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# A Review on Ashwagandha (Withania somnifera (L.) Dunal)

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## Abstract

*Ashwagandha* , commonly known as *Withania somnifera* (L.) Dunal is an important medicinal plant which is used in indigenous medicine for over 3,000 years. Due to its varied therapeutic potential, it has now become a subject of interest for modern scientific attention. Withania is widely claimed to have potent aphrodisiac, sedative, rejuvenating and life prolonging properties. It is also used as a general energy-enhancing tonic known as *Medha Rasayana* ('that which promotes learning and a good memory') and in geriatric problems. More than thirty five chemical constituents are present in the roots of Withania somnifera. The biologically active chemical constituents are alkaloids and steroidal lactones. To explore this drug and its properties we made an effort to collect literature mentioned in ancient textbook backed with recent research evidences. To achieve this, known database like pubmed, medline were selected for studies from 1988 to 2010. Data obtained in English language from clinical and experimental studies on Withania somnifera were considered. Various clinical & experimental studies proved its utility as anti-anxiety, anti stress, anti-inflammatory, antidepressant, antioxidant, antiageing, anticarcinogenic, antibacterial, adaptogenic, hemopoetic & immodulation activity along with cognition enhancing & memory improving activity with effect on Parkinson disease, neuritic regeneration and synaptic reconstruction.

## Keywords

*Ashwagandha* , Withania somnifera (L.) Dunal

## INTRODUCTION

*Withania somnifera* (L.) Dunal is a plant of Solanaceae family which is commonly known as *Ashwagandha*, Indian ginseng, poison gooseberry and winter cherry. It is one of the ingredients of many ayurvedic formulations[1,2] used for musculoskeletal disorders and as general rejuvenator to increase energy, health, longevity and prevention of disease in athletes, elders and pregnancy. It is also used as a general energy-enhancing tonic known as *Medha Rasayana* which means 'that which promotes learning and a good memory' and in geriatric problems.[3,4] It is a thick hairy herb which is found in the forests of

Mandsaur and Bastar in Madhya Pradesh, the foothills of Punjab, Himachal Pradesh, Uttar Pradesh and western Himalayas in India. It is cultivated in Madhya Pradesh, Rajasthan and other drier parts of the country.[5,6] Traditionally it is known as *Ashwagandha, Balya, Vatahara, Madgandhika,*[7] *Gandhata, Varahakarni, Vajigandha, Haya, Havya, Varada, Kustagandhin,*[8] *Vajiava, Vegam, Smarodabhavam,*[9] *Turangahava, Gokaran, Aswavarohakah, Varda, Vrasha,*[10] *Varahakarnya,Turagi, Vajikari, Smrita, Kustagandha, Kandar, Vargatrakari, Punya, Sishtagandha, Pivara,Elaparni, Marughni, Shyamla, Kamrupini*[11] *Dorgunja, Aasandha, Ghodaahuna,*[12] *Kanchuka, Vajikari,*[13] *Kustagandha, Hayahava,Gokarni, Peeta, Bahipicch, Kanchuki* and *Vrishya.*[14] Acharya Charka mentioned this plant under *Balya,*[15] *Brimhaniya*[16] *Mahakashaya* and *Madhur Skanda* while *Acharya Bhav Prakash* described it in *Guduchiyadi Varga.* It is a thick, hairy herb with plumpy roots, fleshy, whitish brown and aromatic. The leaves are simple, round and oval shaped with velvet hairs. The flowers are greenish-yellow and found in clusters. The fruit is a round red berry, enclosed in green leafy structures resembling that of red cherries. The seeds are yellow and kidney shaped many in number.[17] *Ashwagandha* contains compounds such as ergostane type steroidal lactones, including withanolides A-Y, dehydrowithanolide-R, withasomniferin-A, withasomidienone, withasomniferols A-C, withaferin A, withanone and others. Other constituents include the phytosterols sitoindosides VII-X and b-sitosterol, as well as alkaloids (e.g. ashwagandhine, cuscohygrine, tropine, pseudotropine, isopelletierine, anaferine), a variety of amino acids including tryptophan, and high amounts of iron.[4, 18]

On the basis of plant morphology chemical constituents as given below:

**Root** - Among the various alkaloids, withanine is the main constituent. The other alkaloids are somniferine, somnine, somniferinine, withananine, pseudo-withanine, tropine, pseudo-tropine, 3-a-gloyloxytropane, choline, cuscohygrine, isopelletierine, anaferine andanahydrine.[19]

**Leaves** - Leaves contain twelve withanolides, alkaloids, glycosides, glucose and free amino acids, with anon. [20, 21, 22, and 23]. The present study was aimed to collect literature mentioned in ancient textbook backed with recent research evidences. This was achieved by referring known database like pubmed, medline from 1988 to 2013.

Clinical and experimental studies written in English language were considered.

**PHARMACODYANAMIC ROPERTIES**

Table 1 shows the *Ayurvedic* pharmacological properties of *Withania somnifera* (L.) Dunal according to various texts:

**KARMA (ACTION)**

*Rasayana* (rejuvenator), *Balya* (tonic), *Brimhana* (Anabolic) [8, 9, 14] *Sothahara*8, *Vrishya* (aphoristic), *Vatahara*,[9] *Vishagna* (antidote).[14]

**ROGA-HARATWA (THERAPEUTIC INDICATION)**

*Kasa* (cough), *Vrana* (wound healer), *Shwasa* (breathlessness) [14], *Kshaya roga* (emaciation), *Shwitra* (lecucoderma), *Shotha* (oedema) [9, 14] *Daurbalya* (tonic), *Vatavyadhi*,[7] *Granthi* (anti tumor), *Gandmala* (antigoiter), *Vandhyatva* (anti infertility).[11]

**Table 1** Pharmacological properties of *Withania somnifera* (L.) Dunal

| S. No. | Nighantu (Ay.Text) | Rasa | Virya | Vipaka | Guna | Doshaghnata |
|---|---|---|---|---|---|---|
| **1** | P.N.[9] | *Tikta, Katu, Madhur* | *Ushna* | *Madhura* | *Laghu, Snigdha* | *Vata* |
| **2** | R.N.[7] | *Katu,Tikta* | *Ushna* | - | - | *Vata* |
| **3** | S.N.[11] | - | -- | - | - | *Vata* |
| **4** | D.N.[13] | *Kasaya,Tikta* | *Ushna* | - | - | *Vata,Kapha* |
| **5** | B.P.N.[8] | *Tikta,Kasaya* | *Ushna* | - | - | *Vata,Kapha* |
| **6** | K.N.[14] | *Tikta,Kasaya* | *Ushna* | - | - | *Kapha* |
| **7** | M.P.N.[10] | *Kasaya,Tikta* | *Ushna* | - | - | *Vata,Kapha* |
| **8** | M.V.N.[24] | *Tikta,Kasaya* | *Ushna* | - | - | *Vata,Kapha* |

(P.N.-Priya Nighuntu, R.N.- Raj Nighuntu, S.N.- Sodhala Nighuntu , D.N.-Dhanwantri Nighuntu, B.P.N.- Bhav prakash Nighuntu, K.N.- Kaiydeva Nighuntu, M.P.N.- Madanpal Nighuntu, M.V.N.-Madan Vinod Nighuntu)

**CONTRAINDICATIONS**

*Ashwagandha* must be taken cautiously with patients on anticonvulsants, barbiturates and benzodiazepines due to its GABAnergic and sedative properties. *Ashwagandha* is traditionally avoided in lymphatic congestion, during colds, flu.

***Nootropic-like effect***

*Ashwagandha* root extract (50, 100 and 200 mg/kg; orally) improve retention of a passive avoidance task in a step-down paradigm in mice. In the same dose it reverses the scopolamine (0.3 mg/kg)-induced interruption of achievement, retention and attenuated the amnesia produced by acute treatment with electroconvulsive shock (ECS), immediately after training. Chronic treatment with ECS, for six successive days at 24 hr intervals, disrupted memory consolidation on seventh day. Daily administration of *Ashwagandha* for six days significantly improved memory consolidation in mice receiving chronic ECS treatment. *Ashwagandha,* administered on seventh day, also attenuated the disruption of memory consolidation produced by chronic treatment with ECS. On the basis of these findings, it is suggested that *Ashwagandha* exhibits a nootropic-like effect in naive and amnesic mice. [25]

***Cognition enhancing & memory improving activity***

In double-blind, multi-dose, placebo-controlled, crossover study, twenty healthy male participants were randomized to receive two capsules of 250 mg twice daily made from an encapsulated dried aqueous extract of roots and leaves of Withania somnifera or a matching placebo for a period of fourteen days. Cognitive and psychomotor performance was assessed pre-dose (day 1) and at 3 hrs post-dose on fifteenth day using a battery of computerized psychometric tests. After a washout period of fourteen days, significant improvements were observed in reaction times with simple reaction, choice discrimination, digit symbol substitution, digit vigilance, and card sorting tests with Withania somnifera extract compared to placebo. However, no effect can be seen with the finger tapping test. These results suggest that Withania somnifera (WS) extract can improve cognitive and psychomotor performance and may, therefore, be a valuable adjunct in the treatment of diseases associated with cognitive impairment.[26]

*Ashwagandha* has been shown in many studies to enhance all aspects of cognitive function. A double-blind, placebo-controlled clinical study compared the effects of Withania somnifera, Panax ginseng and placebo on psychomotor performance in thirty healthy participants. Sensory-motor function, auditory reaction time, and mental arithmetic ability were improved in the Withania somnifera compared to Panax ginseng and placebo.[27]

In a study, the effect of Withania somnifera (WS) extract prepared by two different methods on behavioral parameters assessed using open field exploratory behavior, behavior despair and passive avoidance tests were compared in young and old stressed Wistar rats. WS extracts prepared with 50% methanol and solvent containing water, ghee and honey were administered orally as fine suspension, during the shock period. The results revealed that stress produced depression anxiety and retention deficit in young and old rats. Administration of WS methanolic extract 250 mg/ kg during shock period in young and old rats attenuated the stress-induced depression and enhanced memory. WS traditional extract 250mg/kg produced memory enhancement in both control and stressed young and old rats. Both the WS extracts failed to reverse the stress-induced anxiety. It can be concluded that in comparison to methanolic extract, traditional extract was found to be more active in memory enhancement than anxiolytic and antidepressant activity. [28]

***Adaptogenic activity***

Adaptogenic activity of a standardized extract of WS roots was investigated against a rat model of chronic stress (CS). The stress procedure was mild, unpredictable footshock, administered once daily for twenty one days to adult male Wistar rats. CS induced significant hyperglycaemia, glucose intolerance, and increase in plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression and mental depression. These CS induced perturbations were attenuated by WS (25 and 50 mg/kg) and by PG (100 mg/kg) orally administered 1 hr before footshock for twenty one days. The results indicated that WS, like PG, has significant antistress adaptogenic activity, confirming the clinical use of the plant in Ayurveda.[29]

In another study, WS methanolic extract for 15 days significantly reduced the ulcer index, volume of gastric secretion, free acidity, and total acidity. A significant increase in the total carbohydrate and total carbohydrate/protein ratio was also observed. Study also indicated an increase in antioxidant defense, that is, enzymes SOD, CAT, and ascorbic acid, increased significantly, whereas a significant decrease in lipid per oxidation was observed. WS inhibited stress-induced gastric ulcer more effectively as compared to the standard drug ranitidine.[30]

***Antidepressant effect***

Prophylactic use of *Ashwagandha* prevent behavioural deficit in animal model of

depression. For this normal rats fed with *Ashwagandha* root extract (100mg/kg orally) for 4 and 8 weeks showed enhanced open field behavior and emotional stability along with a moderate but significant enhancement in the functional sensitivity of 5 HT2 receptors in the brain and a reciprocal sub sensitivity of the 5HT1A receptors chronic *Ashwagandha* treatment (prophylactic) was effective in preventing the behavioral deficit in open field activity in an animal model of depression. This was accompanied by an adaptive super sensitivity of the postsynaptic 5HT2 receptors in the brain. The effect of chronic *Ashwagandha* on 5HT receptor subtypes is similar to the action of chronic ECT treatment and several antidepressant drugs. [31]

***Anti anxiety effects***

Anxiolytic and antidepressant actions of the bioactive WSG, isolated from WS roots, in rats were assessed. WSG was administered orally once daily for 5 days and the results were compared by those elicited by the benzodiazepine lorazepam for anxiolytic activity, and by the tricyclic antidepressant, imipramine. WSG induced an anxiolytic effect was comparable to lorazepam, in the elevated plus-maze, social interaction and feeding latency in an unfamiliar environment, tests. WSG also reduced rat brain levels of tribulin, an endocoid marker of clinical anxiety, when the levels were increased following administration of the anxiogenic agent, pentylenetetrazole. WSG also exhibited an antidepressant effect, comparable with that induced by imipramine, in the forced swim-induced 'behavioural despair' and 'learned helplessness' tests. The investigations supported the use of WS as a mood stabilizer in clinical conditions of anxiety and depression in Ayurveda.[32]

***Effect on neuritic regeneration and synaptic reconstruction***

In a study it is proved that withanolide A (WL-A), isolated from the root of Withania somnifera, could regenerate neurites and reconstruct synapses in severely damaged neurons & the effect of WL-A on memory-deficient mice showing neuronal atrophy and synaptic loss in the brain. Treatment with A beta (10 microM) induced axonal and dendritic atrophy, and pre- and postsynaptic loss in cultured rat cortical neurons. Subsequent treatment with WL-A (1 microM) induced significant regeneration of both axons and dendrites, in addition to the reconstruction of pre- and postsynapses in the neurons. WL-A (10 micromol kg (-1) day (-1), for 13 days, p.o.) recovered A beta

(25-35)-induced memory deficit in mice. At that time, the decline of axons, dendrites, and synapses in the cerebral cortex and hippocampus was almost recovered. WL-A is therefore an important candidate for the therapeutic treatment of neurodegenerative diseases, as it is able to reconstruct neuronal networks. [33]

***Anti-inflammatory activity***

A herbomineral formulation containing roots of Withania somnifera, the stem of Boswellia serrata, rhizomes of Curcuma longa and a zinc complex (Articulin-F), was evaluated in a randomized, double-blind, placebo controlled, cross-over study in patients with osteoarthritis. After a one-month single blind run-in period, 42 patients with osteoarthritis were randomly allocated to receive either a drug treatment or a matching placebo for a period of three months. After a 15-day wash-out period the patients were transferred to the other treatment for a further period of three months. Clinical efficacy was evaluated every fortnight on the basis of severity of pain, morning stiffness, Ritchie articular index, joint score, disability score and grip strength. Other parameters like erythrocyte sedimentation rate and radiological examination were carried out on a monthly basis. Treatment with the herbomineral formulation produced a significant drop in severity of pain ($P < 0.001$) and disability score ($P < 0.05$). [34]

***Antiaging activity***

*Ashwagandha* was tested for its anti-aging properties in a double-blind clinical trial. A group of 101 healthy males, 50-59 years old were given the herb at a dosage of 3 grams daily for one year. The subjects experienced significant improvement in hemoglobin, red blood cell count, hair melanin, and seated stature. Serum cholesterol decreased and nail calcium was preserved. Seventy percent of the research subjects reported improvement in sexual performance. These findings suggest therapeutic use of WS as an *Ayurvedic Rasayana.* The antioxidant effect of active principles of WS root may explain the reported anti-stress, cognition-facilitating, anti-inflammatory and anti-aging effects produced by them in experimental animals, and in clinical situations. [35]

***Antioxidant activity***

Researchers from Banaras Hindu University in Varanasi, India, have discovered that some of the chemicals found in Withania somnifera are powerful antioxidants. Studies conducted on rats' brains showed the herb produced an increase in the levels of three

natural antioxidants superoxide dismutase, catalase and glutathione peroxidase.[36]

In a study the attenuating effect of extracts of Withania somnifera on prevention of hippocampal and cortical cell degenerations of streptozotocin (STZ) diabetic mice is examined. Doses of WS extract's given to experimental animals was based on the evaluation of their total antioxidant activity and also their potency to reduce Fe (3+). The results showed a significant ($P < 0.05$) increase in lipid peroxidation (LPO) and protein carbonyl (PC) in hippocampus and cortical regions of STZ diabetic mice & significant impairment in both motor and memory behavioral functions. However, when diabetic mice were supplemented with the extracts of WS, the oxidative damage in both brain regions was reduced as marked by a significant ($p < 0.05$) declines in both LPO and PC. It conclude that impairments in the hippocampus and cortex in STZ diabetic mice are associated with an increased free radical mediated oxidative damage and that the supplementation of extracts showed preventive effects in attenuating oxidative damage in both brain regions possibly via ant oxidative mechanisms.[37]

***Anticarcinogenic activity***

The alcoholic extract of the dried roots of the plant as well as the active component withaferin A isolated from the extract showed significant antitumor and radiosensitizing effects in experimental tumors in vivo, without any noticeable systemic toxicity. Withaferin A gave a sensitizer enhancement ratio of 1.5 for in vitro cell killing of V79 Chinese hamster cells at a non toxic concentration of approximately 2 microM. The mechanism of action of this compound is not known. The studies so far indicate that W. somnifera could prove to be a good natural source of a potent and relatively safe radio sensitizer/chemotherapeutic agent.[38]

***Antiparkinsonism effect***

Withania Somnifera significantly inhibited haloperidol or reserpine-induced catalepsy and provide hope for treatment of Parkinson's disease.[39] In another study, 6-Hydroxydopamine (6-OHDA) is one of the most widely used rat models for Parkinson's disease. Rats were pretreated with the WS extract orally for 3 weeks. On day 21, 6-OHDA was infused into the right striatum while sham operated group received the vehicle. Three weeks after 6- OHDA injections, rats were tested for neurobehavioral activity and were killed 5 weeks after lessoning for the estimation of

lipid peroxidation, reduced glutathione content, activities of glutathione-S-transferase, glutathione reductase, GPX, SOD and CAT, catecholamine content, dopaminergic D2 receptor binding and tyrosine hydroxylase expression. WS extract reversed all the parameters significantly in a dose-dependent manner.[40]

***Antibacterial activity***

Both aqueous as well as alcoholic extract of the plant (root as well as leaves) were found to possess strong antibacterial activity against a range of bacteria, as revealed by in vitro Agar Well Diffusion Method.[41]

In another study Aqueous root extract of the plant was found to possess strong antibacterial activity against Staphylococcus aureus (MRSA) as revealed by the in -vitro agar well diffusion assay. The separation of the bioactive compounds from the plant extract was carried out using two dimensional thin layer chromatography (TLC) and contact bioautography. Two TLC spots were found to be bioactive against the pathogen with minimum inhibitory concentrations of 2.3 µg/µl and 5.2 µg/µl respectively. One spot was of alkaloids and the other one was a mixture of essential oil and phenolics. The antioxidant activity was estimated to be Trolox Equivalent Antioxidant Capacity of 9.83mg/gm of dry weight of extract and reducing power was 0.11mg/gm of dry weight of extract using ascorbic acid as standard. This suggests that the bioactive fraction separated from aqueous extract of W. somnifera is a potential source of antibacterial compounds with antioxidant property.[42]

***Hypothyroid activity***

Animal studies reveal *Ashwagandha* has a thyrotropic effect.[43] An aqueous extract of dried Withania root was given to mice via gastric intubation at a dose of 1.4 g/kg body weight daily for 20 days. Serum was collected at the end of the 20- day period and analyzed for T3 and T4 concentrations and lipid peroxidation was measured in liver homogenate via antioxidant enzyme activity. Significant increases in serum T4 were observed, indicating the plant has a stimulatory effect at the glandular level. No changes in T3 levels were observed. Withania may also stimulate thyroid activity indirectly, via its effect on cellular antioxidant systems. Withania extract significantly decreased lipid peroxidation in the liver homogenate and significantly increased catalase activity, promoting scavenging of free radicals that can cause cellular damage. These results indicate *Ashwagandha* may be a useful botanical in treating hypothyroidism.[44]

***Immunomodulation and Hematopoiesis***

A series of animal studies show *Ashwagandha* to have profound effects on the hematopoietic system, acting as an immunoregulator and a chemo protective agent.[45]

In a mouse study, administration of a powdered root extract from *Ashwagandha* was found to enhance total white blood cell count. In addition, this extract inhibited delayed-type hypersensitivity reactions and enhanced phagocyte activity of macrophages when compared to a control group.[46]

***Effect on GABA receptors***

A methanolic extract of Withania somnifera inhibited the specific binding of GABA and TBPS, and enhanced the binding of flunitrazepam to their putative receptor sites, suggesting a GABA-mimetic activity.[47]

***Effect on Orofacial Dyskinesia***

Chronic treatment with Withania somnifera root extract for a period of 4 weeks to reserpine treated animals significantly and dose dependently reduced the reserpine induced vacuous chewing movements and tongue protrusions. Oxidative stress might play an important role in the pathophysiology of reserpine-induced abnormal oral movements. [48]

***Toxicity***

Withania somnifera is a widely used medicinal plant for several disorders. Toxicity studies on Withania somnifera are not available. Acute and sub-acute oral toxicities of WS root extract in Wistar rats were evaluated in the present study. In the acute toxicity study, WS extract was administered to five rats at 2000 mg/kg, once orally and were observed for 14 days. No toxic signs/mortality was observed. In the sub-acute study, WS extract was administered once daily for 28 days to rats at 500, 1000 and 2000 mg/kg, orally. No toxic signs/mortality were observed. There were no significant changes ($P < 0.05$) in the body weights, organ weights and haemato-biochemical parameters in any of the dose levels. No treatment related gross/histopathological lesions were observed. The present investigation demonstrated that the no observed adverse effect level was 2000 mg/kg body weight per day of hydro alcoholic extract of WS in rats and hence may be considered as non-toxic. [49]

## CONCLUSION

On the basis of above study it is concluded that *Withania somnifera* (L.) Dunal (*Ashwagandha)* is a medicinal plant used in *Ayurveda* since a long time. Various experimental & clinical trials the ancient

claims of its therapeutic claim as an aphrodisiac, anxiety, cognitive and neurological disorders, inflammation, liver tonic, anti-inflammatory, antibacterial, anti ageing, anti oxidant activity along with its thyrotrophic effects and effect on Parkinson's disease that make a potent & effective herbs. However number of studies is required in future to validation its effectiveness.

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