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SHATAVARI (ASPARAGUS RACEMOSUS) – A COMPREHENSIVE REVIEW.

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Abstract: A climbing Ayurvedic plant called Asparagus racemosus is well-known for its many uses, including treating benign hormonal imbalances, hypertension, angina, dysmenorrhea, anxiety disorders, and urinary tract infections, leucorrhea, and prostatic hyperplasia (BPH). Numerous secondary metabolites, such as steroids, alkaloids, derivatives of dihydrophenanthrene, flavonoids, furan derivatives, and essential oils, are present in this plant. According to information from the literature, steroidal saponins are the principal components of A. racemosus and are primarily in charge of the various biological activities of the species. The paper provides an overview of the data pertaining to A. racemosus culture, morphology, phytochemistry, biological activity, safety profile, marketing status, and conservation methods.

Introduction:

There are over 300 species of the genus Asparagus worldwide, with 22 of those species being found in India. Although A. racemosus is primarily grown in India, it is found around the world, including tropical Africa, Java, Australia, Sri Lanka, and southern regions of China and India. 1 A. racemosus is a significant medicinal plant that is considered a "rasayana," or plant medication that promotes overall health by boosting cellular resilience and vigor. 3. The ancient Ayurvedic literature (Charaka Samhita) mentions the use of A. racemosus. 4. Traditionally, A. racemosus is used to treat epilepsy, vata problems, brain tonics, heart disorders, and hypertension.

Classification:

Kingdom: Plantae

Order: Asparagales

Family: Asparagaceae

Sub family: Asparagoideae

Genus: Asparagus

Species: Asparagus racemosus L

Various common names at various region 2:
Sanskrit: Satavari
Hindi: satavari, shatawar
Bengali: Shatamuli
Tamil: Inli-Chedi

Telegu: Pilli-gaddalu
Kumaon: kairuwa
Rajasthani: Norkanto or Satawar
Gujrati: Satawari
Nepali: Kurilo

It is widely used to treat spermatogenic abnormalities, oligospermia, male genital dysfunctions, and other male illnesses such painful micturition 7, 8. Additionally, it is examined in Ayurvedic formulations for piles, debility, amoebiasis, indigestion, and digestive discomfort 9, 10. In women, doctors recommend medication for recurrent abortions, uterine weakening, and heavy menstrual flow 11. Shatavari has been shown in recent studies and trials to have antidiarrhetic, antispasmodic, aphrodisiac, demulcent, diuretic, galactagogue, nutritional, mucilaginous, refrigerant, stomachic, and tonic qualities in humans (14). It is also known to strengthen the immune system and safeguard important bodily organs including the heart, brain, and others. The cultivation, morphology, phytochemistry, biological activity, safety profile, and conservation methods of this plant are all included in this review.

Cultivation and Morphology: The plant's decorticated roots have long been utilized in Thailand as a treatment for liver and spleen disorders as well as other internal organs, such as avoiding miscarriage 17. The roots have historically been used as a tonic in India to treat fever, tumors, and internal pain 18.

The climbing plant A. racemosus, often known as Shatavari, has tuberous roots 5. As determined on the dried weight basis, A. racemosus contains at least 0.1% of Shatavarin IV, following the Indian Pharmacopoeia 14. The flavor is starchy at first, then slightly bitter, and finally sweet. A. racemosus possesses homogeneous, glossy green phylloclades, or photosynthetic branches, that resemble tiny pin-needles. The roots are sold in parts and measure 5 to 15 cm in length and 2 cm in thickness. These have a white exterior and are either ash-colored or very white inside. When fresh, roots are essentially smooth, but as they dry out, they begin to form longitudinal wrinkles 10. Under a microscope, the inner parenchymatous zone of the cortex is made up of 42–47 layers in the middle tuberous region of the roots and 18–24 layers in the top portion. Cells have round to oral shapes, distinct intercellular gaps, and thin walls made of cellulosic fibers.

Figure 1: Photos of Asparagus racemosus- Tuberous roots, powder, leaves and berries

In certain roots, the three to four layers of cortex that are right next to the endodermis change to form a stone cell sheath around it. It starts producing pulpy berries in September that are puxrplish black after ripening, with seeds that are spherical or obscurely three-lobed brittle and hard 14. Timely execution of weeding operations is required. In general, pests and illnesses do not impact the crops. After 1.5–2 years of transplanting, which continues for 10–15 years, the first harvest is carried out. If seed is needed, both male and female plants are cultivated. 4.

Methods of analysis: RP HPLC technique 22 was used to analyze Shatavarin V from the root extract. Sarsapogenin analysis in A. racemosus extract under isocratic conditions using RP-HPLC 23 has been documented in another investigation. HPLC with an Evaporative Light Scattering Detector (ELSD) and a solvent system of 57.3% have been used to examine Shatavarin I and IV. Methanol 24 contains ethyl acetate. Enzymatic, size exclusion, gas chromatography with flame ionization detector (GC-FID), high pressure anion exchange chromatography (HPAEC), and thin layer chromatography techniques were used to report the presence of fructooligosaccharides (FOS). 25.

Plant-based chemicals: Steroid saponins make up the majority of the varied spectrum of compounds found in A. racemosus, along with alkaloids, flavonoids, furan derivatives, dihydrophenanthrene derivatives, and volatile components (figure 2). There have been reports of 29 steroidal saponins (1-27) from A. racemosus. 3-0-[α-L rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl (1→4)-O-β-D-glucopyranosyl] is an oligospirostanoside (1).-25(S)-spirosta-3β oil, which is derived from A. racemosus, increased antibody synthesis and the immune system's cell-mediated response in rats with weakened immune systems when taken orally.

Chemical class	Phytochemical constituent
1. Steroidal saponins	Shatavarin I-VI
2. 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-2-0 (-2-hydroxy isobutyl) benzaldehyde, Undecanyl cetanoate
3. Kaempferol	
• Trace minerals	Zinc, Manganese, Copper, Cobalt, Magnesium, Calcium, Potassium, Selenium, Iron
• Miscellaneous	Gamma linolenic acid, Vitru11ins A, BI, B2, C and E, Folic acid

Table 1: Phytochemical constituents of Asparagus racemosus

In cultures of human stomach cancer cells (KATO III), sitosterol (20) 32, 33; Shatavaroside A (26) and Shatavaroside B (27) 37; Asparagamine A (28) 38; polycyclic alkaloid (29) 39 and Racemofuran (31) isolated from A. racemosus have antioxidant activity IC50 value of 130 µM 17 and immunomodulatory activity 3 (IC50 = 79. 81µg/ml 39) (figure 2). Components of essential oils: A wide variety of chemical classes, including acids, alcohol, aldehyde, ester, hydrocarbon, ketone, and N-containing compounds, are represented by the fifty-five essential oil constituents that were isolated from aerial sections. The principal ones are as follows: 4-[1 hydroxyethyl] benzaldehyde (45), hexanal (46), furfural (47), decanoic acid (48), undecanoic acid (49), camphor (50), myrtanol (41), pinocarveol (42), 2 ethylhexanol (43) perillaldehyde (44), and 6, 10, 14-trimethyl pentadecanone.

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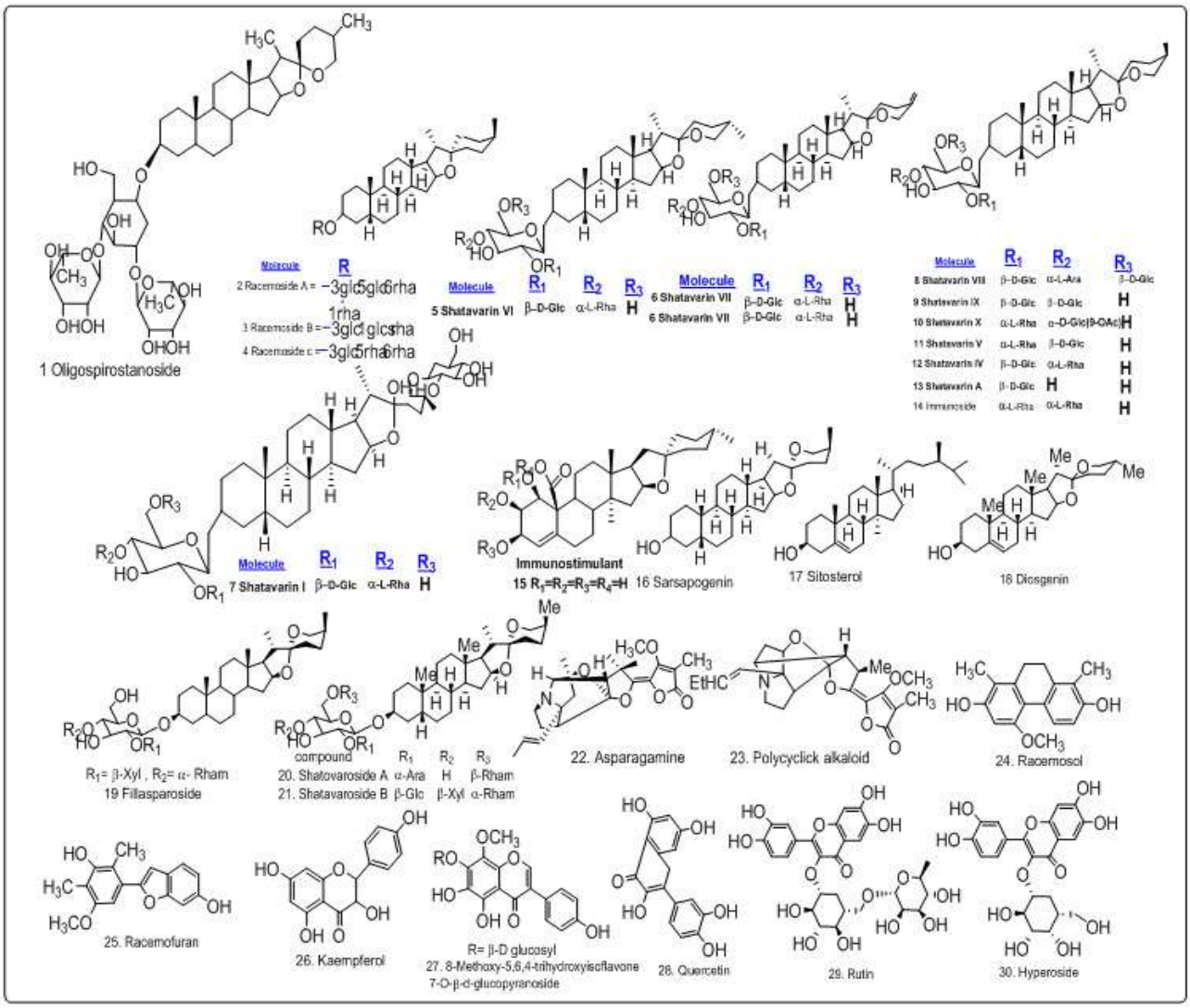

Figure 2: Structures of steroidal saponins, alkaloids, dihydrophenanthrene, furan derivative, flavonoids from asparagus racemosus

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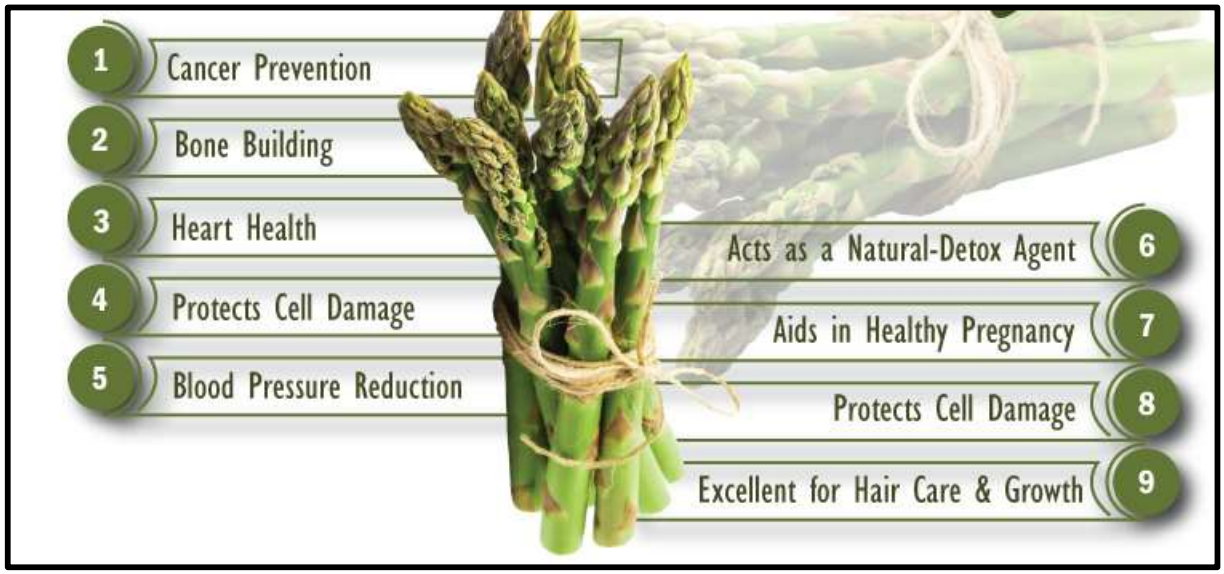

Figure 3: Medicinal properties of Asparagus racemosus

1. **Antioxidant property**: It has been shown that A.racemosus's crude extract and purified aqueous fraction contain antioxidant properties 46. Rat liver cell mitochondrial membrane damage brought on by produced free radicals was used to test the activity. The production of lipid hydroperoxides (LOOH) and thiobarbituric acid reactive compounds (TBARS) 47, 48 served as indicators of the induced lipid peroxidation.
   By offering defense against lipid peroxidation, protein oxidation, and reduction in the levels of protein thiols and the antioxidant enzyme superoxide dismutase, the extract demonstrated an antioxidant action against oxidative damage. In comparison to the crude extract, it was discovered that the purified aqueous fraction, which contained polysaccharides, was a strong antioxidant. (Figure 3)

2. **Diuretic activity:** An appropriate experimental model has confirmed the diuretic characteristic that was highlighted in Ayurveda. The study was conducted using three dose vials of an aqueous extract of the roots (800 mg/kg, 1600 mg/kg, and 3200 mg/kg) to examine the diuretic activity of the medicine in comparison to standard drug (furosemide) and control (normal saline) rats following acute toxicity tests. At a dose of 3200 mg/kg, the extract showed diuretic efficacy without causing any acute toxicity 51.

3. **Antidepressants activity**: The tail suspension test (TST) and the forced swim test (FST) were used to assess activity in mice. The methanolic extract dramatically reduced immobility times in TST and FST, indicating strong antidepressant activity and demonstrating that the extracts' effectiveness was on par with that of the study's reference medications, imipramine and fluoxetine. It has been discovered that the methanolic extract has antidepressant activity, likely by inhibiting MAO-A and MAO-B and through interaction with adrenergic, dopaminergic, serotonergic, and GABAergic systems (Gamma aminobutyric acid). Mice given the extract showed a significant decrease in brain MAO-A (Monoamine Oxidase A) and MAO-B (Monoamine Oxidase B) activity levels 52. Rats have been used in experiments with methanolic extract and put through the learned helplessness test (LH) and forced swim test (FST) and the extract has been shown to have antidepressant action by increasing the avoidance response in LH and decreasing immobility in the FST.

   The results of behavioral experiments showed that the methanolic extract had a strong antidepressant effect mediated through serotonergic, noradrenergic precipitation systems, and antioxidant defenses 53. It also increased the number of head twitches induced by 5-HT (5 hydroxy tryptamine) and clonidine-induced aggressive behavior.

4. **Antiepileptic effect:** Using various extracts, the anticonvulsant effectiveness was assessed on seizures generated in rat models by Maximal Electroshock MES, as well as pentylenetetrazole. The methanolic extract demonstrated a strong anticonvulsant effect in the test, which was predicted based on the finding of a reduction in the duration of the stupor phase, clones, and hind limb extension. GABAergic extracts 55 were the mechanism underlying the extended onset of the tonic clonic seizure caused by pentylenetetrazole in the groups treated with methanolic and aqueous solutions.

5. **Antitussive effect**: It has been reported that the roots' methanolic extract possesses antitussive properties. The mouse model 56 was used to assess the action against coughing caused by sulfur dioxide (SO2). Codeine phosphate was used as a common antitussive reference medication, along with methanolic root extract given at 200 and 400 mg/kg. At doses of 200 and 400 mg/kg, respectively, extract demonstrated a 40% and 58.5% suppression of SO2-induced cough upon oral administration of methanol. Both the extracts and the conventional medication had dose-dependent antitussive effects, which further validated the statements made by practitioners of traditional medicine regarding the effectiveness of A. racemosus in treating cough.

6. **Anti-plasmodial activity**: The anti-plasmodial activity of an ethyl acetate extract of A. racemosus roots has been examined. 60 With an IC50 value of 29µg/mL 61, the extract with a yield value of 7.9% per 100g has demonstrated dose-dependent suppression of the chloroquine-resistant strain of Plasmodium falciparum (3D7).

7. **Immunostimulant**: The category of illnesses known as immunodeficiency disorders is where the body's defense mechanism is weakened, which reduces its ability to repel outside invaders. An immunodeficiency condition patient would consequently have more frequent, typically more severe, and longer-lasting illnesses.

   Research on the immune systems of both healthy and cyclosporine-A-induced immune-suppressed mice revealed that isolated polyhydroxylated steroidal sapogenin acids (13–15) are strong immune system stimulators (30).

   Since T and B lymphocytes are the foundation of the immune system and immunostimulant 63 targets the biology of Th1/Th2 immunity, the study primarily concentrated on lymphocytes and cytokines. The compounds' oral administration has resulted in a notable and dose-dependent rise in Th1/Th2 cytokines and CD3 and CD19 counts. The compounds were found to be strong immune system stimulators, as evidenced by the results, which were similar to those of levamisole. The polymorphonuclear leukocyte function test was used to assess the immunomodulatory activity of steroidal saponins, shatavaroside A (26) and shatavaroside B (27), that were separated from the methanolic extract of A. racemosus. A few more sensitive assays, including nitroblue tetrazolium, nitrous oxide, and chemiluminescence assays, were employed as a confirmatory test for the activity. It was shown that the separated steroidal saponins may function as a strong immunostimulant (37) and were active at nanoconcentrations (5ng/mL).

8. **Antibacterial activity**: Using the conventional cylinder method, the antibacterial activity of A. racemosus root extracts has been investigated. Proteus mirabilis, Kleibsella pneumonia, Pseudomonas putida, Bacillus subtilis, Aureus, Staphylococcus werneri, and Escherichia coli were among the microorganisms that were employed. The extract influenced both gram-positive and gram-negative bacteria. The antibacterial activity of ethanolic extracts with concentrations of 100 mg/ml, 300 mg/ml, and 500 mg/ml was equivalent to that of the reference standard medication, gentamycin (25 µg). Staphylococcus aureus had the most impact on the gram-positive bacteria. 67.

9. **Pregnancy**:
    a. **Antiabortifacient**: In cases where abortions were imminent, medications containing A. racemosus roots (such as Shatavari sidh ghrit) were recommended. 68. The Shatavarin I 69 (7) was the cause of the observed activity. Shatavarin IV (12), also known as saponin A4, had an in vivo effect on the uterine muscles that was comparable to that of estrogen 70. According to reports, the polycyclic alkaloid asparagamine A (28) has an antiabortifacient effect and an anti-oxytocic action (38).
    b. **Prenatal tonic**: According to a clinical experiment with 450 patients, consistent usage of a Sujat pill containing A. racemosus extract throughout the prenatal period enhances fetal weight and lowers the risk of perinatal mortality 71. The prevalence of pregnancy-induced hypertension (PIH) decreased. A lack of PGI2 and NO (nitric oxide), two crucial vasodilators, can result in PIH. Gamma linolenic acid, an essential fatty acid derived from A. racemosus, is known to mediate the production of PGI2 over TXA2 71.

10. **Cardioprotective effects**: Himalayan Drugs produces the Herbo mineral formulation Abana, which has been shown to be effective in managing coronary heart disease, preventing it, and lowering hypercholesterolemia. Abana was reported to lower total cholesterol and triglyceride levels when administered in both normal and essential hypertension and angina pectoris cases. The levels of high-density lipoprotein cholesterol were found to have significantly increased 77. Investigation showed that the main cause of the antihypercholestrolemic effect was increased excretion of cholesterol, neutral sterols, and bile acid, as well as an increase in the hepatic bile acid content. The lipid-lowering effects of A. racemosus root extract were demonstrated in hypercholesteraemic rats. When hypercholesteraemic rats were given powdered A. racemosus root, their HMG-CoA reductase activity increased. Interestingly, normocholesteremic animals under A. racemosus treatment, exhibited no significant variations either in excretion of cholesterol, neutral sterols, bile acid, hepatic cholesterol and bile acid content.

11. **Anti-cancer property**: It was demonstrated that the root extract protected against mammary cell carcinoma 80. Steroidal apoptotic activity was examined in A. racemosus components, which were found to have the ability to kill tumor cells 81

    The MTT assay was used to assess the anticancer activity of shatavarins (containing shatavarin IV) (12) that were isolated from the roots using human breast cancer cell lines MCF-7, human colon adenocarcinoma cell lines HT-29, and human kidney carcinoma cell lines, as well as an in vivo experimental model of Ehrlich ascites carcinoma (EAC) tumor-bearing mice. According to the experimental findings, the extract that contains Shatavarin IV has strong anti-cancer properties. 82

Conservation: Since the medicinal plant's active ingredient is its primary constituent, it is important to cultivate superior clones that can be found using molecular marker methods, and chemo-profiling is a method for enhancing the active ingredient content. The axillary branching method 110 was used to create the micropropagation method, an in vitro protocol for A. racemosus micropropagation. A more effective technique for producing secondary metabolites on a wide scale from plant cells is the cell suspension culture system. (Table 3)

Sr. No.	Product Name	Content of A. racemosus	Medicinal property
1	Abaoa	10 mg root extract per tablet	Hyperlipidaemia conditions, Mild to moderate hypertension
2	Diabecon	20 mg Shatavari root extract per tablet	Microalbuminuria, Monotherapy in non-insulin-dependent diabetes mellitus
3	EveCare	32 mg Shatavari root extract per 5 ml syrup	Dysmenorrhea, Menorrhagia Metrorrhagia, Oligomenorrhea
4	Geriforte	20 mg Shatavari root powder per tablet	Geriatric stress, Stress related anxiety
5	Himplasia	80 mg Shatavari root powder per tablet	Benign prostatic hyperplasia
6	Lukol	40 mg Satavari root extract per tablet	Leukorrhea, Malaise
7	Renalka	50mg Shatavari root extract per 5mL of syrup	Burning micturition, Dysuria. Hematuria
8	Menosan	110 mg Satavari root extract per tablet	Natural menopause, Surgical menopause

Table 3- List of marketed drugs/formulations containing A. Racemosus

Conclusions:

Because it is utilized in indigenous medical systems like Ayurveda, Sidha, and Unani, A. racemosus is a significant medicinal plant of historical significance. Numerous scientific and experimental investigations support traditional practices. This illustrates a plant with enormous possibilities for both trade and healthcare. Although a great deal of research has been done on the biological activities and therapeutic uses of plants, there are still innumerable potential pharmacological uses that require investigation. Antioxidant, diuretic, antidepressant, antiepileptic, antitussive, immunostimulant, hepatoprotective, cardio-protective, antibacterial, and antiulcerative are just a few of the many medicinal uses for plants. Significant research utilizing plant extracts has been documented; nevertheless, the active principle behind these actions still requires investigation. Formulations that include A. racemosus as a key component to treat a variety of illnesses demonstrate the plant's global economic and medicinal significance.

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