

Pharmacological significance of shatavari; The Queen of herbs.

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Abstract

Shatavari (*A. racemosus*) has been used since ages by the rural people as a galactagogue. The herb is a source of phytochemicals like steroidal saponins, saponins, flavonoids (kaempferol, quercetin, and rutin), and poly phenols (secondary metabolites that have high pharmacological importance). These active principals gives medicinal value to the plant as anti-ulcerogenic, anti-oxytocic, anti-tussive, anti-diabetic, immunostimulants, cardioprotective, anti-cancerous, anti-hepatotoxic, anti-bacterial, anti-diarrheal, anti-aging, anti-depressant, anti-lithiatic, and anti-candidal activities. The review has been written in an attempt to enlist the detailed aspects of pharmacological significance of shatavari with the aim to provide a direction for further clinical research to promote safe and effective herbal treatments to cure a number of diseases.

Keywords: *Asparagus racemosus*, Pharmacology, Medicinal herb, Rasayana herb, Plant based preparations

Introduction

Shatavari literally implies "the one who has hundred spouses" as claimed in Ayurvedic literatures that shatavari strengthens a woman to the point where she is being capable of producing thousands of healthy ova. Its roots extract were used since ancient times to supplement as female tonic for promoting women's health by balancing several internal body hormones. Botanically called as *A. racemosus*, a member of family Asparagaceae, considered to be a rasayana herb. Rasayana means rejuvenation. Rasayana consist of the sanskrit word 'rasa' which means taste, essence, flavour, juice, or emotion, while, 'ayana' means path. Therefore, rasayana roughly translates to - The path of the juice. Rasa nourishes body, boosts immunity and helps to keep the body and mind in best of health. The main aim of Ayurvedic rejuvenation therapy or rasayana therapy is to restore spirit and vitality and thereby attain longevity. *A. racemosus* pacifies 'Vata' and 'Pitta' i.e. is useful in the management of diseases resulting from aggravation of Vata/ Pitta or both.

The major bioactive constituents which impart medicinal value to the herb are a group of steroidal saponins, saponins, flavonoids and polyphenols [1]. Saponins possess a variety of biological properties namely, being antioxidants, immunostimulants, anti-hepatotoxic, anti-bacterial, anti-carcinogenic, anti-diarrheal, anti-ulcerogenic, anti-oxytocic, useful in diabetic retinopathy, and as reproductive agents. Flavonoids, and phenolic compounds are widely distributed in plants, have been reported to exert multiple biological effect, including antioxidant, free radical scavenging abilities, anti-inflammatory, anti-carcinogenic etc [2]. We now review supporting pharmacological properties ascribed to *A. racemosus*.

Galactagogue

Shatavari has been mentioned in Ayurvedic texts like the Charak Samhita and Susruta Samhita, and Astanga Samgraha. It is stated that shatavari promotes maternal health and its meticulous use as a galactagogue (enhances breast milk secretion in lactating mothers). Ayurveda has called Shatavari the Queen of herbs and is the primary herb recommended for female health. Oral administration of roots of *A. racemosus* significantly increased the milk yield in rats [3], cows [4], buffaloes [5] and goats [6], thereby confirming its galactagogue property. The crude alcoholic extract of the roots increased the weight of mammary glands in post-partum and oestrogen-primed rats and the uterine weight in oestrogen-primed group [3].

Galactagogue effect was evaluated in 60 lactating mothers by measurement of changes in their prolactin hormone level during the study. The oral administration of roots of *A. racemosus* lead to more than three-fold increase in the prolactin hormone level of the subjects in the research group as compared to the control group. Evaluation of the galactagogue activity of the roots of *A. racemosus* Willd. during clinical trial on lactating mothers having symptoms of deficient lactation exhibits significant galactagogue activity in comparison with the control group without any significant acute toxicity effect. A probable reason for this galactagogue effect could be the presence of steroidal saponins in this plant [7].

Hormonal activity

A. racemosus is mainly known for its phytoestrogenic properties due to the presence of isoflavones in the roots [8]. Initially oestrogen replacement therapy has been envisaged as an effective therapy for the treatment of menopausal symptoms, for the



prevention of cardiovascular disease, and osteoporosis in postmenopausal women [9]. However, the therapy has also been known to increase the risk for endometrial cancer, breast cancer, venous thromboembolic events, and gall bladder disease [10]. Hence, the synthetic oestrogens replacement therapy is now considered as unsafe and ineffective due to known side effects and the interest in plant-derived oestrogens (phytoestrogen) has increased tremendously making *A. racemosus* particularly important. *A. racemosus* is used as hormone modulator [11]. Rao and coworkers [11], demonstrated the inhibitory action of *A. racemosus* on DMBA-induced mammary carcinogenesis in rats. Further, microscopic examination of the treated adult pregnant female albino rats at a dose of 30 mg alcoholic extract of *A. racemosus* rhizome /100 g body weight, daily for 15 days (days 1-15 of gestation), showed proliferation in the lumen of the duct of mammary gland. The workers envisaged an oestrogenic effect of 'Shatavari' on the female mammary gland and genital organs. Further, Ashajoythi and coworkers [12], reviewed the biological activities, pharmacological applications and clinical studies of *A. racemosus* to provide direction for identifying further phytoestrogenic properties, and unexplored areas in which *Asparagus* can be proved to have potential to cure diseases eg., osteoporosis. The worker suggested that the phytoestrogens derived from *A. racemosus* cannot be blindly advocated due to the incomplete understanding and insufficient evidence regarding their potential health effects. Phytoestrogenic herbs are usually extremely potent and not advisable for long term use and therefore the dosage and duration are extremely important.

Antidyspepsia

Dyspepsia, also known as upset stomach or indigestion, refers to a condition of impaired digestion. Dyspepsia is a common problem, and is frequently associated with, gastroesophageal reflux disease (GERD) or gastritis. In a small minority it may be the first symptom of peptic ulcer disease (an ulcer of the stomach or duodenum), and occasionally cancer. *A. racemosus* is used in 'Ayurveda' for dyspepsia ('amlapitta'). A modern inorganic drug, metoclopramide, which is used in dyspepsia to reduce gastric emptying time was compared with powdered root of *A. racemosus* [13]. Gastric emptying half-time (GE t_{1/2}) was studied in 8 healthy male volunteers using a cross-over design. The basal GE t_{1/2} in volunteers was 159.9 ± 45.9 min (mean ± SD) which was reduced to 101 ± 40.8 min by *A. racemosus* (p less than 0.001) and to 85.3 ± 21.9 by metoclopramide (p less than 0.001). Metoclopramide and Shatavari did not differ significantly in their effects on gastric emptying, and its traditional use in dyspepsia may be justifiable. Metoclopramide is a synthetic dopamine antagonist, which is used in therapy as an antiemetic and in patients with dyspepsia to increase the rate of emptying of the stomach. The side effect, galactorrhoea caused by dopamine antagonists has long been documented [14, 15]. Drowsiness is a known side effect of the metoclopramide drug. The usefulness of any potential antidyspeptic drug may therefore possibly be predicted from its effect on gastric emptying [16]. As *A. racemosus*

accelerates gastric emptying rate, thus it can be useful in treating dyspepsia patients.

Anti-tussive Activity

A. racemosus is also commonly used in the treatment of cough as demulcent, and in mild upper respiratory tract infection, worked as an anti-tussive. Methanol extract of *A. racemosus* root (200 and 400 mg/kg, p.o.) showed significant anti-tussive activity on sulfur dioxide-induced cough in mice, the cough inhibition (40.0 and 58.5%, respectively) being comparable to that by 10-20 mg/kg of codeine phosphate (36.0 and 55.4%, respectively) [17]. Codeine phosphate is an alkaloid obtained from opium, common side effects associated with this drug are constipation, dizziness, drowsiness, flushing, lightheadedness, nausea, sweating, tiredness and vomiting as opium is narcotic. Thus, we can explore the possibility of using *A. racemosus* in cough treatment.

Anti-microbial Activity

Microorganisms, apart from being beneficial are also the causative agents of various kinds of acute and chronic diseases. Plants based antimicrobials have enormous therapeutic potential. They are effective in the treatment of infectious diseases without causing many of the side effects that are often associated with synthetic antimicrobials. Many commercially proven synthetic drugs, used in modern medicine, were initially used in crude form in traditional or folk healing practices that suggested potentially useful biological activity [18]. Different concentrations (50, 100, 150 µg/mL) of the methanolic extract of the roots of *A. racemosus* showed considerable in-vitro antibacterial efficacy against *Escherichia coli*, *Shigella dysenteriae*, *Shigella sonnei*, *Shigella flexneri*, *Vibrio cholerae*, *Salmonella typhi*, *Salmonella typhimurium*, *Pseudomonas putida*, *Bacillus subtilis* and *Staphylococcus aureus* that are responsible for a number of ailments. The effects produced by the methanol extract were compared with chloramphenicol, a synthetically derived formulation [19]. Chloramphenicol, a bacteriostatic antimicrobial, associated serious adverse effect is bone marrow toxicity, which may occur in two distinct forms: bone marrow suppression, which is a direct toxic effect of the drug and is usually reversible, and aplastic anemia. Further, Battu and Kumar [20], used leaf extract of *A. racemosus* for its antimicrobial activity against wide range of microorganism including *Bacillus pumilis*, *B. subtilis*, *E. coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *S. aureus*, *A. niger*, and *C. albicans*. Ethanolic root extract (300 mg/ml) inhibited the growth of all the test organisms and the maximum zone of inhibition against gram positive organism was *S. aureus* (14.3 ± 0.2 mm); against gram negative is *E. coli* (14.0 mm); and against fungal organism was *C. albicans* (16.2 ± 0.2 mm). Their study justifies the use of *A. racemosus* in the treatment of boils, scabies and as antiseptic. Further, *A. racemosus* root exhibited significant anti-microbial activity against *Shigella dysenteriae*, *E. coli*, *Salmonella typhimurium* and *Vibrio cholerae*. These pathogens cause a variety of diseases including dysentery, diarrhoea and gastroenteritis in human. Furthermore, Kaushik and

coworkers [21] evaluated leaf extracts of *A. racemosus* against fungal pathogens *Fusarium oxysporum*, and *Aspergillus parasiticus*, reported significant activity of the herb against the fungal pathogens. While, Onlom and coworkers [22] evaluated antifungal activities of the *A. racemosus* root extracts against *Malassezia furfur* and *M. globosa*, frequently associated with dandruff and seborrhoeic dermatitis and suggested for potential use in anti-dandruff formulation of *A. racemosus*.

Anti-leishmanial activity

Leishmaniasis remains a major health problem of the tropical and subtropical world, caused by protozoan parasite *Leishmania* species. The most common type of Leishmaniasis is cutaneous leishmaniasis, however, other types are visceral leishmaniasis, diffuse cutaneous leishmaniasis, and mucocutaneous leishmaniasis. The visceral form causes the most fatalities if left untreated [23]. Racemoside A, a water-soluble steroidal saponin purified from the fruits of *A. racemosus*, is a potent anti-leishmanial molecule effective against antimonial-sensitive (strain AG83) and unresponsive (strain GE1F8R) *L. donovani* promastigotes. Dramatic increases in the rates of infection and drug resistance and the non-availability of safe vaccines have highlighted the need for identification of novel and inexpensive anti-leishmanial agents [24].

Immunological Activity

The use of *A. racemosus* dried root powder modulates the activity of the immune system. That, in turn, decreases the inflammatory response. It stimulates the immune system to fight against immunodeficiencies (like AIDS), infections and cancers. It may be helpful in obtaining higher protective antibody against different vaccinations including more effective cell mediated immune response for protection against various bacterial, viral and other diseases. Several workers has studied the effect of *A. racemosus* root extract in augmentation of humoral and cell mediated immune responses providing better protection level against infections.

Effect of *A. racemosus*, was evaluated in an albino rats, intraperitoneal adhesions induced by caecal rubbing [25]. Macrophages appear to play a pivotal role in the development of intraperitoneal adhesions, and modulation of macrophage activity, therefore, is likely to provide a tool for prevention of adhesions, was tested by the workers. A significant decrease was observed in the adhesion scores attained by animals receiving oral dose 200 mg/ kg of *A. racemosus* as total root extract. This was associated with significant increase in the activity of macrophages (70.1 +/- 2.52), compared to that in surgical controls (53.77 +/- 10.8). The workers findings provide a novel approach for the prevention and management of post-operative adhesions.

Further, immunoadjuvant potential of aqueous root extract of *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 ($P = 0.0052$) in antibody titers to *Bordetella*

pertussis as compared to untreated (control) animals. The plant therefore, serves as a potential immunoadjuvant that also offers direct therapeutic benefits resulting in less morbidity and mortality [18]. Extracts of *A. racemosus* have also shown immunopotentiating effects in cyclophosphamide treated mouse with ascetic sarcoma [26]. Further, Kumari *et al.* [27], determined the immuno-modulatory effects of *A. racemosus* extract treated feed, and to analyze the role of T and B cells in host defense against Newcastle disease in one week old normal, and immuno-compromized broiler chicks. After the treatment, significant ($P < 0.01$) positive effects were observed in both humoral and cell mediated immune responses of the birds, which was found to be evident by increased antibody titer after Hemagglutination inhibition (HI) test. Furthermore, Veena and coworkers [28] investigated immunomodulatory and antioxidative potential of milk fortified with freeze dried aqueous extract of *A. racemosus* using mice animal model, and reported immunomodulatory activity, ascertained by increased activity of macrophages and proliferation of lymphocytes.

Anti-oxidant potential

Plant extracts are a large source of natural anti-oxidant. Reactive oxygen species (ROS) including hydrogen peroxide (H_2O_2), and superoxide radical (O_2^-) are produced by a number of cellular oxidative metabolic processes [29] involving xanthine oxidase, NAD(P)H oxidases, metabolism of arachidonic acid by cyclooxygenases and lipoxygenases, monoamine oxidases, and the mitochondrial respiratory chain. Overproduction of such free radicals in human body can cause oxidative damage to biomolecules (e.g. lipids, proteins, DNA), eventually leading to many chronic diseases, such as atherosclerosis, cancer, diabetes, aging, and other degenerative diseases in humans [30, 31]. The sequential univalent reduction of oxygen generates superoxide, hydrogen peroxide and hydroxyl radical [32]. Several enzymes, including superoxide dismutase, glutathione peroxidase, glutathione reductase and catalase, are endogenous antioxidants that possess specific free radical scavenging properties. As plants produce a lot of anti-oxidants to control the oxidative stress caused by sunbeams and oxygen, they can represent a source of new compounds with anti-oxidant activity. Natural anti-oxidants strengthen the endogenous antioxidant defense from ROS ravage and restore the optimal balance by neutralizing the reactive species. Racemofuran, a compound isolated from *A. racemosus* root, revealed antioxidant property against DPPH (1, 1-diphenyl-2-picryl hydrazyl) [33]. Kamat and coworkers [34] observed the possible antioxidant effects of crude extract and a purified aqueous fraction of *A. racemosus* against membrane damage induced by the free radicals generated during gamma-radiation. Further, antioxidant effects are evidenced by significant recovery of SOD (superoxide dismutase), and CAT (catalase) enzyme level after drug treatment to the rat brain hippocampus given 4hrs immobilization/swim daily up to 30 days in unpredictable manner. These enzymes are part of antioxidant defense of the body against free radicals, and thus their significant increase after the drug treatment is indicative of free radical scavenging properties of both

these plant based drugs used in study. A significant increase in LDH (Lactic dehydrogenase) activity after stress but significant decrease after drug treatment is indicative of reduced lipid peroxidation in the brain area studied [35]. Anti-oxidant and free radical scavenging properties of methanolic root extract of *A. racemosus*, suggested moderate antioxidant activity of the plant [36].

Hypocholesteremic and Hyperlipidemic Activity

Hyperlipidemia/hypercholesteremia is major risk factors for atherosclerosis and cardiovascular diseases. The potent therapeutic phyto-components present in *A. racemosus* root i.e. phytosterols, saponins, polyphenols, flavonoids and ascorbic acid, could be responsible for increased bile acid production, elimination of excess cholesterol and elevation of hepatic antioxidant status in hypolipidemic and hypercholesteremic conditions [37, 38]. Normal and hypercholesteremic male albino rats were administered with root powder of *A. racemosus* (5 and 10g % dose levels) along with normal and hypercholesteremic diets, respectively, for duration of 4 weeks. Plasma and hepatic lipid profiles, fecal sterol, bile acid excretion and hepatic antioxidant activity were assessed. Inclusion of *A. racemosus* root powder in diet, resulted in a dose-dependant reduction in plasma and hepatic lipid profiles, increased fecal excretion of cholesterol, neutral sterol and bile acid along with increases in hepatic 3-hydroxy-3- methylglutaryl coenzyme A (HMG-CoA) reductase activity and bile acid content in hypercholesteremic rats. Further, *A. racemosus* root also improved the hepatic antioxidant status (catalase, SOD and ascorbic acid levels). *A. racemosus* root appeared to be useful as a dietary supplement that offers a protection against hyperlipidemia/hypercholesteremia in hypercholesteremic animals [37, 38].

Ceribroprotective effect

A stroke or brain attack occurs when a blood clot blocks the blood flow in a vessel or artery or when a blood vessel breaks, interrupting blood flow to an area of the brain. When either of these things happens, brain cells begin to die [39]. It has been suggested that some herbal medicines [39], or their products, may improve microcirculation in the brain and protect against ischemic reperfusion injury possess neuroprotective properties [40], and inhibit apoptosis [41], thus justifying their use in ischemic stroke patients. The potential of methanolic extract of *A. racemosus* roots has been explored against kainic acid (KA)-induced hippocampal and striatal neuronal damage in mice [42]. Intra-hippocampal and intra-striatal injections of KA to anesthetized mice resulted in the production of excitotoxic lesions in the brain. After KA injection, impairment of hippocampus and striatal regions of brain was observed accompanied by increased lipid peroxidation, increased protein carbonyl content, decreased glutathione peroxidase (GPx) activity, and reduced glutathione (GSH) content. GSH is an important anti-oxidant which acts as a nucleophilic scavenger of toxic compounds and as a substrate in the GPx-mediated

destruction of hydroperoxides which would otherwise accumulate to toxic levels in brain tissues. The mice treated with *A. racemosus* extract showed an enhancement in GPx activity and GSH content, and reduction in membranal lipid peroxidation and protein carbonyl. Nandagopal and coworkers [43], investigated the role of methanolic root extract of *A. racemosus* Willd. (MEAR) in the levels of antioxidants, metabolic enzymes, neurotransmitters, and histopathology studies in a model of global cerebral ischemia in rats. Global cerebral ischemia was induced by temporarily and the animals were pretreated with MEAR (200 and 400 mg/kg) for 7 days before induction. This protection was evident from, the significant decrease in the elevated levels of malondialdehyde (lipid peroxidation); reversal of the decreased GSH contents, catalase and SOD activities and protein levels, decrease in elevated levels of acetylcholine esterase, glutamate and reversal of decreased dopamine and serotonin levels, and the significant reduction in neuronal cell death in the hippocampal CA1 region to nearly normal levels after forebrain ischemia. These observations suggest that MEAR may be a clinically viable protective against a variety of conditions where cellular damage is a consequence of oxidative stress. In addition, MEAR may have the potential to be used in the prevention of neurodegenerative diseases such as cerebral ischemia.

Anti-depressant activity

Adaptogenic drugs are those which are useful as anti-stress agents by promoting non-specific resistance of the body. Adaptogenic herbs have traditionally helped prevent the imbalances that can result from stress and thus may prevent or slow down the development and progression of the central nervous system (CNS) disorders. In an Ayurvedic system of traditional medicine in India, 'Medhya Rasayana' is a group of herbal preparations known for their effects on nervous system. Few of them are also classified as adaptogen. Evaluation of antidepressant effect of methanolic extract of roots of *A. racemosus* standardized to saponins (62.2% w/w) revealed significant antidepressant activity, and the effect is probably mediated through the serotonergic and the noradrenergic systems, and augmentation of antioxidant defenses [44].

Anti-cancerous activity

Modern biomolecular science has contributed to the interpretation of the anticancer effects of medicinal plants, which are helpful against cancer, especially useful in improving survival and quality of life in patients suffering from advanced cancer. The anticancer potential of *A. racemosus* has been explored by several workers due to the presence of saponin in tuberous roots. Saponins have been long recognized to show cytotoxic activity in various cancerous cell lines. Apoptosis is an attractive endpoint of cancer therapy, it was believed that compounds that induce apoptosis are more likely to show a therapeutic window (tumor/normal tissue) compared to compounds that induce necrosis. Inhibitory effect of *A. racemosus* on 7,12-Dimethylbenz(a)anthracene (DMBA) - induced mammary tumorigenesis in rats of Holtzman strain,

revealed a sharp decline in mammary tumor incidence when virgin female rats, normal or primed with 17- β -estradiol treatment, were put on diets containing 0.25%, 0.5%, 1% or 2% *Asparagus* root extract powder, prior to their exposure to DMBA. The workers further reported that Shatavarin-I has been shown to have anticancer activity in DMBA induces carcinogenesis in rats [11].

Histopathological studies of the hepatic tissues of Wistar rats treated with diethylnitrosamine, once a week, for 2 weeks, followed by treatment with DDT (dichlorodiphenyltrichloroethane), a tumor promoter, for 2 weeks and kept under observation for another 18 weeks, demonstrated the development of malignancy. Pretreatment of Wistar rats with the aqueous extract of the roots of *A. racemosus* prevented the incidence of hepatocarcinogenesis. Aqueous extract of the roots of *A. racemosus* has the potential to act as an effective formulation to prevent liver cancer induced by treatment with diethylnitrosamine [45].

Further, a series of steroidal constituents, from *A. racemosus* were screened for their ability to induce cell death, and apoptosis of colon carcinoma cells. The carbohydrate moieties linked to the steroid backbones were found to strongly influence cytotoxic activity and cell death mode (apoptosis or necrosis). Immunoside, from *A. racemosus* was found to be a potent inducer of apoptosis. Immunoside has a similar overall structure to shatavarin IV, Shatavarin IV is also cytotoxic, but does not induce apoptosis [46].

Anti-ulceric activity

Ulcer is one of the burning problems in developing, and even developed countries. It is caused due to an imbalance among aggressive factors especially gastric acid and pepsin, and protecting factors, including gastric mucus, bicarbonate and prostaglandin. On the other hand, *Helicobacter pylori* also play an important role in the pathogenesis of peptic ulcer. The incidence of chronic peptic ulcer is steadily increasing and is fast becoming an alarming social problem. Shatavari is useful in pacifying the symptoms like 'Sula' and 'Daha' in patients. Shatavari roots act as a coating agent and bind to the ulcer bed thereby neutralizing, the gastric acid secretion in addition to increasing the life span of gastric mucosal epithelial cells as well as, the secretion and viscosity of gastric mucus [47]. Sairam and coworkers [48], studied the ulcer protective effect of methanolic extract of fresh roots of *A. racemosus* (ARM), 25–100 mg/kg given orally, twice daily for 5 days, on different gastroduodenal ulcer models. ARM 50 mg/kg, twice daily, orally (total saponins 0.9%) showed significant protection against acute gastric ulcers induced by cold restraint stress (CRS), pyloric ligation and aspirin, plus pyloric ligation, and duodenal ulcers induced by cysteamine. Further, antisecretory and antiulcer activity of methanolic extract of *A. racemosus* and its action against indomethacin (a non-steroidal anti-inflammatory synthetic drug), plus pyloric ligation (PL)-induced gastric ulcers in rats revealed that, *A. racemosus* as an effective antiulcerogenic agent whose activity can well be compared with that of ranitidine hydrochloride. *A. racemosus* causes an inhibitory effect on release

of gastric hydrochloric acid, and protects gastric mucosal damage [49].

Anti-diarrhoeal activity

Diarrhoea has long been recognized as one of the most important health problems in the developing countries [50]. Venkatesan and coworkers [51], evaluated the effect of ethanol and aqueous extracts of *A. racemosus* on gastrointestinal tract motility after charcoal meal administration and prostaglandin E₂ (PGE₂) induced intestinal fluid accumulation (enteropooling) in Albino Wistar rats for its anti-diarrhoeal potential against several experimental models of diarrhea. The result showed significant ($P < 0.05$) inhibitory activity against castor oil induced diarrhoea and PGE₂ induced enteropooling in rats, when tested at 200 mg/kg. Both ethanol and aqueous extracts delayed the onset of diarrhoea and 100 and 80% of rats were protected against castor oil induced diarrhoea at four hour, respectively. The extracts also significantly inhibited the PGE₂ induced enteropooling. The workers concluded that, significant anti-diarrhoeal activity was due to its inhibitory effect both on, gastrointestinal propulsion and fluid secretion. The inhibitory effect of the extract, justifies this use of the plant as a non-specific anti-diarrhoeal agent in folk medicine [51].

Hepatoprotective activity

Liver is chief site for intense metabolism and excretion. Therefore, it has a surprising role in the maintenance, performance, and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction [52]. The major functions of the liver are carbohydrate, protein and fat metabolism, detoxification, secretion of bile and storage of vitamin. Plant based preparations can serve as safe and effective approach for the treatment of various liver disorders such as hepatitis, cirrhosis, and alcoholic liver disease. Rahiman *et al.* [53], and Kumar *et al.* [54], demonstrated simultaneously aqueous extract of *A. racemosus* root (150 mg/kg and 250 mg/kg), and ethanolic root extract (150 and 250 mg/kg, p.o.) of *A. racemosus* against paracetamol induced hepatic damage in albino rats. The effect of aqueous and ethanol extract of *A. racemosus* on wet liver weight, bio chemical parameters such as, alanine aminotransferase (ALT/SGPT), aspartate aminotransferase (AST/SGOT), serum Alkaline phosphatase (SALP) and serum total bilirubin, along with anti-oxidant studies such as SOD, CAT, and also histopathological studies, were conducted to find out the possible mechanism of hepatoprotection. Paracetamol-induced a significant rise in wet liver weight, AST, ALT, ALP and total bilirubin with a reduction of superoxide dismutase (SOD) and catalase, elevation in AST and ALT level is indicative of cellular leakage and loss of functional integrity of cell membrane in liver. The scientists reported that, extracts of *A. racemosus* has reversal effects on the levels of above mentioned parameters. The extract of *A. racemosus* functions as a hepatoprotective agent, and the activity may be due normalization of impaired membrane function activity.

Anti-aging effect

Aging is characterized by slow, progressive, structural, and functional changes that take place at cellular, tissue, and organ level. These changes resulting in gradual functional decline, decreased adaptability, and ability to face stress which, increased the probability of age associated diseases including cardio vascular disease, cancer, diabetic, Alzheimer's etc. In the year; 2007, Velavan and Hazeena Begum [55], reported the salubrious role of *A. racemosus* root extract (ARRE) on accumulation of oxidative damage products such malondialdehyde (MDA), protein carbonyls (PCO), lysosomal marker enzymes, acid phosphatase and cathepsin D activity, aging marker lipofuscin and membrane bound H⁺ ATPase activity in heart lysosome of aged rats. ARRE (500 mg kg⁻¹ b.wt.) has inhibiting effect on the accumulation of age-related oxidative damages in addition to restoring the enzyme activity, and decreasing the lipofuscin content in heart lysosomes. This restorative activity of ARRE was mainly attributed to its enriched therapeutic phytochemical constituents, which act synergistically to alleviate the indices of oxidative stress, associated with aging.

Again in the year 2011 [56] the same workers suggested that, supplementation of *A. racemosus* root (500mg/kg body weight) is beneficial to aged rats as it reduces age associated increases in insulin, cholesterol, triglyceride, low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C), apart from increasing the age associated decreased high-density lipoprotein cholesterol (HDL-C). *A. racemosus* regulated the plasma lipids in aged rats as like young rats. Supplementation of *A. racemosus* root to young rats could maintain the plasma parameters, and increase HDL-C, which is anti-atherogenic cholesterol. Like in their preceding study, this lipid regulating activity of *A. racemosus* root was mainly attributed to its enriched therapeutic phytochemical constituents. However, in this work the authors specified the enriched therapeutic phytochemical constituents as; flavonoid, polyphenol, polysaccharide and vitamin C. It was further concluded that, *A. racemosus* roots possess hypolipidemic or antiatherogenic activity.

Memory Enhancement

Dementia, a major health problem in normal life as well as in various pathological conditions such as Alzheimer's disease, Pick's disease, cerebrovascular disease, hypoxic and ischemic encephalopathy, Parkinson's disease, alcoholism, drug abuse, brain tumor and infections like HIV and syphilis [57]. Senile dementia is a clinical syndrome affecting the elderly persons with loss of memory and cognition [58, 59]. Cure of cognitive disorders such as amnesia, attention deficit and Alzheimer's disease is still a nightmare in the field of medicine. Herbal medicines offer therapeutics for age related disorder like memory loss [60]. *A. racemosus* has been used to treat neurodegenerative disorders such as senile dementia associated with Alzheimer disease [61, 62]. Further, methanolic extract *A. racemosus* roots was evaluated [63] for its reversal effect on memory deficits in mice. Two doses of the extract (75 and 150 mg/kg, i.p.) were administered for seven

consecutive days. Scopolamine (0.4 mg/kg, i.p.), sodium nitrite (75 mg/kg, i.p.) were used to induce memory deficits (amnesia). Elevated plus maze (EPM) and Morris water maze (MWM) were employed to evaluate short and long term memory respectively. Scopolamine and sodium nitrite treatments produced significant impairment of elevated plus maze and Morris water maze performance indicating impairment of memory. The methanolic root extract dose of 150 mg/kg, i.p., significantly (p<0.05) improved EPM and MWM performance of scopolamine and sodium nitrite treated mice. The results indicated towards the memory deficit relieving potential of the plant [63].

Anti-lithiatic effect

A. racemosus root is a natural diuretic that is useful for preventing kidney stones. Christina and coworkers [64] evaluated the ethanolic root extract of *A. racemosus* for its 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 ionic chemistry of urine was altered by ethylene glycol which, elevated the urinary concentration of crucial ions viz. calcium, oxalate, and phosphate, thereby contributing to renal stone formation. The ethanolic extract, however, significantly (p < 0.05) reduced the (elevated) levels of these ions in urine. It also, elevated the urinary concentration of magnesium, which is considered as one of the inhibitors of crystallization. The high serum creatinine level observed in ethylene glycol treated rats was also reduced, following treatment with the *A. racemosus* extract. The histopathological findings also showed signs of improvement after treatment with the extract. All these observations provided the basis for the conclusion that this plant extract inhibits stone formation induced by ethylene glycol treatment.

Anti-candidal Activity

Candida albicans can cause infections (candidiasis or thrush) in humans and other animals, especially in immunocompromised patients. Many *Candida* species are harmless commensals or endosymbionts of animal hosts including humans [65]. *In vitro* anti-candidal activity of *A. racemosus* roots tubers extract against *C. albicans*, *C. tropicalis*, *C. krusei*, *C. guilliermondii*, *C. parapsilosis* and, *C. stellatoidea*, which are isolated from vaginal thrush patients, showed high degree of activity against all the *Candida* strains. The inhibitory effect of the extract against all the *Candida* tested was found comparable with that of standard antibiotics used [66].

Anti-diabetic activity

Diabetes mellitus (DM) is a major cause of disability and hospitalization that presents a significant burden on societies worldwide [67, 68]. In Asia and Africa, there are limitations on presently available therapeutic options for diabetes, such as oral hypoglycaemic agents and insulin [69, 70, 71]. In such circumstances, herbal medicines for the treatment of diabetes become significant. *A. racemosus* roots have been reported to

reduce blood glucose level in rats, and rabbits [72, 73]. Hannan *et al.* [74], evaluated the effects of the ethanol extract and five partition fractions of the root of *A. racemosus* on insulin secretion together with exploration of their mechanisms of action. The ethanol extract and each of the hexane, chloroform and ethyl acetate partition fractions concentration dependently stimulated insulin secretion in isolated perfused rat pancreas, isolated rat islet cells, and clonal β -cells. Ethanol extract and five fractions increased intracellular Ca^{2+} , consistent with the observed abolition of insulin secretory effects under Ca^{2+} -free conditions. The findings of the study revealed that constituents of *A. racemosus* root extracts have wide-ranging stimulatory effects on physiological insulinotropic pathways. Future work assessing the use of this plant as a source of active components may provide new opportunities for diabetes therapy.

Percutaneous permeation enhancer

The interaction of steroidal saponins, of *A. racemosus* root extract, with the skin membrane lipids can be expected to enhance the permeation of drugs from transdermal formulations. Saponins are characterized by their surface active properties and, hence, possess great potential for use as percutaneous permeation enhancer. Sapro and coworkers [75] investigated the effect of *A. racemosus* extract and chitosan (CTN) in facilitating the permeation of carvedilol (CDL) across rat epidermis. Transdermal flux of carvedilol through heat-separated rat epidermis was investigated *in vitro*. Biochemical estimations of cholesterol, sphingosine, and triglycerides were carried out for treated excised as well as viable rat epidermis. The permeation of carvedilol across excised rat epidermis was significantly higher ($p < 0.05$) when *A. racemosus* extract, CTN, or *A. racemosus* extract-CTN mixture were used as donor vehicle, as compared to propylene glycol/ethanol (7:3) mixture. Epidermis obtained after 12 h treatment of viable rat skin with *A. racemosus* extract-CTN mixture showed significantly higher ($p < 0.05$) permeability to CDL, as compared to those epidermis, obtained after treatments with *A. racemosus* extract or CTN. Estimation of micro constituents in rat epidermis revealed maximum extraction of cholesterol, sphingosine, and triglycerides after treatment with *A. racemosus* extract-CTN mixture. This was manifested in altered lipid and protein-specific thermotropic transitions. Further, increase in intercellular space, disordered lipid structure, and corneocyte detachment suggested a great potential of *A. racemosus* extract for use as percutaneous permeation enhancer. The developed transdermal patches of CDL containing *A. racemosus* extract-CTN mixture exhibited better performance as compared to oral administration in controlling hypertension in rats. The worker suggested promising role for, *A. racemosus* extract-CTN combination, as an effective and safe percutaneous permeation enhancer in transdermal formulations.

Anti-resorptive activity

De Pompo and coworkers [76] investigated antiresorptive properties of *A. racemosus* along with three other plants for potential efficacy in the treatment of bone-loss diseases. *A. racemosus* decoction inhibited osteoclastogenesis similarly to alendronate (standard drug) at the highest doses, and the workers suggested use of *A. racemosus* decoction as alternative therapeutics for the treatment of diseases caused by increased osteoclast activity.

Side Effects

Despite of the studies claiming immense medicinal value of the herb, Goel and coworkers [77] reported potential side effects of *A. racemosus*. The workers emphasized that *A. racemosus* should be cautiously used in pregnancy as its exposure during that period may cause damage to the offspring. Methanolic extract of *A. racemosus* roots (1000 mg/kg/day for 60 days) showed teratological disorders in terms of increased resorption of fetuses, gross malformations e.g. swelling in legs and intrauterine growth retardation with a small placental size in Charles Foster rats. Pups born to mother exposed to methanolic extract of *A. racemosus* for full duration of gestation showed evidence of higher rate of resorption and therefore smaller litter size. Live pups showed significant decrease in body weight and length and, delay of various developmental parameters when compared to respective control groups.

Formulations of *A. racemosus*

Satavari mandur (SM)

A herbo-mineral preparation 'Satavari mandur' (SM), containing *A. racemosus*, finds mention in ancient Indian texts for treatment of gastric ulcers. Datta *et al.*, [24], studied the ulcer protective effect of SM on cold restraint stress-induced gastric ulcer in rats. 125-500 mg/kg of SM was administered orally, twice daily for three, five and seven days. The effective regimen was observed to be 250 mg/kg; given for five days and, hence, was used for further experiments. Though, SM showed significant protection against acute gastric ulcers induced by pyloric ligation, it was found to be ineffective against aspirin- and ethanol-induced ulcers. Further, gastric juice studies revealed that, whereas, SM significantly increases mucosal defensive factors like, mucus secretion, it has little or no effect on offensive factors like, acid and pepsin secretion.

Mentat

A human trial on the efficacy of 'Mentat' in promoting memory and ameliorating mental fatigability was conducted by Sharma *et al.*, [78], in patients suffering from anxiety neurosis and minor depression. 'Mentat' treatment improved the memory quotient significantly in cases of anxiety neurosis by bringing it to normal levels. In cases of depression however, the memory quotient though raised, did not reach statistical significance. Further, mental fatigability that, had also been observed in both groups earlier, was

reduced significantly on account of treatment with 'Mentat'. The workers therefore concluded that, 'Mentat', seems to have specific effect on memory and power of concentration. It is pertinent to note that, 'Mentat' (BR-16A), an herbal psychotropic preparation, contains 'shatavari' (*A. racemosus*); besides others.

D-400

'D-400', a polyherbal formulation containing 20mg root extract of *A. racemosus*, besides others, has proven antidiabetic activity in experimental animal models as well as in human clinical trials. D-400 was investigated for its interaction with oral hypoglycaemic agents like, tolbutamide and glibenclamide, in alloxan-induced diabetic rabbits. Whereas, administration of 'D-400', significantly elevated plasma tolbutamide and glibenclamide concentrations along with, simultaneous reduction of blood glucose levels, the concentration of above compounds were observed to be significantly lowered, after withdrawal of 'D-400' treatment. After withdrawal of 'D-400'; however, elevation of plasma tolbutamide was observed only for the first 4 h, followed by its decline towards normal levels. Further, no significant differences between 'D-400' treated and control group was observed at the end of 8 hrs; as well [79].

The role of *Asparagus* in controlling diabetes mellitus (DM) can also be inferred by the following work of Kundu and Chatterjee [80], who conducted meta-analysis to analyze the efficacy and safety of Diabecon® tablets that contain, 20 mg 'shatavari' root extract per tablet; among others. Results of this study indicated significant beneficial effects in patients given 'Diabecon' tablets. Significant improvements were observed in fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycated hemoglobin, plasma insulin, microalbuminuria, etc. The workers observed similar results, in studies that used, 'Diabecon' along with OHA or insulin in OHA-resistant cases. 'Diabecon' treatment also significantly improved lipid profile [total cholesterol, HDL-cholesterol (HDL-c), LDL-cholesterol (LDL-c)] as well as diabetic retinopathy and microalbuminuria. The findings from clinical trials with 'Diabecon' clearly indicated their beneficial effects in controlling DM and related complications with additional advantage of long-term safety.

Menosan®

The mechanism of action of phytoestrogens in the biological system and the role of *Asparagus* in treatment of post-menopausal symptoms can be inferred through the works mentioned below: Gopumadhavan *et al.*, [81], observed that, Menosan®, containing 110 mg *A. racemosus* extract per tablet; among others, another polyherbal formulation, causes an increase in uterine weight and uterine glycogen; without altering serum oestrogen and progesterone levels in immature rats; however. The study indicated that, the phytoestrogen performs its function by binding directly to the oestrogen receptor, without enhancing the endogenous oestrogen levels.

'Menosan' has also been studied for the treatment of post-menopausal symptoms in trials on women [82]. Significant relief from such symptoms as depression (90% relief), insomnia (83.33% relief), irritability (50% relief), weight gain (50% relief), bone and joint pains (40%), sweating (37.88%) and hot flashes (37.03%) were observed, post 'Menosan' treatment. On account of the known anti-bacterial and phytoestrogenic activities of *A. racemosus*, the workers concluded that, menosan is responsible for relief from symptoms like hot flashes and night sweats.

EveCare®

Similarly, the contribution of *Asparagus* in treatment of menstrual disorders: dysmenorrhoea and menorrhagia can be inferred through the work of Mitra *et al.*, [83]. The workers utilized 'U-3107' or EveCare®, containing 32 mg *A. racemosus* extract per 5ml syrup; among others, in an open clinical trial conducted on thirty five female patients in the reproductive age group of 19-45 years, with a history of abnormal uterine bleeding. Progressive decline in bleeding was observed after one and three months of treatment with Evecare. By the end of 3 months of this study, all the subjects noticed a significant decrease in bleeding. The workers thereby concluded that, 'Evecare' can effectively avert the multifactorial aetiology of dysmenorrhoea and menorrhagia, without producing any undesirable side effects [83]. It may be noted that EveCare® is an herbal preparation formulated by the Himalaya Drug Co., Bangalore, to treat various menstrual disorders and threatened abortion.

Ricalex®

Similarly, the galactagogic effect of the roots of *A. racemosus* can be inferred through the work of Joglekar *et al.*, [84], who observed an increase in milk secretion of nursing mothers, after administration of Ricalex® tablets, to women suffering from deficient milk secretion. It may be noted that Ricalex® tablets, Aphali pharmaceuticals, contains 40 mg concentrated root extract of *A. racemosus* per tablet. The aphrodisiac nature of *A. racemosus* has been established by the work of Garg and Gupta [85], who administered milk and aqueous decoction of *A. racemosus* roots, for testing their aphrodisiac activity in male albino rats. Results were compared with untreated; control group. The rats were evaluated for impact of treatments on anabolic effect. 200 mg/ kg body weight of milk decoction, showed a significant difference in the sexual behavior of animals. Further, reduced hesitation time, an indicator of attraction towards female; in treated rats, also indicated an improvement in sexual behavior of extract treated animals. The observed effects appear to be attributable to the testosterone-like effects of the milk decoction of *A. racemosus*. In addition the saponin content was found to be appreciably higher in the milk decoction as compared to, that observed in the aqueous decoction of *A. racemosus*.

Conclusion

Shatavari, an herb with immense medicinal value has been reviewed with the aim to explore the different pharmacological studies via several in vitro and in vivo techniques of biological evaluation, and to facilitate safe and effective herbal treatments for biological problems (diseases). The active principals responsible

for medicinal value includes: steroidal saponins, sapogenins, flavonoids (kaempferol, quercetin, and rutin), and poly phenols. The review dealt with pharmacological significance of shatavari with the aim to provide a direction for further clinical research.

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