diarrhea), Ykshma (Tuberculosis), Mutrakrishya (Urinary infection), Apsmar (Epilepsy), Pradar (Leucorrhea), Grabhsrav (Miscarriage), Arsha (Piles) and Timir (Loss of vision) etc. *A. racemosus* is useful in several diseases postulated to be induced by stress [6].

Cultivation of *A. racemosus*

The plant prefers light (sandy), medium (loamy) and heavy (clay) soils and requires well-drained soil. Black, well drained and fertile soil is good for cultivation. But can be cultivated in loose and medium black soil. The tamarind is adapted to semiarid regions of the tropics and can withstand drought conditions quite well. They require minimum irrigation so avoid over-watering. Flowering of asparagus takes place in August–November, produces small white scented flowers. The fruits appear in December-January

and collection period is September to October. One acre land need about 2.5 kg seeds. The plants are harvest after 3 years. The roots (tubers) are dug out, collected and cleaned. The tubers are peeled off with the help of sharp knife immediately after harvesting. After removing the skin it is cut in to small pieces and dried in shade.

Macroscopic

The stem is covered with recurved spines. The leaves are linear green and needle-like it bear tutts of cladodes axillary to minute scales. Root occurs in cluster offascicle at the base of the stem. Root tuberous, 10 to 30 cm in length and 0.1 to 0.5 cm thick, tapering at both end with longitudinal wrinkles; colour cream; taste sweetish [8].

Microscopic

Microscopic characters showed an outer layer of piliferous cell, ruptured at places, composed of small, thin-walled, rectangular asymmetrical cell, a number of cell elongated to form unicellular root hair. Cortex consist of 25 to 29 layers, distinct in two zones, outer & inner cortex, stone cells present in either singly or in groups, form a discontinuous to continuous ring in the upper part of this region. Raphides of calcium oxalate present in the region, 2 or 3 layers of the stone cells encircle the endodermis. Endodermis composed of thin-walled cells of parenchyma, pericycle present below endodermis, stele exarch and radial in position. Xylem composed of vessels and parenchyma. Xylem vessels have pitted thickening, phloem consists of usual element. Pith composed of circular to oval cells of parenchyma a few cells slightly lignified [9].

Ethnopharmacology

Ethnopharmacological knowledge is most common and import among tribal populations but much of the information is empirical at best lacking scientific validation. Despite widespread use of plant resources in traditional system of medicines, bioassay analysis of few plant species have been conducted to evaluate their pharmacological profile, and to ascertain safety and efficacy of traditional remedies [10]. Medicinal plants help in alleviating human suffering and are widely used for subsistence, home remedies, and trade [11]. It is estimated that 70-80% of people worldwide rely on traditional herbal

medicine to meet their primary health care needs [12]. The global demand of herbal medicine is growing and its market is expanding at the rate of 20% annually in India [13]. Numerous drugs have entered into the international market through exploration of ethnopharmacology and traditional medicine with extensive uses of medicinal plants [14]. Traditionally, roots and rhizomes of *A. racemosus* were used as an tonic, diuretic, aphrodisiac, carminative, appetizer. Literature survey revealed that plant is strongly recommended for the treatment of mental disorders, in diarrhoea and dyspepsia [10].

Phytochemistry

The major active constituents of *A. racemosus* are steroidal saponins (shatavarins I-IV), isoflavones, asparagamine (an alkaloid substance similar to aspirin) and polysaccharides. Shatavarin I is the major glycoside with 3 molecules of glucose and rhamnose moieties attached to sarsasapogenin (fig. I&II) [15]. Other active constituents are Asparagamine, (a polycyclic alkaloid) (fig. III) Racemosol, cyclichydrocarbon (9,10-dihydrophenanthrene) (fig-IV) [16] and Isoflavones including 8-methoxy-5, 6, 4'-trihydroxyisoflavone and 7-O-beta-D-glucopyranoside [17]. Shoots contain thiophene, thiazole, aldehyde, ketone, vanillin, asparagusic acid, and its methyl and ethyl esters used as flavours. Flowers and mature fruits contain rutin (fig V), quercetin (fig VI), hyperoside. Leaves contain diosgenin and quercetin-3-glucuronide [18].

Bioactivity of *A. racemosus*

Phytoestrogenic effects

The phytoestrogen are plant derived non-steroidal compound which are found in many foods [19]. Shatavarin isolated from roots of shatavari mimic like female estrogen hormone and even replace it from its receptor [20]. Oestrogen replacement therapy is recommended primarily for the treatment of menopausal symptoms and for the prevention of cardiovascular disease and osteoporosis in postmenopausal women [21]. U-3107 (EveCare containing 32 mg *A. racemosus* extract per 5ml syrup) is a herbal preparation formulated by The Himalaya Drug Co. Bangalore with different plant extracts. Administration of U-3107 in normal rats significantly increased the wet and dry

uterine weight. It also resulted in marked increase of oestrogen levels with no change in progesterone levels as compared to control [22]. The alcoholic extract of its rhizome was administered orally to adult pregnant female albino rats at a dose of 30 mg/100 g body weight, daily for 15 days (days 1–15 of gestation). The macroscopic findings revealed a prominence of the mammary glands, a dilated vaginal opening and a transversely situated uterine horn in the treated group of animals. The weight of the uterine horns of the treated group was found to be significantly higher ($p < 0.001$) but the length was shorter ($p > 0.01$) [23]. Alcoholic extract of root of *A. racemosus* containing saponin glycoside was showed to produce a specific and competitive block of the pitocin induced contraction and spontaneous uterine motility shown the positive response in order to treatment of premenstrual syndrome in women [24].

Galactogogue effect

The root extract of *A. racemosus* is prescribed in Ayurveda to increase milk secretion during lactation [25]. Study revealed that due to presence of corticoids or prolactin in aqueous extract of *A. racemosus* roots increased the weight of mammary glands and uterine weight in post-partum and oestrogen-primed rats [26]. Another report observed an increase in milk secretion after administration of *A. racemosus* in the form of Ricalex® tablets (Aphali Pharmaceuticals Ltd. Ahmednagar; 40 mg concentrated root extract per tablet) to women suffering from deficient milk secretion [27]. In another report, *A. racemosus* (capsule 200mg & granules 15mg) along with some other herbs in the form of lactare (TTK Pharma, Chennai) have been reported to enhance milk output in women complaining of scanty breast milk, on 5th day after delivery [28]. The poly nutrient formulation, Galactin vet bolus of The Himalaya Drug Company, Bangalore contains powders of *Leptadenia reticulata*, *A. racemosus* (200mg/kg), *Withania somnifera*, *Arundo donax*, *Cissampelos pareira*, *Foeniculum vulgare*, and extracts of *Eclipta alba* and *Solanum nigrum* improved milk yield during treatment period to the extent of 9.12% compared to pretreatment period [29].

Teratogenicity

Methanol extract of roots of *A. racemosus* at the dose of 100 mg/kg showed teratological disorders in terms of increased resorption of fetuses, gross malformations e.g. swelling in legs and intrauterine growth inhibition with a small size of placenta in Charles Foster rats. Pups born to mother exposed to *A. racemosus* extract for full duration of gestation showed evidence of increase rate of resorption and therefore smaller litter size. The live pups showed significant reduce in body weight and length and delay of various developmental factors when compared to respective control groups. *A. racemosus* therefore, should be used in pregnancy cautiously as its exposure during that period may cause damage to the offspring [30].

AntiLithiatic effect

The alcohol extract of *A. racemosus* root at the dose of 200 mg/kg showed significant inhibitory potential on lithiasis (stone formation), induced by oral administration of 0.75% ethylene glycolated water to adult male albino Wistar rats for 28 days. The study revealed that ionic chemistry of urine was changed by ethylene glycol, which elevated the urinary concentration of crucial ions viz. calcium, oxalate, and phosphate, leading to renal stone formation. The alcoholic extract significantly reduced the increased level of these ions in urine. The high serum creatinine level observed in ethylene glycol-treated rats was also reduced, by the treatment with the extract [31].

Antibacterial effect

Methanol extract of the roots & rhizome of *A. racemosus* at different concentrations (50, 100, 150 µg/mL) showed significant antibacterial activity against *Escherichia coli*, *Shigella dysenteriae*, *Shigella sonnei*, *Shigella flexneri*, *Vibrio cholerae*, *Salmonella typhi*, *Salmonella typhimurium*, *Pseudomonas putida*, *Bacillus subtilis* and *Staphylococcus aureus* comparable to chloramphenicol [32].

Antidiabetic effect

D-400, a polyherbal formulation containing roots extract *A. racemosus* (20mg) along with other herbal extract and powder has proven antidiabetic activity in experimental

models as well as in clinical trials. D-400 has been investigated for its interaction with oral hypoglycaemic agents like, tolbutamide and glibenclamide in alloxan-induced diabetic rabbits. Administration of D-400 at a dose of 1 g/kg for 15 days significantly elevated plasma tolbutamide and glibenclamide concentrations with simultaneous reduction of blood glucose level. Plasma concentrations of tolbutamide and glibenclamide were significantly lowered after withdrawal of D-400 treatment. Elevation of plasma concentration of tolbutamide was observed only for the first 4 h after which it declined towards normal levels and no significant difference between D-400 treated and control group was observed at the end of 8 hrs [33]. The D-400-treated group showed significant lowering of triglycerides and HDL cholesterol. The pancreas of diabetic rats under treatment of D-400 therapy showed significant increase in islet number of β cells and appeared to bring about blood sugar homeostasis by increasing insulin secretion and regeneration of endocrine pancreas [34-35].

Immunomodulatory effect

Steroidal saponins (Shatavarin IV, Immunoside®) from aqueous root extract of *A. racemosus* used to study effects of that extract on Th1/Th2 immunity. The sheep red blood cells (SRBC) specific antibody titres and delayed type hypersensitivity (DTH) responses were also monitored as markers of Th2 and Th1 responses, respectively. Cyclosporin, cyclophosphamide and levamisole were used as controls. Treatment with extract (100 mg/kg) resulted in significant increase of cluster of differentiation (CD3+ and CD4/CD8+) percentages suggesting its effect on T-cell activation. The extract treated animals showed significant up-regulation of Th1 (IL-2, IFN-g) and Th2 (IL-4) cytokines suggesting its mixed Th1/Th2 adjuvant activity. Consistent to this, extract also showed higher antibody titres and DTH responses. The extract in combination with lipopolysaccharide (LPS), SRBC, produced a significant proliferation suggesting effect on activated lymphocytes [36]. The immunoadjuvant potential of aqueous extract of root & rhizome *A. racemosus* was evaluated in experimental animals immunized with diphtheria, tetanus, pertussis (DTP) vaccine. Oral administration of test material at 100 mg/kg per day dose for 15 days resulted significant increase in antibody titers to

Bordetella pertussis as compared to untreated (control) animals. Results indicate that the treated animals showed significant increase in antibody titers as compared to untreated animals [37].

Antioxidant activity

Aqueous extract of root of *A. racemosus* showed antioxidant activity against membrane damage induced by the free radicals generated during γ -radiation. γ -Radiation, in the dose range of 75–900 Gy, induced lipid peroxidation as assessed by the formation of thiobarbituric acid reactive substances (TBARS) and lipid hydroperoxides (LOOH). The antioxidant effects of *A. racemosus* extract were studied against oxidative damage in terms of protection against lipid peroxidation, protein oxidation, depletion of protein thiols, levels of the antioxidant enzymes and superoxide dismutase. An active fraction consisting of polysaccharides (termed as P3) was effective even at a low concentration of 10 μ g/ml. Both the crude extract as well as polysaccharides fraction significantly retarded lipid peroxidation and protein oxidation [38]. A new antioxidant compound named racemofuran along with two known compounds asparagamine A and racemosol isolated from root & rhizome of *A. racemosus* showed antioxidant activity against DPPH (diphenyl-picrylhydrazyl) [39]. The acetone extract of roots of *A. racemosus* showed antioxidant activity against kainic acid (KA) – induced hippocampal and striatal neuronal damage. The extract treated mice displayed an improvement in glutathione peroxidase activity, reduced glutathione (GSH) content, reduction in membranal lipid peroxidation and protein carbonyl [40].

Antiulcer effect

The methanol extract of fresh roots of *A. racemosus* 50 mg/kg, orally (total saponins 0.9%) showed significant protection against acute gastric ulcers induced by cold restraint stress (CRS), pyloric ligation, aspirin plus pyloric ligation, and duodenal ulcers induced by cysteamine. Further, gastric juice and mucosal studies indicate that above extract significantly increased the mucosal defensive factors like mucus secretion, cellular mucus

and life span of cells [41]. In another report *A. racemosus* showed the peptic ulcer healing properties against psychological stress and faulty food habits which are the key factors for causing and complicating the pathogenesis of peptic ulcer [42]. Satavari mandur (SM) is a herbo-mineral preparation containing *A. racemosus*, which showed ulcer protective effect at the dose of 125-500 mg/kg against cold restraint stress-induced gastric ulcer in rats [43]. In another report methanol extract of roots of *A. racemosus* and *W. somnifera* (100mg/kg/day p.o.) given for 15 days significantly reduced the gastric ulcer index, volume of gastric secretion & total acidity against indomethacin and stress-induced ulcer in Wistar rats [44].

Adaptogenic effect

Adaptogenic activity of milk decoction of *A. racemosus* was tested by determining anti stress effect using forced swimming stress model at the dose 200mg/kg. Various behavioral parameters (anxiety level, memory, muscle relaxation and locomotor activity) were also assessed in mice. The results indicated that milk decoction of *A. racemosus* has significant antistress adaptogenic activity [45]. Siotone (ST) is herbal formulation containing *W. somnifera*, *Ocimum sanctum*, *A. racemosus*, *Tribulus terrestris* and *Shilajit*, which are reputed to promote physical and mental health, improve defence mechanisms of the body and enhance longevity. Adaptogenic activity of ST against footshock stress induced perturbations in behaviour (depression), glucose metabolism, suppressed male sexual behaviour, immunosuppression and cognitive dysfunction was investigated albino rats. *Panax ginseng* (PG) was used as the standard adaptogenic agent for comparison. The result showed that effects were attenuated by administration of ST and PG [46].

Antiosteoporotics effects

Methanol and aqueous root extract of *A. racemosus* at the 50mg/kg and 250mg/kg showed significant effect on mineralization, ossification and osteoclastic activity suppression. Treatments of ovariectomized rats by extract significantly reduced serum alkaline phosphatase activity, serum calcium and also inhibited the ovariectomized induced excessive loss of calcium in urine, also improved biomechanical parameters [47].

Aphrodisiac Activity

The roots of *A. racemosus*, *Chlorophytum borivilianum*, and rhizomes of *Curculigo orchioides* are popular for their aphrodisiac properties. Lyophilized aqueous extracts of the roots of *A. racemosus*, along with root of *C. borivilianum*, and rhizomes of *C. orchioides* were studied for sexual behaviour effects in male albino rats. Administration of aqueous extracts of 200 mg/kg has showed pronounced anabolic effect in treated animals, evidenced by weight gains in the body and reproductive organs. There was a significant variation in the sexual behaviour of animals as reflected by reduction of mount latency, ejaculation latency, post ejaculatory latency, intromission latency, and an increase of mount frequency [48].

Neuroprotective Effect

Due to Long term stress and aging the most of the nervous system disorders from simple dementia to Parkinson's and Alzheimer's etc. are characterized by nerve cell loss in specific brain areas, such as hippocampus, substantia nigra, cerebral cortex [49-52]. Methanol extract of root of *A. racemosus* showed the neuroprotective potential both in animal models and clinical patients. Mice were subjected to 3 hour unpredictable swim stress daily up to 30days to develop region specific neurodegeneration. *A. racemosus* root extract were given to separate group of animals at the dose (100mg/ kg) daily up to 30 days,. Histological and behavioural studies were carried out which showed retardation of neurodegeneration. For clinical study registered patients both male and female of approximately same age groups, were selected they were subjected to memory retention and recall test. Cytological studies demonstrated that total normal cell count in various regions of hippocampus (CA1, CA3, CA4 and Dg) was significantly high in treated group as compared to stress group [53].

Anti-diarrhoeal Effect

Ethanol and aqueous extracts of *A. racemosus* showed the antidiarrhoeal activity against

castor oil-induced diarrhoea model in rats. Loperamide was used as positive control. The plant extracts showed significant inhibitory activity against castor oil induced diarrhoea and PGE2 induced enteropooling in rats when tested at the dose of 200 mg/kg. Both extracts also showed significant reduction in gastrointestinal motility in charcoal meal test in rats [54].

Antitussive Effect

The methanol extract root of *A. racemosus* at dose of 200 and 400 mg/kg showed significant antitussive potential on sulfur dioxide-induced cough in mice. The cough inhibition being comparable to standard drug codeine phosphate (10-20 mg/kg) [55].

Hepatoprotective

Alcoholic extract of root of *A. racemosus* significantly reduce the enhanced levels of alanine transaminase, aspartate transaminase and alkaline phosphatase in CC14-induced hepatic damage in rats, indicating antihepatotoxic potential of *A. racemosus* [56]. The Polyherbal formulation (PHF08) containing *A. racemosus* (200mg/kg & 600 mg/kg) along with other herbal extract showed significant hepatoprotective activity against carbon tetrachloride (CCl4) induced hepatotoxicity in rats [57-58].

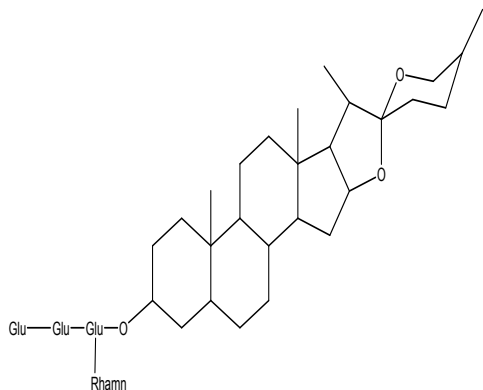
Anti-dyspepsia effect

The roots powder of *A. racemosus* at dose of 2mg/kg showed central dopaminergic effect in male rats similar that of modern allopathic drug metoclopramide (dopamine antagonist) by reduced gastric emptying time resulting anti-dyspepsia effect [59].

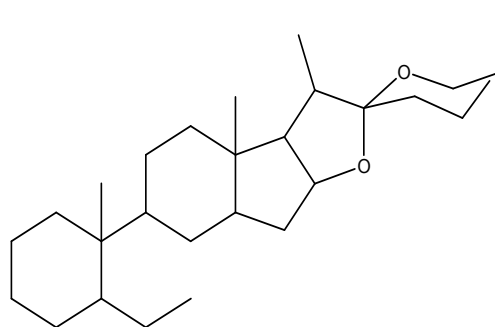
Conclusion

In recent years, ethnomedicinal studies received much attention as this brings to light the numerous little known and unknown medicinal virtues especially of plant origin. The scientific research on *A. racemosus* suggests a huge biological potential of this plant. It is strongly believed that detailed information as presented in this review on the phytochemical and various biological properties of the extracts might provide detailed evidence for the use of this plant in different medicines. Root extract of this plant are

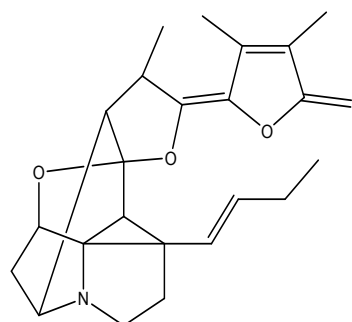
mostly used for their therapeutic action. *A. racemosus* plant contain steroidal saponins, isoflavones, asparagine and polysaccharides, make this plant a natural chemical source which play a major role in treatment of diarrhoea and dysentery. The plant also has potent antioxidant, antitussive, immunostimulant, *antidyspepsia*, galactogogue also as antiulcers and anticancer activity. At the same time, the organic and aqueous extract of *A. racemosus* could be further exploited in the future as a source of useful phytochemical compounds for the pharmaceutical industry.



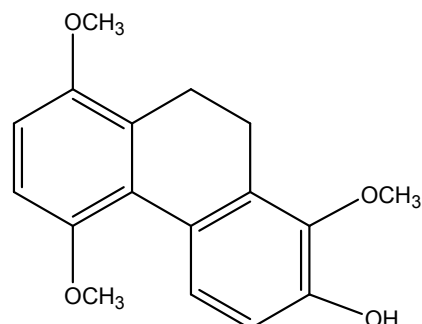
(Fig.-1) Shatavarin I



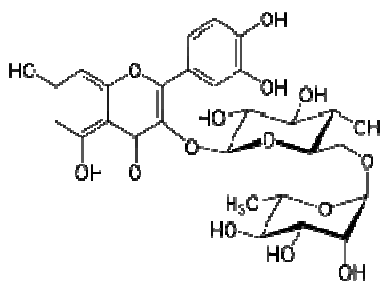
(Fig.-II) Sarsasapogenin



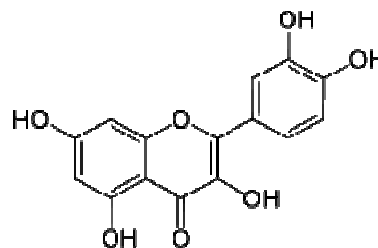
(Fig.-III) Asparagine



(Fig.-IV) Racemosol



(Fig.-V) Rutin



(Fig.-VI) Quercetin

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