Review Article

Indian Journal of Ancient Medicine and Yoga
Volume 8 Number 3, July - September 2015
https://dx.doi.org/10.21088/ijamy.0974.6986.8315.6

Ashwagandha: Solution to Stress and Insomnia

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Abstract

Hectic and unhealthy life style has been a prime factor for various life style disorders including Alzheimer's disease, arthritis, atherosclerosis, metabolic syndromes, obesity, sleep disorders etc. Sleep disorders are serious enough to interfere with normal physical, mental, social and emotional functioning [1]. Sleep disorders include hyposomnia, hypersomnia and insomnia. Insomia is the most common problem of present generation. Stress is the one of commonest causes attributed to insomnia [3]. *Nidra* is one of the *Upastambhas* described in ancient classics [2]. Ayurveda, with its holistic approach can help in this condition with its unique way of life style management and drug therapy. *Whithania somnifera* (L.) Dunal (family Solanaceae), commonly known as *Ashwagandha* (Indian ginseng), has been used to treat a number of medical condition in Ayurveda [4]. In *Bangsen, Ashwagandha* has been indicated for the treatment of insomnia [5]. This herb is considered as an adaptogen. *Ashwagandha* effectively alleviates insomnia but does not act as sedative. It's rejuvenative and nervine tonic properties produce energy which in turn helps the body to settle and sleep [6]. It reduces significantly the cortisol level which is an indicator for stress and anxiety. Thus *Ashwagandha* can prove wonderful for the treatment of sleep disorders specifically insomnia.

Keywords: Stress; Insomnia; Ayurveda; *Ashwagandha.*

Ashwagandha (*Withania somnifera* Linn, Solanaceae)

Ashwagandha has been extensively used in therapeutics in Ayurveda. A review of *Ashwagandha* is being reproduced here:

S. No		
1.	*Balya Mahakashay [7], Bringhaniya Mahakashay [8], Madhur skandha [9]*	*Charak Samhita*
2.	*Guduchyadi Varga*	*Bhavprash Nighantu [10], Dhanvantari Ninghantu [11], Sodhal Nighantu [16], Shaligram Nighantu [17] Haritakyadi Nighantu [18]*
3.	*Shatahvadi varga*	*Raj Nighantu [12]*
4.	*Aushadhi varga*	*Kaiyadev Nighantu [13]*
5.	*Vividhaushadhi varga*	*Madhav dravyaguna [14]*
6.	*Haritakyadi varga*	*Madanpal Nighantu [15]*
7.	*Ekpad varga*	*Hridayadeepak Nighantu [19]*

Classical Synonyms [21]: Ashwagandha, Varahakarni, Vajikari, Kandara, Punya, Elaparni, Kamarupani, Turangi, Ashwarohak, Sishtgandha, Marutaghni, Balya, Kusthagandha, Varagatrakari, Pivara, Syamala.

Pharmacological properties [22]

Rasa -Madhur, Tikta, Katu; Guna-Laghu, Snigdha; Virya-Usna; Vipaka-Madhur

Taxonomical Classification [23]

Kingdom: Plantae

Order: Solanales

Family: Solanacae

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Genus: Withania

Species: Withania somnifera

Binomial Name: Withania somnifera (L) Dunal.

Morphology

Height usually 30-60 cm can grow up 170 cm, upright stout shrub with central stem. Branches star shaped, branches covered with fine hairs. Leaves – alternate, ovate, up to 10 cm long, 5 cm wide. Flowers – yellow petals inside with a green outer covering layer [24]. Root straight, unbranched, thikness varying with age. Root bears fiber like secondary roots, outer surface buff to grey-yellow with longitudinal wrinkles, crown consist of 2-6 remains of stem base. Odor characteristics – taste bitter and acrid [25].

Phytochemistry

In Israel 3 ecotype of the plant were identified on the basis of semi-quantitative analysis of withanolides. They had difference in concentration of their major components and were related to various localities. Withanolide Y has been isolated from a hybrid developed from Chemotype II (Israel), Withanolide D, occurring in leaves. From the chemotype II, several chlorinated withanolides have been isolated and characterized as D-deoxyphysalolacton, withanolides D, and withanolides C. Analysis of dried plant material revealed the presence of various mineral elements viz. Ca, Cu, Fe, Mg, Zn, Ba, K, Na, Al, Ce, Sr, Co, Ag. The root contains Fe, K, Mg, Ni along with other elements, which are reported to play a significant role in the diuretic and aphrodisiac activity of the drug. Two glycowithanolides isolated from the root, viz. sitoindosite-IX and sitoindosite-X produced significant immunomodulatory and anti-stress activity in albino mice and rats [26]. Other main therapeutically active phytochemicals reported are withaferin-A and dihydrowithaferin-A_2 (Seeds), visamine (plant), anaferin (leaves), tropine, pseudotropine, anahygrine, hygrine , a pyrazole alkaloids withasomine, c-28 steroid lactone, withaniol, nicotine, somniferine, somniferine withanine, sucrose, choline (root), steroidal lactone of withanolide series i.e., Withanolides N, O, D, G, P & S, Q & R, somnitol, glucose, withanone, nitrogen free compounds A1, A2 , A3, A4 & A5. aminoacids including proline, valine, tyrosine, analine, glyecine, hydroproline, aspartic acid, glutamic acid, cystine and cysteine (berries) and fatty acid (seed oil) [27].

Classical Uses

Insomnia: The powder of *Ashwagandha* mixed with sugar taken with *ghee* alleviates insomnia and brings sleep quickly [28].

Rasayana: Ashwagandha taken with milk, *ghee*, oil or tapid water for a fortnight promotes development of body [29]. *Ashwagangha, mandukparni (Centella asciatica* Linn. Scrophulariaceae), *sankhpuspi (Convolvulus pluricaulis* Chois, Convolvulaceae), and *shatavari* (*Asparagus racemosus* Willd., Liliaceae) should be used in order to promote intellect, life-span, stability and strength [30]. One who takes powdered *Ashwagandha* root in late winter mixed with honey and ghee along with milk regains youthfulness even in old age [31].

Bronchial asthma: The ash (alkali) of *Ashwagandha* should be taken with honey and ghee [32].

Granthi visarpa (Erysipelas): The part should be sprinkled with hot decoction of leaves of eranda (*Ricinus communis* Linn., Euphorbiaceae) etc. and cow's urine or warm paste of *Ashwagandha* should be applied externally on the affected part [33].

Urustambha (Stiffness in thigh muscle): The root of *Ashwagandha* or *arka* (*Calotropis procera* Ait., Asclepiadaceae) or *nimb* (*Azadirechta indica* A.Juss, Meliaceae) or *devadaru* (*Cedrus deodara* Roxb., Pinaceae) mixed with honey, mustard (*Brassica compestris* Prain., Brassicaceae) and ant-hill earth should be anointed thickly and applied as paste in urustambha [34].

Cardiac Disorder: The paste (powder) of *Ashwagandha* and *bibhitaka* (*Terminalia bellirica* Roxb., Combretaceae) mixed with jaggery taken with tapid water alleviates *vata* located in heart [35].

Accidental Wound: One affected with accidental wound should lick the powder of *Ashwagandha* with jaggery or *ghee* or should take with milk. It also acts as Rasayana [36].

Suppression of Urine: Decoction of *Ashwagandha* alleviates suppression of urine and promotes urination [37].

For conception in sterility: Milk processed with *Ashwagandha* should be taken by the woman in proper time. It helps conception [38].

Balasosa (Emaciation in children): Ghee cooked with one-fourth paste of *Ashwagandha* with ten times milk promotes development of body in emaciated children [39].

Udararoga (Diseases of Abdomen): Devadaru (C. devdara), shobhanjana (Moringa pterygosperma Gaertn., Moringaceae) and apamarga (Achyranthes

aspera Linn., Amaranthaceae) or *Ashwagandha* pounded with cow's urine alleviates severe *udararoga*, worms and edema [40].

Excessive Emaciation: In case of excessive emaciation *Ashwagandha* etc. should be used [41].

Consumption: Powder of *Ashwagandha, tila* (*Sesamum indicum Linn., Pedaliaceae)* and *masa (Vigna mungo* Linn., Fabaceae) taken with goat's *ghee* and honey [42].

In Folklore: In the Mewat region of Haryana, the leaves are heated and applied to painful joints and boils [43]. The Chenchu tribes of Andhra Pradesh pound the roots / tubers of herb along with leaves of *Sanseviera roxburghiana* Schult. F., Liliaceae, tuberous roots of *Asparagus racemosus* Willd., Liliaceae and fruit of *Solanum surrattense* Burm.F., Solanaceae, in cow's milk and add equal quantity of sesame oil. The preparation is stored in bottles and applied on male sexual organ to strengthen it. In Kachchh district of Gujarat, roots are used as uterine tonic in sterility [44].

Pre-clinical Pharmacology

Anti Stress Activity: Anti-stress effect of *Ashwagandha* was investigated in rats using cold water swimming stress test. The drug treated animals showed better stress tolerance. Withanolide-free aqueous fraction isolated from the roots of *W. somnifera* exhibited anti-stress activity in a dose dependent manner in mice. *Ashwagandha* has been evaluated for its adaptogenic activity. Administration of *Ashwagandha* with other drugs in experimental animals exposed to a variety of biological, physical and chemical stressors was found to offer protection against these stressors [45].

Anti-ageing and antioxidant activity [46]: Ashwagandha, traditionally used as an anti-ageing herb, increases longevity, promotes resistance to disease and improves both mental and physical health. Culturally, it is considered a strong tonic. Ant-oxidant properties are suggested by animal research, and this is a viable explanation of ageing effect.

Cardioprotective Activity: Marutham, a polyherbal formulation containing *W. somnifera* has been found to be cardio-protective and anti-oxidant in isoproterenol-induced ischemic rats [47].

Hypothyroidism: Animal studies reveal *Ashwaganda* has a thyrotropic effect. 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 that *ashwaganda* may be a useful herb in treating hypothyroidism [48].

Anticancerous activity: The root extract of the plant and Alferin-A isolated from the extract kills tumour cells on its and in combination with modern cancer therapy. The extract when administered with radiotherapy in mice, produced power full synergistic effect against cancer. The best result, however, was obtained when the extract was administered with radiotherapy and hyperthermia (heat treatment). Withanolide D, occurring in the leaves, exhibited significant anti-tumour activity in *vivo* against Sarcoma 180 and Ehrlich ascites carcinoma and in *vitro* against cells derived from human epidermoid carcinoma of nasopharynx [49].

Anti-arthritic activity: The root powder (1000 mg / kg body weight) when orally fed to adjuvant arthritic rats for 15 days, corrected the body weight loss and brought marked reduction in the swelling of paw. It prevented the bony degenerative changes occurring during the arthritic condition. It also had modulating effect on serum levels of Cu, Zn and Fe suggesting beneficial effect of these minerals in arthritis. The crude extract of the plant showed anti-inflammatory activity [50].

Antibiotic activity: The antibiotic activity of the roots as well as leaves has recently been shown experimentally. Withaferin A in concentration of 10µg / ml inhibited the growth of various Gram-positive bacteria, acid-fast and aerobic bacilli, and pathogenic fungi. It was active against *Micrococcus pyogenes var aureus* and partially inhibited the activity of *Bacillus subtilis* glucose-6-phosphate dehydrogenase. Withaferin A inhibited Ranikhet virus. The shrub's extract is active against Vaccinia virus and *Entamoeba histolytica*. *Ashwagandha* showed the protective action against systemic Aspergillus infection. This protective activity was probably related to the activation of the macrophage function revealed by the observed increases in phagocytosis and intracellular killing of peritoneal macrophages induced by *Ashwagandha* treatment in mice. Antibiotic activity of Withaferin A is due to the presence of the unsaturated lactone-ring. The lactone

showed strong therapeutic activity in experimentally induced abscesses in rabbits somewhat stronger than that of Penicillin. It substantiates the reputation of the leaves as a cure for ulcers and carbuncles in the indigenous system of medicine [51].

CInical Evidences for classical therapeutic indications

Insomnia and depression: A research conducted at the Department of Pharmacology, University of Texas Health Science Center indicated that extract of *Ashwagandha* produce GABA-like-activity, which may account for the herb's anti-anxiety effect. GABA (Gamma Amino Butyric Acid) is an inhibitory neurotransmitter in the brain. Its function is to decrease neuron activity and inhibit nerve cell from over firing. This action produces a calming effect. Excessive neuronal activity leads to restlessness and insomnia, but GABA inhibits the number of nerve cell fire in brain, and help to induce healthy sleep, uplift mood, and reduce anxiety[50]. In one of the most complete human trials to date, researchers studied the effect of a standardized extract of *Ashwagandha* on the negative effect of stress, including elevated levels of the stress hormone cortisole. Many of the adverse effect of stress are thought to be related to elevated levels of cortisole. The results were impressive. The participants subjectively reported increased energy; reduced fatigue, better sleep and an enhanced sense of well being [52].

Anti-ageing and antioxidant effect: Double-blind clinical trial carried out to study the effect of plant on prevention of ageing in 101 normal healthy males in 50-59 years age group. Root powder (0.5 g) was given orally three times a day for 1 year. Results showed statistically significant increase in Hb, RBC, hair melanin and seated stature in treated group in comparison to placebo group. Decrease in serum cholesterol was more in treated group than in placebo group[53]. Researchers from Banaras Hindu University have discovered that some of the chemicals found in *W. somnifera* are powerful antioxidants. The antioxidant effect of active principles of *W. somnifera* 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 [54].

Cardioprotective Effect: Myocardial infarction (AMI) and myocardial ischemia-reperfusion injury (MI-R), which occurs in a wide spectrum of patients, ranging from survivors of out-of-hospital cardiac arrest to AMI victims and patients undergoing cardiac surgery and represents a major public health burden. *W. somnifera* treatment found to increase the heart rate, contractility, relaxation and decrease preload along with improved antioxidant enzymes and inhibition of lipid-peroxidation comparable to vitamin E, a known cardio-protective antioxidant. In addition to antioxidant activity, the anti-apoptotic activity which contributes to cardio protection was evidenced by up-regulated Bcl-2, an anti-apoptotic protein and decreased Bax, a pro-apoptotic protein as well as attenuation of terminal deoxynucleotide-l transferase biotin-dUTP nick end labelling (TUNEL) positivity; a hallmark of apoptosis . Similarly, Thirunavukkarasu *et al*. found the energy boosting properties of a formulation comprising of *W. somnifera* in I-R compromised heart and recommended its use as a dietary supplement for cardio-protection. The formulation favourably altered the myocardial energy substrate, improved cardiac function and reduced infarct size [55].

Aphrodisiac effect: The presence of therapeutic amount of Zn and Cu in the herb clearly indicates its major use as aphrodisiac in the traditional system of medicine. The herb is used with *Mucuna prurita* Hook. (Fabaceae) orally as an aphrodisiac [56].

Musculotropic Activity: The total alkaloids of *W. somnifera* showed relaxant and antispasmodic effects against several spasmogens on intestinal, uterine, bronchial, tracheal and blood vascular muscles. The pattern of smooth muscle activity of the alkaloids was similar to that of papaverine which suggested a direct musculotropic action [57].

Conclusion

Ashwagandha has been a focus drug for researchers world over. Its classical uses, biological activities and subsequent clinical trials have proved that the herb is capable of correcting physiological processes involved in the genesis of stress and strain. The drug is being used as an anti-stress drug for centuries together and has got the potential to be the drug of choice for stress and disorders originating out of present day lifestyle.

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