

Ashwagandha and Health Attributes: A Mini Review

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Abstract

Withania somnifera (WS) is commonly known as Ashwagandha, Indian ginseng and winter cherry is an important plant in Ayurvedic medicinal system. It is also known as Medhya Rasayana (boost learning and memory) and Rasayana (enhance endurance, prevents aging, imparts resistance, and ameliorate immune system). WS shows possess pharmacological effects such as antioxidant, immunomodulatory, and anti-inflammatory. In view of these facts, the present review article highlights role of WS in neurodegenerative disease and related issues.

Introduction

The plants lead significantly diverse lifestyle. Approximately 10% of all vascular plant species have medicinal use every component of the plant is beneficial to all living organism in the universe. These plants are crucial to protecting human health since they contain numerous types of useful treatments [1] Many plant species that are employed in remedies along with certain of that possess therapeutic properties are included in the category of medicinal plants. Medicinal plants known as excellent resources for the synthesis and discovery of novel drugs. [2] Plants have been used for medicinal reasons for over five centuries, as indicated by their use in Indian, Egyptian, Chinese, Greek, and roman culture to cure ailments and revitalize the human body. [3] Application of natural treatment different kinds of physical illness continues to grow at an alarming rate on a global scale. Natural cures are rapidly gaining popularity and public attention in nations that are developed as well as underdeveloped. The majority of the population that lives in poor nations get their healthcare primarily from herbal medical remedies. The majority of the population that lives in poor nations get their healthcare primarily from herbal medical remedies. [1]

In India, medicinal value is widely utilized by all demographic groups, as processed pharmaceutical industry products as well as traditional medicines in a variety of native medical systems including Siddha, Unani and Ayurveda. [4] Indian cuisine makes extensive use of an extensive range of herbs and spices, including fenugreek, fennel, ajwain, bay leaf, hing, clove, cardamom, cinnamon, cumin, and turmeric. All of them are used in ayurvedic medicine, whether as drugs or diets. [5]

Herbal treatments such as ashwagandha and brahmi can boost immunity, promote nutrition, heal body cells, and increase vitality. Ashwagandha (*Withania somnifera*) a tiny to medium sized bushes that grows in india's harsh terrain. It's an aphrodisiac, anabolic, and nervine tonic. [6] Additionally, rheumatism and general weakness are treated with it.

This review's plot explores the latest research and offers a thorough summary of what is currently known about the possible applications of Ashwagandha as well as about the recent studies. Ashwagandha (*family. Solanaceae*) is most generally referred as "Indian Ginseng" and "Indian Winter cherry." Due to its extensive range of health advantages as shown in fig.1, it has been used as a Rasayana for millennia and is regarded as one of the significant Ayurvedic herb in the Indian traditional medicine system.[6]

This is a part of numerous formulas suggested for a variety of musculoskeletal disorders (like arthritis and rheumatism), In addition, for overall use to stimulate energy, improve overall longevity and health, and diseases in pregnant women, the elderly, and sportsmen. Several pharmacological research have been performed to investigate the qualities of ashwagandha and justify its usage as a diverse therapeutic aid.

Neurological illnesses were found to benefit from it. It has been demonstrated to encourage dendritic development and to have a GABA mimic action. It enhances energy levels and mitochondrial health and has anxiolytic properties. It functions as an anti-arthritic and anti-inflammatory drug.

Ashwagandha is rich in antioxidants, hemopoietic, anti-inflammatory, anticancer, antistress, and rejuvenating qualities. Additionally, it seems to have a favorable impact on the CNS (central nervous system), the endocrine system, and the heart. [7] Indian Pharmacopoeia-1985 mentions *W. somnifera* as a recognized medication. Both the Ayurvedic and Unani medical traditions make substantial use of the plant's roots. According to reports, 0.13–0.31% of the following substances are found in roots: starch, volatile oils, reducing sugars, amino acids, steroids and glycosides.[6]

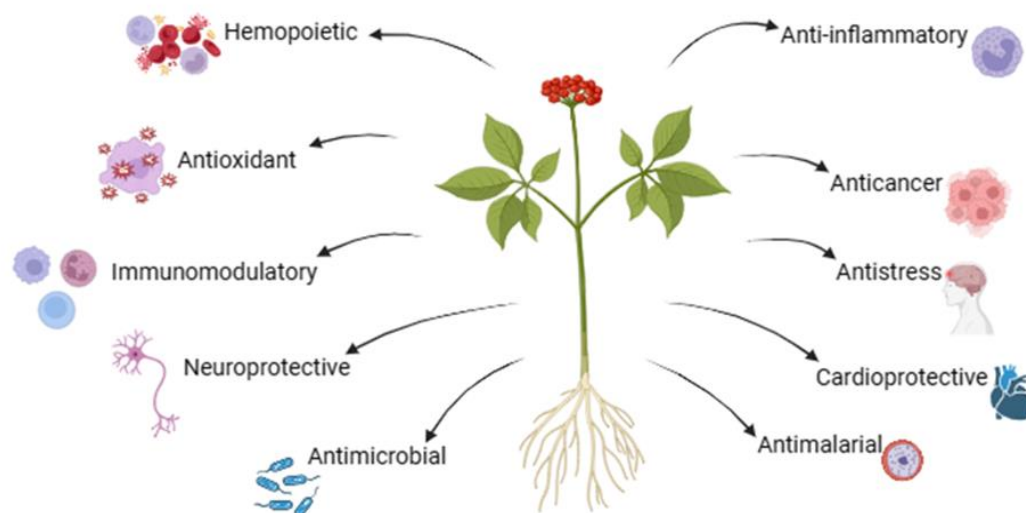


Fig.1 Therapeutic properties of Ashwagandha

Chemical composition of Ashwagandha

Ashwagandha contains withanolides, withaferins (steroidal lactones), saponins, and alkaloids (1-(2-Piperidiny)-2-propanone, anaferine, cuseohygrine, anahygrine, etc.) that are biologically active chemical components as mentioned in fig,2 Depending on where the extract is coming from (root or leaves, for example), Ashwagandha has different amounts of active components. [6] In addition to enhancing cell-mediated immunity, Ashwagandha root has strong anti-inflammatory and antioxidant properties that protects cells from harm caused by mediators of inflammation and free radicals. These actions enhance the body's resistance against chronic illnesses. [8] Ashwagandha is mostly composed of alkaloids and steroidal lactones. The phytochemical makeup of the plants varies according to its geographical location. Withanine is important alkaloid. In the Indian variant 13 alkaloids test positive with Dragendroff's reagent have been identified. Withaferin A is primary active withanolides derived from Ashwagandha, 24-dienolide. Withanolides are distinguished by a 6-membered aromatic lactone ring linked to a C28 steroidal nucleus and a C9 side chain. [9]

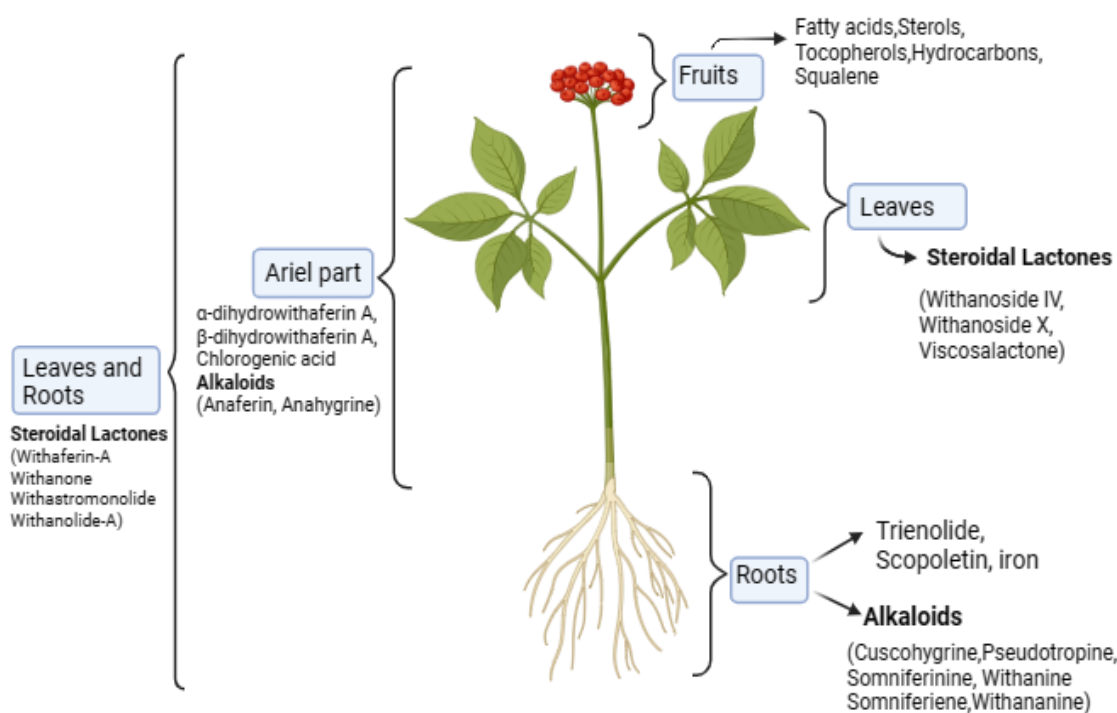


Fig.2 Distribution of chemical constituent of Ashwagandha

Prior studies on phytochemicals have revealed the Key phytochemicals derived from various plant parts include, alkaloids, steroidal lactones saponins, tannins, flavonoids saponins, phenolic compounds, starch, carbohydrates, sitoindosides, withanolides, β -sitosterol, anahygrine, anaferine, β -sitosterol, cysteine, chlorogenic acid, cuscohygrine, withanine, pseudotropine, withananine, scopoletin, somniferinine, somniferiene, 14- α -hydroxywithanone, tropanol, and 6,7 β -Epoxywithanon. Historically, the roots, stems, bark, leaves, flowers of plants have been utilized to treat a variety of ailments, such as sexual dysfunction, discomfort, liver problems, fever, respiratory infections, wounds, ulcers, and heart problems [10]

Medicinal effects of phytoconstituents from Ashwagandha

Anti-Inflammatory Effect

White blood cell activation and the production of cytokines and their release are two of the many phases that make up the inflammatory response. In several pharmacological in-vivo models of inflammation caused by pharmaceuticals, such as cotton pellet inflammation, adjuvant-induced arthritis condition, and induction of inflammation by carrageenan, It has been demonstrated that ashwagandha possesses anti-inflammatory qualities. Granuloma tissue's glycosaminoglycan content was lower following hydrocortisone therapy. In adjuvant-induced arthritic rat models, WA (withaferin A), the physiologically active steroidal lactone present in leaves extraction, exhibits effects comparable to hydrocortisone sodium succinate therapy. Its ability to stabilize the activity of lysosomal enzymes is another potential method of action. [9] The withaferin-A inhibited I κ B (I κ b) kinase activation and phosphorylation, which in turn impeded the translocation of Nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B). NF κ B-DNA binding, and transcription [11]. Consequently, by altering the amount of inflammatory signalling molecules and catalyst despite having any adverse effects, the botanical components of ashwagandha may be a potential anti-inflammatory and anti-arthritic drug in comparison to other anti-inflammatory and non-steroidal treatments. [9]

Antioxidant effect

Antioxidants are essential for defending against reactive species of oxygen and radicals that are free. harm

to nerves by free radicals may be a factor in both the normal aging process and neurodegenerative disorders of the brain like Parkinson's schizophrenia, and epilepsy. The active compounds of ashwagandha, glycowithanolides (withaferin A) and sitoindosides VII-X, can modify the activity of key enzymes involved in free radical scavenging, including GPX (glutathione peroxidase), CAT (catalase), and SOD (superoxide dismutase). This effect has been observed in the frontal cortex and striatum regions of the rat brain. [12] Lipid peroxidation (LPO) and SOD activities were reported to be normalized by glycowithanolides. It can increase the activity of GPX and CAT in the striatum and frontal cortex of chronic foot shock-stress-induced rat brain models. [13] The ingestion of Ashwagandha's root extract has recovered the lower glutathione levels and dramatically decreased LPO. [14]

The antioxidant properties of Ashwagandha's active principles may help to explain, at least in part, the effects that the plant has been shown to have on stress reduction, cognitive function, inflammation, and aging in both clinical and experimental settings. [14]

Anti-cancer and apoptotic effect

Severe side effects from radiation and chemotherapy include baldness, nausea, vomiting, pulmonary fibrosis, ulceration of the mucosa, toxicity to the liver and heart, and more. Medicines that can get rid of these adverse effects can be very helpful for treating cancer. [14] The leukemic THP-1 cell (monocytic cell) survival and PBMC (peripheral blood mononuclear cells) can be affected by aqueous root extracts of Ashwagandha. These extracts can also boost caspase and oxidant scavenging activities while lowering levels of GSH (glutathione), TNF- α (tumour necrosis factor-alpha), and IL-10 (interleukin) [14]. In the leukemic murine mouse model, withanolide D is shown to reduce the expression of anti-apoptotic genes Telomerase Reverse Transcriptase.

(TERT), Puma and Bcl-2 (B-cell lymphoma 2). [14]. A new peptide fractions derived from Ashwagandha roots could potentially induce mitochondria-mediated programmed cell death in cells of triple-negative breast cancer. [14]

Immunomodulatory effect

The immune system defends the body against numerous malignancies and invasive infections. An essential

obstacle in managing of infectious diseases, autoimmune diseases, tumor immunity, and organ transplantation has been immune system modulation. The immune-regulating qualities of Ashwagandha are well-established and have been utilized in "rasayana" preparations, which strengthen the body's defenses against illness without causing adverse consequences. [9]

In Swiss albino mice, Ashwagandha extracts significantly increased leukocytes and thrombocytes counts, reduced ovalbumin-induced edema, and prevented immunoglobulin E-mediated anaphylaxis. Additionally, they prevented the potentiation of the Delayed-type hypersensitivity (DTH) reaction induced by cyclophosphamide. [15]

Antibacterial effect

Antimicrobial compounds can be found in abundance in medicinal plants. Antibacterial activity of Ashwagandha extracts is demonstrated opposed to Gram-negative and Gram-positive microorganisms. [16]

The plant's methanolic leaf extract shown notable antibacterial efficacy as an opposition to Gram-positive isolates of *Enterococcus sp.* derived from Methicillin-resistant *Staphylococcus aureus* and pus samples (MRSA). [17]

Furthermore, it demonstrated possible antibacterial activity against *Proteus mirabilis*, *salmonella typhi*, *E. Coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Citrobacter freundii*, which are Gram-negative bacteria. [18]

Such reports on the antibacterial properties of Ashwagandha against human infections 100 have been published recently. Because of their effectiveness and safety, Ashwagandha extracts are a good option for both conventional and combination therapy. [9]

Antimalarial effect

When the rodent malaria parasite *Plasmodium berghei* was When Ashwagandha extracts were intraperitoneally injected into Swiss albino mice for an in vivo study, There was a substantial drop in the outcomes in 2:13 PMParasitaemia percentages compared to the controls. [19]

Additionally, When coupled with chloroquine, ashwagandha (root bark) demonstrated statistically important and enhanced suppressions towards chloroquine-resistant PbNK65 (*Plasmodium berghei* NK65) in mice. [20]

Cardio-protective effect

Polyherbal mixtures with Ashwagandha offer cardio-protection for cardiovascular system towards damage induced by doxorubicin in animals. They activate a transcription factor called Nrf2 (nuclear factor-erythroid-2), that triggers enzymes for phase-II detoxification and inhibits programmed cell death in HL-1 cardiomyocytes in a Nrf2-dependent manner [21–25]. Additionally, Ashwagandha treatment not only reduces myopathologic heart degeneration and TUNEL-positive (apoptotic) cells in rat models but also significantly reestablishes the balance between antioxidants and myocardial oxidants, as well as pro- and anti-apoptotic factors in Wistar rats [26–29].

Neuroprotective effect

The increasing loss of a neuron's composition or purpose, such as neuron's death, is known as neurodegeneration. Researchers have demonstrated that Ashwagandha stimulates the regeneration of neuronal cell dendrites, that allow neurons to connect with one another. Thus, Ashwagandha can exhibit the regeneration of healthy and damaged nerve cells and mend the changes in neural tissue brought on by memory loss, suggesting that the herbs may maintain the health of each ill and healthy brain cells.. [30-31]

In experimental mice, withanolide included in the leaf extract can shield glial and neuronal cells from the toxicity caused by scopolamine. A number of markers for neuronal cells, consist GAP-43 (growth-associated protein 43), PSD-95 (postsynaptic density protein 95), neurofilament (NF)-H, and MAP-2 (microtubule-associated protein 2). Ashwagandha extracts are reported to drastically lower oxidative stress markers of DNA and the glial cell indicators (glial fibrillary acidic protein, or GFAP).

While withanolides VI and IV expanded the dendrites, withanolide A typically lengthened the dendrites and axons. But rat Neurons in the cortex injured by amyloid-b (Ab) were able to regenerate synapses and produce new axons and dendrites thanks to withanoside-IV. [32-33] It has been shown that the plant's root extracts are extremely effective in treating various neurological disorders such as anxiety, depression, senile dementia, cognitive impairment, and a variety of other neurological conditions, such as (Alzheimer's and Parkinson's disease). Due to their superior lipid peroxidation and inhibitory characteristics, glycowithanolides, one of the extract's many ingredients, are primarily responsible for its neuroprotective activity. Subsequent research has confirmed that sitoindosides (VII–X) and withanolides have the ability to increase the activities of glutathione peroxidase and catalase. [34]

The extract demonstrated remarkable potential in reviving nerve cells and preventing lipid peroxidation. By repairing synapses and growing new neurites, it may be able to restore severely injured neurons. [35]

Ashwagandha demonstrated the capacity to counteract neuropathogenesis triggered by β -amyloid. The plant extract's withanosides and withanolides have the potential to displace and lessen the proliferation of $A\beta$ (β -amyloid peptides) and oligomers in the brain. [36-37]

After being treated with Ashwagandha, the activity of some neural receptors were increased. These included the dopaminergic D2 receptor, LRP, or low-density lipoprotein receptor-related protein, and neprilysin, a protease that breaks down β -amyloid peptide. [38]

In male Wistar rats, an oral dosage of Ashwagandha leaf water extract reduced lipopolysachhride (LPS-mediated neurotoxicity and cognitive impairment. [45]

Anti-Parkinson's disease (PD) activity

PD (Parkinson's disease) is one of disorders which comes under the motor system disorders that arise from the death of brain cells that produce dopamine. Ashwagandha extract was tested using 6-hydroxydopamine (6-OHDA) rat models, and the results indicated anti-parkinsonian properties. Oxidant stress is the mechanism by which 6 OHDA produces its harmful effects. This particular study assessed the level of LPO, reduced activities of glutathione-S-transferase, GSH content, GPX, GSR (glutathione reductase), CAT, SOD, and dopaminergic D2 receptor binding, and tyrosine hydroxylase expression and catecholamine content, in rats three weeks following 6-OHDA injections. [9] [40][41]

Postural irregularities (stooped posture), resting tremors, and signs such as an engorged gait, akinesia, and bradykinesia are characteristics of PD. [42]

The disease's pathological characteristics include Downie bodies in the neurons that survive and the loss of neurons in the nigrostriatal tract of the brain [43]

MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) induced motor disorder in animal models has been demonstrated to induce oxidative harm, dysfunction of the mitochondria, and dopaminergic loss in the the striatum, in addition to closely mimicking the physical signs of patients with PD. [44]

A specific degeneration of catecholaminergic neurons occurs. 6-OHDA-induced dopamine neurotoxicity is linked to oxidative stress caused by hydrogen peroxide (H₂O₂) and hydroxyl radicals. Additionally, it lowers SOD activity and decreases GSH content, which raises striatal malondialdehyde (MDA) levels. [45–46] It has been shown that the ethanolic root extract of ashwagandha can enhance motor function, decrease MDA and NO levels, boost catalase activity, and restore TH-positive neurons. In the end, these reductions in oxidative stress protect dopaminergic neurodegradation.. [47]

Anti-Alzheimer's disease (AD) activity

AD (Alzheimer's disease) is a degenerative, irreversible neurological illness that progressively reduces one's cognitive functions (ability to think clearly, remember things, and carry out every day activities). [48] A complex pathophysiology underlies AD, marked by a gradual decline of recall and recognition of people or objects, an incapacity to carry out tasks, psychologically abnormal characteristics such as depression, anxiety, depression and mental disturbance, and language deficits mainly brought on by toxic A β (β -amyloid) plaques, dystrophic neuritis, gliosis, abnormal NFTs (neurofibrillary tangles), and insufficient levels of the neurotransmitters required for typical neuron communication. [49–50] Studies have revealed that A β cytotoxicity is the unique pathologic characteristic of AD pathogenesis. [51–52] Oxidative stress caused by an excess of ROS (reactive oxygen species) has been discovered as a signal to start apoptosis early in the neuronal death process. [52–53] The withanolide that was isolated from ashwagandha reduced acetylcholinesterase, an enzyme that degrades one of the main chemical transmitters in the brain, in a concentration-dependent manner. [54] The role of ashwagandha root aqueous extract against Hydrogen peroxide and toxicity induced by β -amyloid was investigated in vitro. [54] It was discovered that ashwagandha extract significantly reversed overall characteristics in a dose-dependent manner. Consequently, the study implies that isolated extract of Ashwagandha help Parkinson's sufferers avoid neuronal damage. [54]

Sleep inducing, anxiolytic and antistress properties

The upkeep of the mammalian body's physical and mental health depends heavily on sleep. Lack of sleep or insufficient sleep can lead to a variety of physiological, metabolic, and mental disorders that can cause stress, anxiety, obesity, and other neurocognitive dysfunctions. When sleep is completely lost, two brain regions linked to memory and perception—the hippocampus and the pyriform cortex—lose their ability to function. [55-58] Sleep-inducing refers to the ability of Ashwagandha to prevent motor impairment, anxiousness, and intellectual deficiencies in animals that have lack of sleep . [59] employed Ashwagandha root aqueous extract to clarify the plant's ability to induce sleep.

Rats that were sleep deprived for 12 hours showed neuromotor dysfunction and memory deficits in the study, but these symptoms may be reversed by pretreating with Ashwagandha extract for 15 days prior to sleep deprivation. Additionally, pre-treatment was observed to enhance rats' exploratory nature, recognition memory, and alertness. [60]

Studies performed on Ashwagandha to evaluate different pharmacological effects

According to some medical research, Ashwagandha may also have a number of beneficial qualities, including the ability to maintain immune homeostasis, control inflammation, suppress pro-inflammatory cytokines, and have protective effects on a variety of organs, including the brain and the nervous system. The aggregate data from the investigative investigations conducted on ashwagandha is shown in the table no 1.

Table1: Ashwagandha and pharmacological activities

S.no	Pharmacologic effect	Extract/Chemical constituent	Model induction	MOA	Reference
	Neuroprotective	Glycowithanolides, Withanolides and sitoindosides	restraint stress	Reduced lipid peroxidation, elevated catalase, and increased GPx	[75]
	Immunomodulatory	Root extract	gamma radiation	An increase in bone marrow and white blood cell counts overall.	[62]
	Antimicrobial	Root extract	parasitaemia induced In-vitro model	certainly damaging bacterial cell envelopes— more research is needed	[63]
	Anti-inflammatory	Root extract	pristane induced	inhibiting effect on inflammatory mediators, like interleukin-6, Tumour necrosis factor- α , and other inflammatory indicators	[61]

	Anticancer	Withaferin A	Destruction due to MI/R (myocardial ischemia/reperfusion)	Inhibition of cancer cell proliferation	[64]
	Cardioprotective	Withaferin A	MI/R(myocardial ischemia/reperfusion) injury	cardioprotective action by increasing AMP-activated protein kinase (AMPK) phosphorylation, which in turn upregulates the mitochondrial anti-apoptotic pathway.	[64]

Conclusion

In conclusion, Ashwagandha extract has been extensively studied for its rich content of bioactive substance, including flavonoids, phenols, steroids and alkaloids. Its antioxidant properties make it promising in treating brain disorders associated with oxidative damage, while its ability to promote neuronal health suggests its significant for neurodegenerative recovery. Research also suggests its significant role in preventing and treating psychiatric conditions such as depression, memory loss, and insomnia. With a focus on its traditional medical uses and diverse biological activities, particularly its neuroprotective and psychotropic effects, Ashwagandha presents immense therapeutic potential.

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