

"Exploring Therapeutic Potential: *Asparagus racemosus* in Neurodegenerative Disorders and Enhanced Delivery through Nanoformulations"

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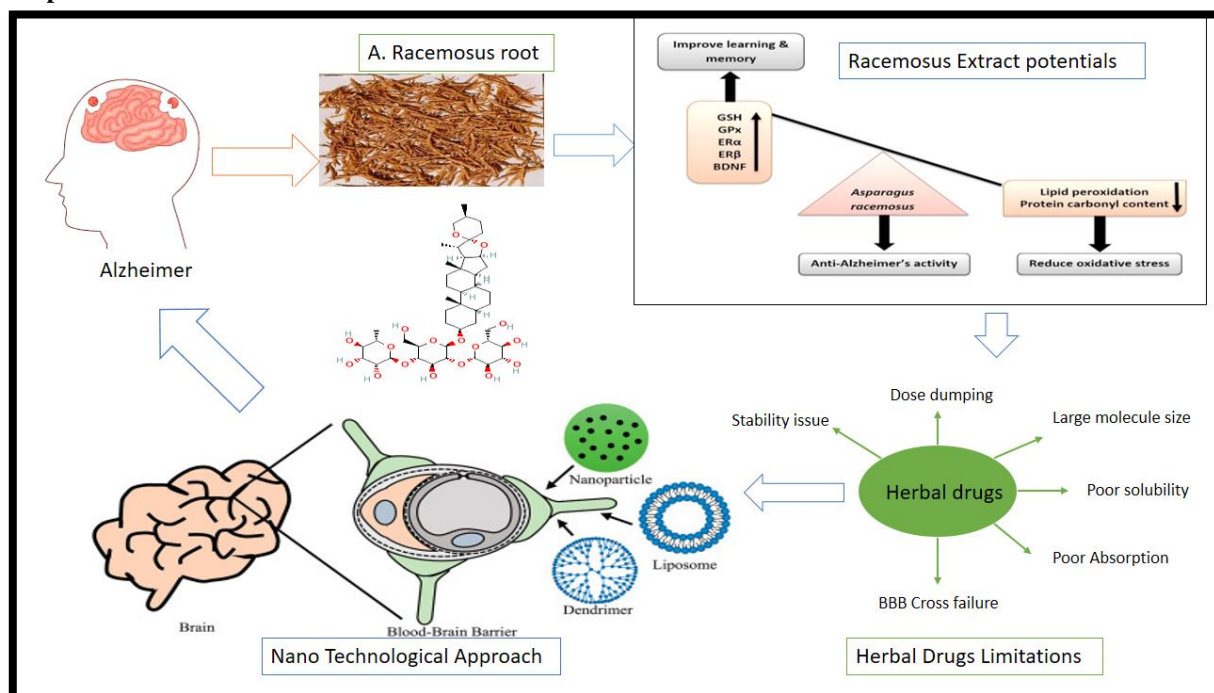
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Graphical Abstract



Abstract

This ample review decipher the therapeutic values of *Asparagus racemosus* cutting-edge framework of neurodegenerative diseases, notably Alzheimer's. As a key herb in Ayurveda, *Asparagus racemosus* is recognized for its diverse phytochemical composition, acting as a nervine tonic that enhances memory function, reinforces antioxidant defenses, and demonstrates neuroprotective effects. The article delves into the rich traditional knowledge surrounding this herb, emphasizing its significance in Ayurvedic practices. A pivotal focus of the review is the transformative impact of nanoformulations on herbal drug delivery, specifically highlighting compounds derived from *Asparagus racemosus*. Nanoformulations facilitate encapsulation in nanoparticles, offering advantages such as targeted delivery, sustained release, and improved stability. This innovative approach holds promise for optimizing the worth of herbal therapies, particularly cutting-edge the complex landscape of neurodegenerative disorders like Alzheimer's. In summary, the review bridges traditional herbal wisdom with modern nanotechnology, presenting a holistic perspective on *Asparagus racemosus*. By elucidating its neuroprotective attributes and exploring the potential of nanoformulations, the article underscores a promising avenue for the development of effective therapies in the field of neurodegenerative diseases, marking a significant step toward integrative and personalized approaches to healthcare.

Keywords: Alzheimer's disease, *Asparagus racemosus*, Neurodegenerative diseases, Phytochemicals, Shatavari

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Introduction

Herbal plants are utilized by nearly 80% of the biosphere's population, particularly in underdeveloped nations, for primary healthcare, because of their cultural acceptability, tolerance with the human body, and lack of side effects.^[1] Botanical treasures are a major source of a diverse collection of secondary metabolites that endure in varied disease prevention and therapy. Medicinal plants have long been recognized for their distinct and productive properties across the world.^[2] In recent years, bioactive phytochemical constituents have developed as therapeutic agents for the management of ailments caused by ROS (reactive oxygen species).^[3] An enormous range of therapeutic plants and their bioactive components, such as *Asparagus racemosus*,^[4] *C. longa*,^[5] *W. somnifera*,^[6] and *O. basilicum*,^[7] have already been documented and are already in use for their promising bioactivity as antioxidants and immune modulators.

Shatavari (*Asparagus racemosus* wild) remains a significant herb that has tremendous medicinal potential belonging to the Asparagaceae family. It is a rising shrub that grows in the near to the ground backwoods of India.^[8] From ancient era it has been utilised in Ayurveda and other old-style medicine practice to indulge a variety of disorders, as well as immune disorders, cancer, also reproductive health in women.^[4] ^[9] Shatavari is described as a Rasayana medicine in the Rig Veda and the Atharvaveda. It is recommended as a soothing agent, uterine tonic in Ayurveda.^[8] The root of Shatavari contains pyrrolizidine alkaloids, flavonoids, carbohydrates, tannins, phenolic compounds, saponins,

terpenes, and steroids.^[10] It also contains vitamins, resin, essential oils, arginine, asparagine, and tyrosine as some other primary chemical constituents.^[11] It is also used for the management of rheumatism, dysentery, diarrhea, anxious collapse, and as an aphrodisiac stimulant.^[9] Recent research has shown that asparagus root extract has neuroprotective properties in an *in vivo* model of aluminium and paraquat-induced neurodegeneration.^[1] NDDs are nervous system disorders that are traditionally defined as a selective loss of neurons.^[12] NDDs are characterised by a progressive loss of neuronal structure and function, and they have presented a major challenge to society as a whole as well as to persons with Parkinsonism, , dementia.^[2] AD is a neural illness that affects people as they get older and affects their memory. It is extremely debilitating, starting with cognitive issues and escalating to total dependency and inability to conduct daily tasks. Several experiments have been carried out to try to uncover therapeutic options for AD, but no cure has yet been found.^[13] *Asparagus racemosus* contains a number of neuropharmacological qualities that support better memory and cognition, making it a recognized nervine tonic in herbal medication.^[14] By preventing membrane lipid peroxidation and protein carbonylation, *Asparagus racemosus* extracts lower oxidative stress and enhance cognitive function by raising levels of GSH (reduced glutathione), GPx (glutathione peroxidase), ERα (oestrogen receptor alpha), and BDNF (brain-derived neurotrophic factor).^[15] An extensive analysis of the medicinal qualities and phytochemicals of *Asparagus racemosus* in the management of AD is provided in this review. We

also look at the new area of nanoformulations, emphasising how *Asparagus racemosus* chemicals can be encapsulated in nanoparticles to transform drug delivery and provide targeted and improved efficacy in the treatment of neurodegenerative disorders.

Methodology

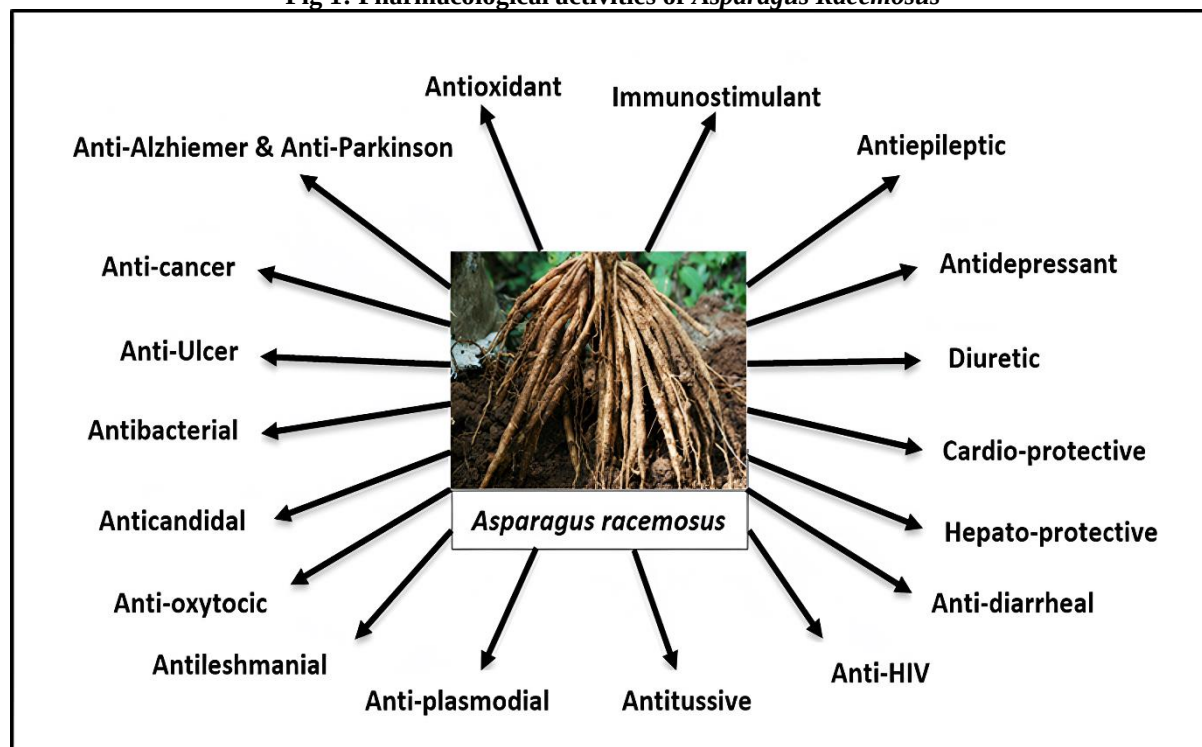
To locate relevant publications covering the time span from each database's launch date to December 20, 2024, a thorough search of Scopus, PubMed, and Science Direct was conducted. Terms such as Shatavari (conditions related to the nervous system); *Asparagus* (reactive oxygen species, oxidative stress, inflammation, Parkinson's disease, Alzheimer's disease); and *Asparagus racemosus* (phytochemicals, bioactive constituents, alkaloids, steroids, flavonoids, extracts), immunostimulant with antidepressant and antiepileptic activity were used were combined. Terms like dementia, cognitive impairment, neuroinflammation, stress, and anxiety were also merged with the preceding terms in PubMed, however the limit to keyword feature was used in Science Direct and Scopus. Only English-language studies were included.

Asparagus racemosus (Shatavari): Morphology and Multifaceted functions

Asparagus racemosus is an extraordinary Asparagaceae medicinal plant and found in India, Sri Lanka, and the Himalayas. Roots are mostly used in medical purposes and are known locally as 'Shatavari or Shatavar'.^[16] Up on the piedmont plains, at an elevation of 1300–1400 metres, this climbing plant, which can reach two metres in height, likes to settle in hard gravelly soils.^[17] White blossoms with short spikes adorn the tiny, uniform leaves that resemble pine needles. *Asparagus* is a genus

of plants that was newly relocated from the Liliaceae family to the afresh established Asparagaceae family.^[18] It was first described botanically in 1799. The demand for Shatavari is always increasing due to its numerous applications. Because to habitat destruction, forest loss, and aggressive harvesting, the herb is currently recorded as endangered in its natural environment.^[16] There are more than 300 species of asparagus worldwide, but only 22 of those have been identified in India. As a valuable medicinal plant, *Asparagus racemosus* is categorised as a "Rasayana," or plant therapy that enhances cellular resilience and vigour to support general health. India has long utilised the roots as a remedy for internal pain, fever, tumours, and as a tonic.^[19] The secondary metabolites identified by the phytochemical screening of the plant include alkaloids, flavonoids, steroids, essential oils, dihydrophenanthrene derivatives, and furan derivatives. Steroid saponins, the primary bioactive constituents of *Asparagus racemosus*, are primarily responsible for a variety of biological functions. The major bioactive components of Shatavari are Saponins, or Shatavarins I–IV, found in the roots.^[20] As per the Indian Pharmacopoeia, as measured in dried weight, *Asparagus racemosus* has a minimum of 0.1 percent Shatavarin IV. It tastes starchy at first, then a little bitter, and then sweet.^[21] The root of *Asparagus racemosus* has promising results (**Figure 1**) and is advised in cases of neuropathy, diarrhoea, inflammations, tumours, hepatopathy, bronchitis, cough, hyperacidity, and several infectious infections.^[17] It is also well known for boosting immunity and safeguarding important body organs, including the cardiovascular system, the nervous system, and other organs.^[22]

Fig 1: Pharmacological activities of *Asparagus Racemosus*



Phytochemical constituents present in *Asparagus racemosus*

Flavonoids, alkaloids, furan derivatives, dihydrophenanthrene derivatives, and volatile components are among the many bioactive and therapeutically relevant substances found in *Asparagus racemosus*.^[23] Steroid saponins make up the majority of these compounds (**Figure 2 & 3, Table 1**). In addition to being a rich source of sapogenins, this plant contains 29 steroidal saponins, of which have been identified. Five percent oil, 4.18 percent inorganic matter, 5.44 percent saponins, 17.93 percent crude fibre, 2.95 percent protein, and 52.89 percent carbohydrates are found in powdered root, according to the study.^[24] Phytochemicals and glucose, galactose, and modest levels of arabinose are among the polysaccharide components (MW, 2000 kDa) present in Shatavari root. There were, however, different relative percentages of monosaccharide present: 54% galactose, 28% the sugar glucose, 8% arabinose, 5% xylose, 4% rhamnose, and 1% others.^[25] A broad spectrum of organic classes, including alcohol, acids, aldehyde, ketone, hydrocarbon, ester and N-containing chemicals, are represented among the 55 essential oil constituents that are extracted from aerial parts. The principal ones are 4-[1-hydroxyethyl] benzaldehyde 6-10, 14-trimethyl pentadecanone, [E]-4-hexadecen-6-yne, borneol, hexanal, myrtanol, furfural, pinocarveol, camphor, decanoic acid, 2-ethylhexanol, undecanoic acid, perillaldehyde, and 6,10,14-trimethyl pentadecanone. Smaller levels of the remaining chemical classes, which included compounds containing S, N, and ester, were found. Borneol, myrtenol,^[97] and paraldehyde made up just three of the compounds that made up 45.09 percent of the composition.^[26] Among the components of essential oils, thymol and eugenol have strong fungicidal effect, preventing the growth of spores, whilst the other elements have mild antifungal action.^[8] Isolated and characterised 'Asparagamine A', a poly-cyclic alkaloid with exceptional anti-oxytotic activity and a distinct cage-type structure from *Asparagus racemosus*.^[27]

Eventually, a novel derivative of 9, 10-dihydrophenanthrene, called racemosol, was derived from the root Shatavari. Most phytoestrogens are classified as flavonoids, a broad class of substituted phenolic chemicals. According to research, isoflavones, prenylated flavonoids, coumestans are the three types of flavonoid phytoestrogens that have the strongest estrogenic effects.^[28] Saxena and Chourasia have provided the spectra files of a newly obtained isoflavone, 8-methoxy-5, 6, 4'trihydroxyisoflavone 7-O - β - d-glucopyranoside. Through autography-directed DPPH (α diphenyl- β picrylhydrazyl) isolations, a novel antioxidant molecule from *Asparagus racemosus* was identified: racemofuran. Asparagamine A and racemosol, two isoflavones, have been found to possess antioxidant properties.^[29] Leaves of the Shatavari plant contain aflatin and aflavonoid glycoside, also known as quercetin-3-glucuronide. Fully developed fruits of *Asparagus racemosus* included cyanidin-3-glucorhamnoside and cyanidin-3-galactoside, while fruits still in development contained quercetin, rutin, hyperoside, and steroidal saponin glycosides.^[8, 30] A class of steroidal saponins is Shatavari's primary bioactive component.^[31] Using a range of cutting-edge extraction techniques, phytoestrogen components, such as shatavarins I, II, III, IV, V, and VI-X (steroidal saponins), have been identified from the Shatavari root powder. Shatabavin I is the major glycoside that is connected to sarsasapogenin and contains 3-glucose and rhamnose moieties.^[32] Sarsasapogenin's glycoside derivative, shatavarin IV, has a saponin content of above 15%.^[33] The impact of steroidal saponins (Shatavarin IV, Immunoside) on Th1/Th2 immunity was investigated using the aqueous root extract of Shatavari.^[34] This plant also contains the following vitamins: B1, P, Fe, A, Ca, Mg, E, C, B2, folic acid. *Asparagus racemosus* has been found by Negi et al. 35 to have 165.03.2 mg/kg of zinc, indicating that it may be used as an herbal remedy to treat mental illnesses, growth issues, and hair loss.

Fig. 2: Phytochemicals present in *Asparagus racemosus*

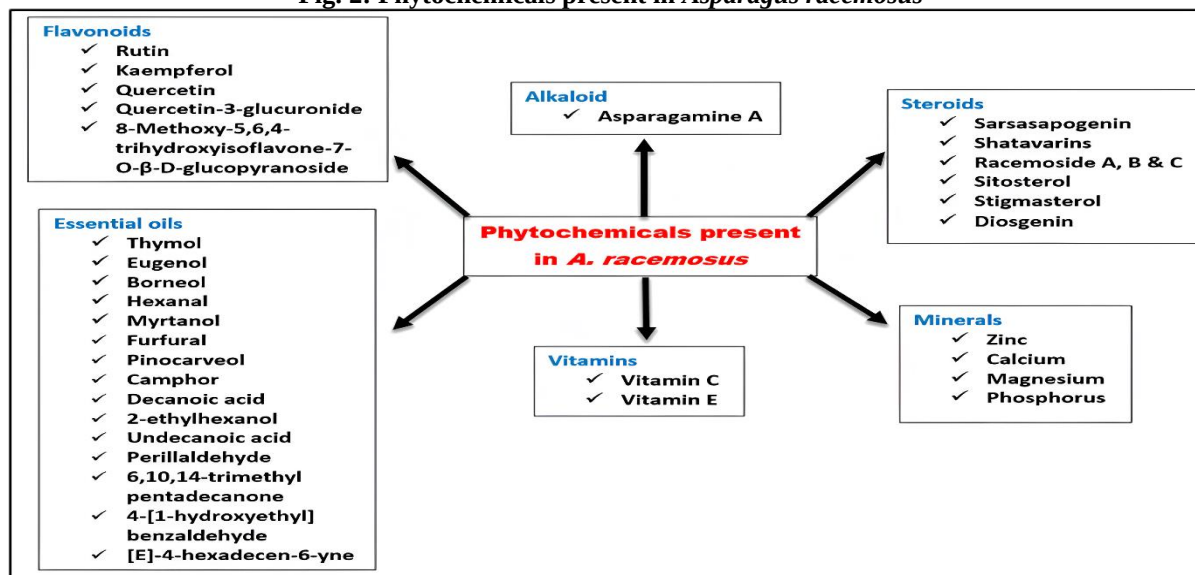


Fig. 3: Structure of Phytochemical constituents from *Asparagus racemosus*

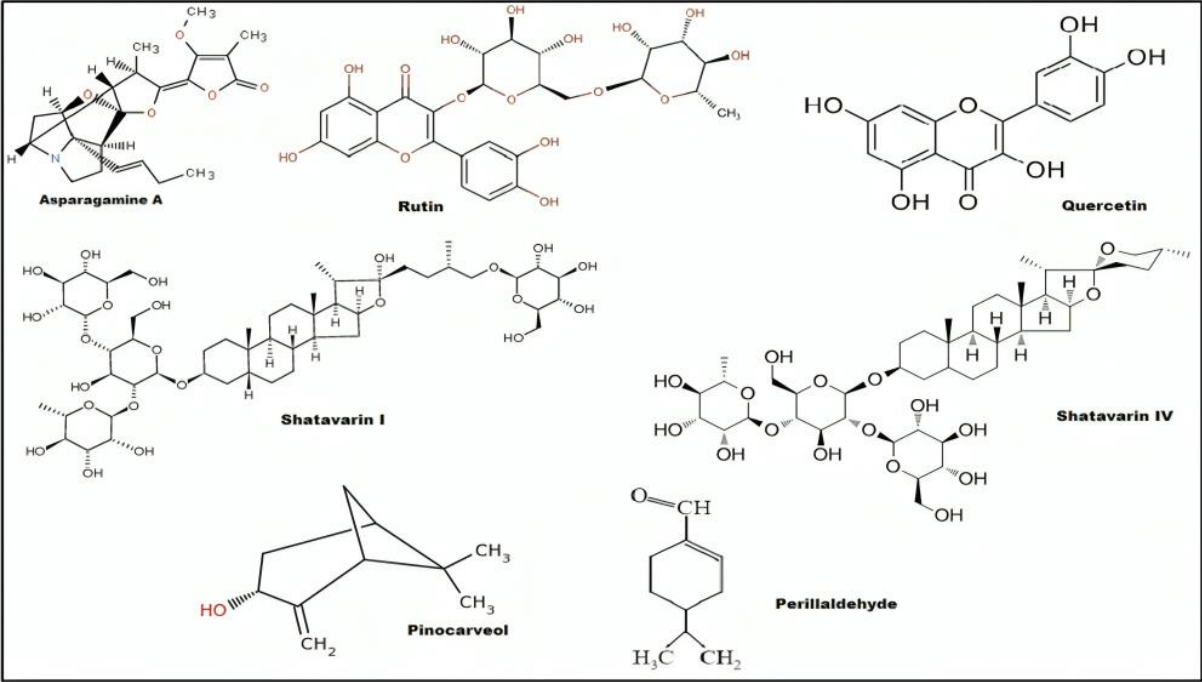


Table 1: The biological activities of the phytochemical components of the *Asparagus racemosus* plant.

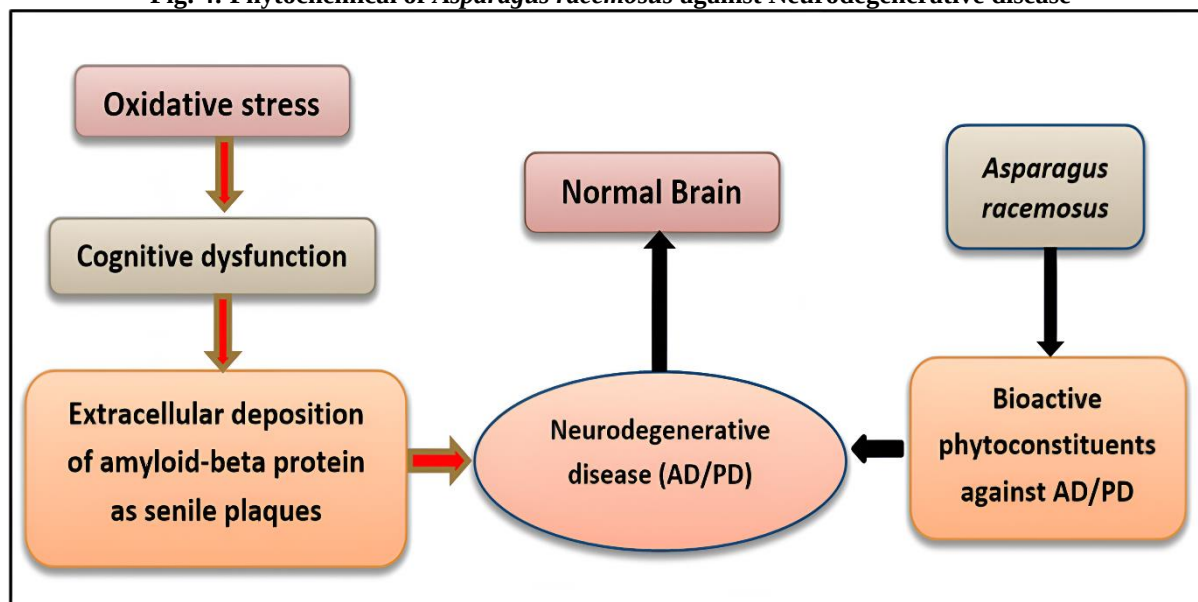
Sl. No.	Phytochemical constituent	Bioactive secondary metabolites	Biological activities	References
1	Alkaloid	Asparagamine A	Acts as an antioxidant & Immunomodulator	[30]
2	Flavonoid	Rutin, Kaempferol, Quercetin, Quercetin-3-glucuronide, 8-Methoxy-5,6,4-trihydroxyisoflavone-7-O- β -D-glucopyranoside	Neuroprotective effects, antioxidant activity	[8, 36]
3	Steroid	Sarsasapogenin, Shatavarins, Racemoside A, B & C, Sitosterol, Stigmasterol, Diosgenin	Improve memory dysfunction, Antioxidant	[37, 38]
4	Vitamins	Vitamin C Vitamin E	Neuroprotective and may improve cognition Power to inhibit neuronal death caused by inflammatory processes	[39] [40]
5	Minerals	Zn Ca, Mg, P	Cure mental disorders Antioxidant	[35] [8]
6	Essential oils	Thymol and eugenol Borneol, hexanal, myrtanol, furfural, pinocarveol, camphor, decanoic acid, 2-ethylhexanol, undecanoic acid, perillaldehyde, 6,10,14-trimethyl pentadecanone, 4-[1-hydroxyethyl] benzaldehyde, [E]-4-hexadecen-6-yne	High fungicidal activity Moderate antifungal activity	[8] [8]

Neurological degenerative diseases

EuMil is a Multicomponent herbal blend of standardised derivative that has been used as an anti-stress drug for a range of stress-related illnesses. Extract restored the normal levels of DA (dopamine), NA (norepinephrine), and 5HT (5-hydroxy tryptamine) during a prolonged

period of electroshock stress. A reduction in neuro-biochemical release in the brain is indicative of the preparation's efficacy in neural diseases.^[41] It has been noticed to be helpful in the controlling neurological conditions similar Parkinsonism and Alzheimer case. (Figure 4).

Fig. 4: Phytochemical of *Asparagus racemosus* against Neurodegenerative disease



Alzheimer's syndrome

Alzheimer is a world-wide health issue rendering to the World Health Organization. As the average age of the global residents rises, so does the rate of AD and it affects an estimated 47 million people worldwide, and researchers are still trying to figure out what causes it. Alzheimer's syndrome is the primary reason of dementia, a condition characterised by a loss of mental skills also independence in doing daily tasks. AD is a brain illness that degrades cells.^[42] The brains of AD patients exhibit two unique characteristics. The extracellular deposits of amyloid-beta ($A\beta$), a protein produced by the degradation of $A\beta$ precursors, are known as senile plaques. An abnormal deposit of $A\beta$ has also been discovered in blood vessels. Neurofibrillary tangles, or thick bundles of aberrant fibres formed by a modified form of the microtubular-associated protein, are originate in the cytoplasm of neurons among persons with AD.^[43,44]

Parkinson's disease

Parkinson's disease (PD) presents a multifaceted neurological condition featuring symptoms such as tremors, stiffness, bradykinesia, and, in later stages, postural instability for some patients. It stands as the second most common neurological disease afterward Alzheimer's disease (AD). While the loss of dopaminergic innervation in the nigrostriatal pathway is a key aspect of PD pathology, neurodegeneration isn't limited solely to nigral dopaminergic neurons; it also affects cells in other parts of the neural network.^[54]

Multifaceted actions of *Asparagus racemosus*

Asparagus racemosus is widely used for a variety of reasons, and its therapeutic value has long been recognized by Ayurveda. Diverse portions of this herbal plant, such as fruits, flowers, roots, greeneries leaf, and so on, have been shown to have natural therapeutic effects, but the roots and young shoots, in particular, have been found to have considerable medicinal properties.^[16] The extract of this plant has various phytoconstituents, each of which has a significant amount of medicinal properties are briefly described below:

Anti-Alzheimer's activity of *Asparagus racemosus*

Asparagus racemosus is recognized as a prominent nerve tonic within Ayurvedic medicine. It has been shown to have neuroprotective properties in copious studies.^[81,83] It has been investigated the result of an alcoholic extract of roots on kainic acid-mediated hippocampal and striatal neuron injury.^[15] The anesthetized rodent developed excitotoxic brain lesions after being given kainic acid. The study revealed damage to the striatal and hippocampal areas of the brain, along through elevated levels of lipid peroxidation and protein carbonyls, as well as decreased activity of glutathione peroxidase (GPx) and abridged glutathione (GSH). The researchers emphasized the importance of GSH as a vital antioxidant, acting as a scavenger for harmful chemicals and a substrate in GSH peroxidase-mediated protection against hydroperoxide damage, which could otherwise reach lethal stages in brain nerves. Mice treated with *Asparagus racemosus* extract showed enhanced GPx activity, lowered GSH levels, and reduced levels of

protein carbonyl and lipid peroxidation, indicating that the extract has antioxidant qualities that may help prevent oxidative damage brought on by free radicals.^[45] Rats undergoing ovariectomy were used in the study to examine the effects of an alcoholic fraction of *Asparagus racemosus* root on alterations in BDNF (brain-derived neurotrophic factor) levels and ER subtypes. The research discovered that the hippocampal and frontal cortex of ovariectomized rats had significantly lower amounts of BDNF and down-regulated oestrogen receptor- α and - β .^[46] Additionally,

these rats' treatment with 17 α -ethynylestradiol and *Asparagus racemosus* root extract increased the levels of BDNF and oestrogen receptor- α and - β in the frontal cortex and hippocampal regions. A possible connection between the neuroprotective properties of *Asparagus racemosus* root distillate in ovariectomized rodent and an upsurge in BDNF and oestrogen receptors is indicated. **(Table 2)** lists the antioxidant, anticholinergic, neuroprotective, and cognitive-enhancing qualities of the plant compounds.

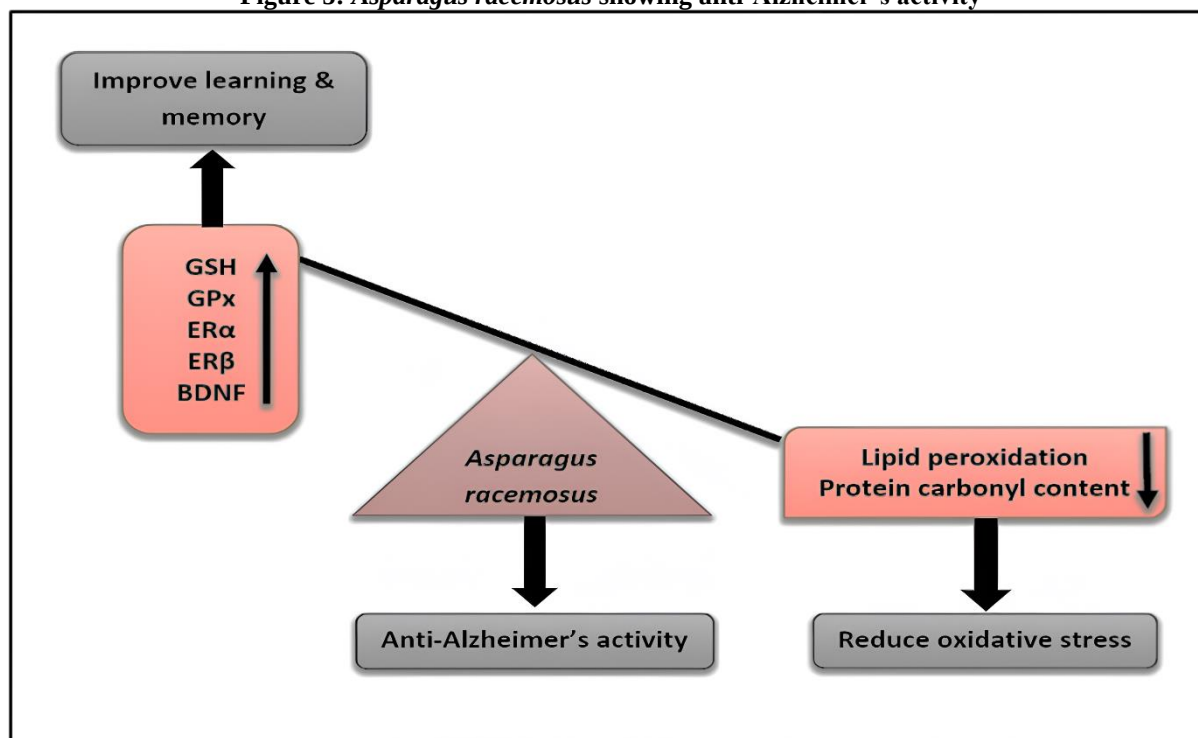
Table 2: Therapeutic properties of different extracts of *Asparagus racemosus*

Sl. No.	Extracts	Plant parts	Therapeutic effects	References
1	Acetone extract	Root	Neuroprotective effects Antioxidant activity	[15]
2	Aqueous extract	Root	Neuroprotective in hippocampus region	[47]
3	Ethanol extract	Root	Antioxidant activity Cholinergic properties Neuroprotective effects	[48]
4	Ethanol, hexane, propylene glycol extract	Root	Cognitive enhancing	[49]
5	Hydro-alcoholic extract	Root	Neuroprotective effects	[50]
6	Methanolic extract	Root	Antioxidant activity Neuroprotective & Cerebroprotective effects	[51]

Asparagus racemosus possesses several neuropharmacological actions that aid with memory and cognition (**Figure 5**). The neuroprotective properties of *Asparagus racemosus* root extract were investigated in 16 medical cases of a clinic with recognised stress-related illnesses, such as patients undergoing therapy for mental alterations and reminiscence deficits. A recall and memory retention test was also performed on these. When compared to those in the stress group, those who

were given extract had much higher test results.^[51] Females, in contrast to males, were found to have a lesser stress effect on short-term memory. As a result, oestrogen has the potential to have a significant impact on cognition.^[52] Moreover, oestrogen is widely recognised for its neuroprotective properties, which has prompted many investigators to explore novel approaches or breakthroughs in the prevention of neurodegenerative and cerebrovascular illnesses.^[53]

Figure 5: *Asparagus racemosus* showing anti-Alzheimer's activity



Anti-Parkinson's activity of *Asparagus racemosus*

Shatavarin IV reduces oxidative stress by reducing intracellular ROS and oxidative damage, such as protein carbonylation, while simultaneously promoting longevity.^[55] SIV also raised the mRNA expression of stress-sensitive genes such as sod-1, 2 & 3, gst-4 & 7, and ctl-2, implying that it has antioxidant properties that may help to reduce oxidative stress and promote longevity. SIV also helped with PD symptoms by lowering alpha-synuclein aggregation, lipid buildup, and increasing dopamine levels.^[56, 57]

Antioxidant activity of *Asparagus racemosus*

Antioxidants play a crucial role in eliminating free radicals that are produced within the body. Even though our bodies have antioxidants to protect us, it's always a good idea to consume an antioxidant-rich diet to strengthen our immune systems.^[58] Researchers examined the protective effects of *Asparagus racemosus* crude extract and purified aqueous fraction on rat liver mitochondria's membranes against injury from free radicals produced by gamma rays. The evaluation of lipid peroxidation was done by generating lipid hydroperoxides and reactive compounds with thiobarbituric acid.^[59] By blocking protein oxidation, lipid peroxidation, a decrease in protein thiol levels, and a decline of antioxidant enzyme superoxide dismutase, the extract demonstrated antioxidant qualities that avoided oxidative injury. When compared to the crude extract, the purified aqueous fraction containing polysaccharides was found to be a powerful antioxidant. The filtered fraction more efficiently suppressed lipid peroxidation than the raw extract's antioxidant activity did at reducing protein oxidation.^[60,61]

Anti-inflammatory activity of *Asparagus racemosus*

The body's natural defense against infection is inflammation. Inflammation must be minimized before beginning therapy for any form of illness to treat patients more effectively and lessen pain. While synthetic anti-inflammatory drugs are widely available, herbal extracts are always a safer option because they don't harm humans. Studies have shown that extraction of the roots of *Asparagus racemosus* have anti-inflammatory qualities. The root distillate reduces skin thickness, myeloperoxidase activity, and the production of pro-inflammatory cytokines. Furthermore, histological evidence supporting the anti-inflammatory activity was found.^[15]

***Asparagus racemosus* as an Immunostimulant**

The body's immune system weakens as a result of a class of illnesses known as immunodeficiency diseases, rendering it less capable of repelling outside invaders. As a result, an immunocompromised patient may experience more infections, which will also typically be more severe and long-lasting than usual. In order to examine the immunity of both normal and cyclosporine-

A administered immunosuppressed mice, isolated polyhydroxylated steroidal saponin acids were employed. According to the findings, the substance is a strong immune system stimulator. The steroidal saponins shatavaroside A and shatavaroside B were extracted using the alcoholic extract of *Asparagus racemosus*.^[62] The immunomodulatory action of these substances was assessed by means of a polymorphonuclear leukocyte functional test, in addition to few additional specific assays such as nitrous oxide, nitroblue tetrazolium and chemi-luminescence assays. Researchers found that the steroidal saponins that were extracted were effective at nano concentrations of 5 ng/mL and were a strong immunostimulant.^[63, 64]

Antidepressant activity of *Asparagus racemosus*

Depression is by far the most frequent psychological disorder. Synthetic medications used to treat depression frequently cause a variety of adverse effects. Furthermore, maximum of the medications are only successful for a small number of the patients.^[65] Herb extracts with antidepressant properties can help patients cope with the side effects of synthetic medications. Different herbal concoctions have been utilized to treat psychiatric problems since ancient times. Shatavari's antidepressant efficacy has been studied in cell line and animal model in numerous investigations.^[66] The antidepressant properties of the methanolic extract on rats were investigated using the forced swim test (FST) and the learned helplessness test (LH). According to the findings, the extract enhanced the LH's avoidance response and reduced the FST's rigidity.^[67] Mice were tested for antidepressant activity. The methanolic extract significantly shortened motionlessness periods in both the TST and FST, suggesting a strong antidepressant effect and emphasising that the extracts' effectiveness was on par with that of imipramine and fluoxetine, the study's reference medications.^[68] In mice, the methanolic extract decreased the levels of MAO-A and MAO-B activity in the brain. The methanolic extract was found to have antidepressant efficacy; this was probably due to interactions with the dopaminergic, adrenergic, serotonergic, and GABAergic systems as well as inhibition of MAO-A and MAO-B.^[63]

Antiepileptic activity of *Asparagus racemosus*

The anticonvulsant efficacy of various extracts was tested in rat models of seizures caused by maximum electroshock and pentylenetetrazole. Reductions in the duration of the stupor phase, clones, and hind limb extension suggested a significant anticonvulsant effect from the methanolic extract in the test. Pentylenetetrazole-induced tonic clonic seizures in the groups given methanolic and aqueous extracts were delayed in starting, which can be explained by the GABAergic nervous system.^[69] Other therapeutic properties are recapitulated in the tabular form as given below (**Table 3**).

Table 3: Other therapeutic activities of *Asparagus racemosus*

Sl No.	Therapeutic properties	Activity	References
1	Anticancer activity	Prevents the UOK 146 renal cancer cell line from growing	[70]
2	Antiurolithiatic activity	Declined urea levels, creatinine, phosphorus, also calcium in the blood	[71]
3	Anti-stress activity	In rodent macrophage cells, there's inhibition of nitric oxide production and pro-inflammatory cytokines like interleukin 1 β and tumor necrosis factor α .	[72]
4	Antihepatotoxic activity	Reduce elevated levels of alanine transaminase, aspartate transaminase, and alkaline phosphatase in rats with CCl ₄ -induced liver damage.	[73]
5	Antiulcerogenic activity	In rats treated with indomethacin for gastric ulcerative rats, effective in decreasing gastric ulcer.	[74]
6	Antibacterial activity	The ability of the plant extract to prevent bacterial pathogen development.	[75]
7	Hypoglycemic activity	Markedly elevated insulin release levels and lowered serum glucose levels	[76]
8	Adaptogenic activity	Cisplatin was shown to have both reversible and adjustable effects on gastric emptying and intestinal hypermotility.	[8]
9	Aphrodisiac activity	Differences in latency times during mounting, ejaculation, post-ejaculation, and intromission reflect significant variations in animal sexual behavior.	[77]
10	Antiamnesic activity	Scopolamine and sodium nitrite reversed the increase in transfer latency on an elevated plus maze, indicating anti-amnesic effects.	[78]
11	Cardio-protective	Potential components reduce lipid peroxidation and lower levels of LDL, VLDL, and triacylglycerols in the blood.	[66]
12	Antitussive activity	Demonstrated significant antitussive effects against sulfur dioxide-induced cough in mice.	[79]
13	Antiprotozoal activity	Root extract showed inhibition of <i>Eintamoeba histolytica</i> growth in vitro.	[17]
14	Antileishmanial activity	There was a dose-dependent elimination of phagocytosed amastigotes, and treated <i>L. donovani</i> promastigotes showed signs of programmed cell death.	[80]
15	Antiplasmodial activity	Dose-dependent inhibition of chloroquine-resistant <i>Plasmodium falciparum</i> strain.	[81]

Nanoformulation in Therapeutic Management of Neurodegenerative Diseases

Neurodegenerative diseases pose a substantial and growing challenge to global healthcare, necessitating innovative therapeutic strategies. The field of nanoformulation is changing as it relates to treating diseases of the brain. The convergence of nanotechnology and neuroscience has spurred a paradigm shift, offering promising avenues for improved drug delivery, enhanced bioavailability, and targeted therapeutic interventions.^[84]

In Cognitive decline disorders like dementia, Parkinsonism, and Huntington the structure and function of the nervous system gradually decline. Conventional therapeutic modalities encounter significant obstacles, including restricted medication delivery via the blood-brain barrier (BBB) and inadequate targeting of particular brain areas.^[84] Nanoformulation, leveraging nanotechnology principles, has emerged as a transformative strategy to overcome these barriers and revolutionize therapeutic management. Nanoformulations, such as liposomes, polymeric nanoparticles, and dendrimers, exhibit unique physicochemical properties that facilitate their interaction with biological systems. Notably, these nanoparticles can traverse the BBB, a critical obstacle in delivering therapeutic agents to the brain. Receptor-mediated endocytosis and surface modifications enable efficient entry into the central nervous system,

enhancing drug concentration at target sites.^[86] One of the hallmarks of nanoformulation is its capability for targeted drug delivery. By encapsulating therapeutic agents within nanoparticles, drugs can be selectively released at specific neuronal or glial cells, minimizing off-target effects and reducing systemic toxicity. Additionally, nanoformulations provide sustained release profiles, ensuring prolonged therapeutic effects and potentially mitigating the need for frequent administrations.^[84]

The diverse nanoformulation strategies employed in neurodegenerative diseases. This includes the application of polymers, solid lipid carriers, liposomes, metal-based carriers, and antibody-tethered nanoparticles. Nanoformulations offer neuroprotective effects by enhancing antioxidant defenses, reducing oxidative stress, and modulating inflammatory responses. Furthermore, they hold promise for disease-modifying interventions by facilitating the targeted delivery of therapeutic agents designed to alter the course of neurodegenerative processes.^[84,86] Considering the impact of functional modifications on systemic administration is crucial when designing nanoparticles (NPs) for biomedical applications.^[84] In recent decades, there has been a significant rise in the development of therapeutic nanomedicine in neuroscience, holding potential for improving human health and fostering interdisciplinary research. Notably, previous studies indicate that nanoparticles, utilizing

receptor-mediated endocytosis, can traverse the blood-brain barrier, benefiting from T80 encapsulation that attracts apolipoproteins and mimics lipoprotein particles.^[84]

Research has shown that rivastigmine, an anti-Alzheimer's medication, is more readily absorbed by AD rats when it is bound to poly (n-butyl cyanoacrylate) nanoparticles smeared with 1% T80 for instance opposed to when the drug is administered free via intravenous injection.^[87] Similar positive outcomes are observed with the administration of rivastigmine and tacrine using chitosan-based nanoparticles coated with 1% T80 in rats, indicating their potential efficacy in AD treatment. Strategies such as conjugation with hydrophilic surfactants like polyethylene glycol (PEG) or modification with a neutral surface charge are employed to prevent exclusion through the reticuloendothelial system and facilitate BBB transport.^[88] Various natural derived compounds containing nanoparticles and nanocarriers have been demonstrated in animal models to have minimal

cytotoxicity, offering novel avenues for effective AD-targeted therapies. Various nanotechnology-based strategies are employed for the management of neurological conditions like Alzheimer's disease, Parkinson's disease, epilepsy, and other associated disorders. Nanoparticles come in various forms, including metal-based carriers, lipid carriers, polymer-based nanoparticles, lipoprotein-based nanoparticles, inorganic nanoparticles, magnetic nanoparticles, curcumin-loaded nanoparticles, cubosomes, nanoparticle conjugates, antibody-tethered nanoparticles, dendrimers, emulsions, and nanocomposites. These diverse types offer a range of options for targeting specific aspects of neuroprotection and neuroregeneration, presenting promising avenues for therapeutic intervention in debilitating conditions.^[96] These advancements present promising opportunities for developing targeted and effective therapies tailored to address the complexities of Alzheimer's disease (**Table 4**).

Table: 4- Nanoparticles in Neurodegenerative Diseases: Effects and References

Nanoparticle Type	Disease	Effects	Reference
Poly(carboxybetaine methacrylate) (pCB)	Alzheimer's Disease (AD)	Improved pharmacokinetics of Curcumin (Cur), Inhibition of A β 42 fibrillation	[88]
Lipid-based NPs	Parkinson's Disease (PD)	Increased bioavailability and reduced aggregation of alpha-synuclein fibrils	[89]
Liposomes	Alzheimer's Disease (AD)	Increased affinity for A β 1-42 fibrils and improved pharmacokinetics quality	[90]
Polyethyleneglycol-polylactide (PEG-PLA)	Alzheimer's Disease (AD)	Increased Curcumin (Cur) bioavailability	[91]
Chitosan Solid Lipid Nanoparticles (CSLNs)	Huntington's Disease (HD)	Decreased mitochondrial swelling, ROS, lipid peroxidation, and protein carbonyl levels.	[92-94]
Solid Lipid Nanoparticles (SLNs)	Alzheimer's Disease (AD)	Recuperation from aluminium chloride's harmful neurological consequences.	[92-94]
Nanoparticles conjugated with trimethylated chitosan and coenzyme Q10 6-coumarin, encapsulated in PLGA.	Alzheimer's Disease (AD)	Enhanced bioavailability, reduced senile plaques, and improved memory impairment.	[92-94]
Nanoparticles made of lactoferrin-conjugated N-trimethylated chitosan (Lf-TMC NPs) containing HupA.	Alzheimer's Disease (AD)	Sufficient sustained-release, higher bioavailability, and better targeting capacity.	[92]
Berberine coated multi-walled carbon nanotubes (MWCNTs) with phospholipid and polysorbate.	Alzheimer's Disease (AD)	Reduced AChEI activity and corrected memory impairment	[93]
Hesperetin Nanocrystal	Alzheimer's Disease (AD)	Enhanced activity of antioxidant enzymes and improved detection of memory consolidation.	[94]
Nanospheres based on Vitamin E and polyethylene glycol (PEG).	Alzheimer's Disease (AD)	Enhanced vitamin E antioxidant effectiveness	[94]
Polymeric nanoparticles containing retinoic acid (RA).	Parkinson's Disease (PD)	Noteworthy benefit to dopaminergic neurons' neuroprotection	[92-94]
Chrysin SLNs	Alzheimer's Disease (AD)	Enhanced scavenging of free radicals, reduced neuronal damage, and increased oral bioavailability	[92-94]
Nanoparticles comprising sialic acid, peptide-B6, and selenium.	Alzheimer's Disease (AD)	prevented A β aggregation and disintegrated A β fibrils	[92-94]
Cysteine Selenium nanoparticles	Alzheimer's Disease (AD)	Decreased ROS, prevented A β aggregation	[92-97]

Future Prospectives

In recent years, the integration of traditional medicinal plants, such as *Asparagus racemosus* (shatavari), with modern nanotechnology has emerged as a promising avenue for addressing neurodegenerative diseases. Shatavari, a key remedial herb in Ayurveda and Himalayan traditional medicine, boasts a rich profile of phytoconstituents, including steroidal saponins, polycyclic alkaloids, flavonoids, and trace minerals. The therapeutic potential of these compounds has been extensively explored, particularly in the context of neuroprotection. One significant challenge in utilizing the active components of shatavari in the treatment of neurological disorders, lies in their limited permeability through the blood-brain barrier. To overcome this obstacle, nanoformulations of shatavari have been proposed as a potential solution. Nano drug delivery systems offer the advantage of enhanced bioavailability and improved penetration of therapeutic agents into the brain, thereby enhancing their efficacy in managing neurodegenerative conditions. The antioxidative potential of shatavari root has been demonstrated to prevent reactive oxygen species (ROS)-mediated oxidative damage. This, coupled with its traditional use and the identified therapeutic compounds, positions shatavari as a promising candidate for neuroprotective interventions. However, it is crucial to emphasize that rigorous clinical validation is imperative before shatavari can be incorporated into mainstream neuroprotective medicine. Efforts to integrate traditional herbal knowledge with modern pharmacology present exciting possibilities for the development of personalized and effective therapies. Collaborative research endeavors between traditional medicine and contemporary nanotechnology may unlock transformative interventions in neurotherapeutics. The synergy of *Asparagus racemosus* and Shatavari within nanoformulations not only aligns with Ayurvedic principles but also serves as a bridge between traditional wisdom and cutting-edge technology.

Conclusion: the exploration of *Asparagus racemosus* and Shatavari nanoformulations holds promise as a holistic and Ayurvedic-inspired approach to addressing neurodegenerative diseases. This convergence of traditional herbal remedies and advanced nanotechnology provides a foundation for innovative strategies in neurotherapeutics, offering potential breakthroughs in the management and treatment of these challenging conditions.

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