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REVIEW ARTICLE

WITHANIA SOMNIFERA (ASHWAGANDHA): A SOURCE OF THERAPEUTIC AGENTS

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Abstract

Withania somnifera is a plant in the Solanaceae family commonly known as Ashwagandha. Ashwagandha root is among the most prominent herbal preparations used in Ayurveda, a holistic system of medicine that originated in India. Ashwagandha is referred to as the "Prince of Herbs" in Ayurveda because it has an impressively broad range of therapeutic effects. It is an exotic Indian herb, has significant stress-relieving properties analogous to those of powerful drugs used to treat depression and anxiety. Ayurvedic practitioners have been using it for thousands of years as a potent rasayana (a tonic for greater vitality and longevity). The root of this small evergreen shrub is primarily acknowledged for its adaptogenic properties. The herb has conventionally been used for nervous exhaustion, calming the mind, arthritis, relieving weakness and for building sexual energy. Ashwagandha contains flavonoids and many active ingredients of the withanolide class. The present communication constitutes a review on the medicinal properties, major phytochemical constituents and pharmacological activities of *Withania somnifera*.

Keywords: *Withania somnifera*, Ayurveda, arthritis, withanolide, pharmacological activities

Introduction

Withania somnifera (Family: Solanaceae) is an ayurvedic herb that has been used for centuries in India as an adaptogenic herbal remedy to improve overall health, vitality and longevity. It is a well-liked Indian medicinal plant and is also known as Ashwagandha, Ginseng, and Winter cherry (Gurib and Schmelzer, 2012).

In Sanskrit Ashwagandha means “the smell of a horse,” signifying that the herb imparts the vigor and strength of a stallion, and it has traditionally been prescribed to help people strengthen their immune system after an illness (Choudhary et al., 1995).

It has been a vital herb in the ayurvedic and indigenous medical system for over 3000 years. Ashwagandha is a short woody shrub native to the Indian subcontinent that grows naturally in India, Afghanistan, Pakistan, Spain, parts of the Middle East Africa and the Canary Islands (Chopra et al., 1980). Ashwagandha is now also grown in North America and other temperate climates as its popularity increases. It is listed in the Indian Materia Medica, and is part of Ayurvedic, Siddha, and Unani traditions (Anonymous, 1982).

The plant is characteristically close to two feet tall at full height. They form small, green flowers that contain the red fruit in the center, resembling a small berry (Mirjalili et al., 2009). Leaves are simple, ovate, glabrous, and up to 10 cm long.

Several components of this plant are used in herbal medicine. The root is used medicinally, although the

seeds, shoots, juice and leaves have all been used traditionally as well. Ashwagandha has been as a natural therapy for ages (Bone, 1996). There are many reasons and benefits for using Ashwagandha and it's been used in South Asia and Africa to heal inflammation, fevers, and as an overall tonic. It has also been used to supercharge the immune system, enhance memory, and to encourage overall well-being (Chatterjee and Pakrashi, 1995). In addition to its excellent defensive effects on the nervous system, Ashwagandha may be a capable substitute treatment for a variety of degenerative diseases such as Alzheimer's and Parkinson's (Jesberger and Richardson, 1991). This plant has powerful antioxidant properties that seek and destroy the free radicals that have been concerned in aging and numerous disease states. Even more remarkable, emerging evidence suggests that Ashwagandha has anti-cancer benefits as well (Scarfiotti, 1997).

It is beneficial to people who do physical labor or exercise a lot to help the body adapt to physical stress. It has also been used for strengthening the female reproductive system. Ashwagandha contains flavonoids and many active ingredients of the withanolide class. Numerous studies over the past two decades indicate that it has anti-inflammatory, rejuvenating, anti-stress, antioxidant, mind-boosting and anti-tumor properties (Kirtikar et al., 1980; Nadkarni, 1982).

Medicinal uses

1. Ashwagandha is used for anxiety, trouble sleeping (insomnia), tuberculosis, tumors, asthma, bronchitis, a skin condition marked by white patchiness (leukoderma), backache, fibromyalgia, menstrual problems, hiccups, and chronic liver disease (Ali, 1997; Anonymous, 2007).
2. This herb is well thought-out an adaptogen which is a nontoxic herb that works on a nonspecific basis to normalize physiological function, working on the HPA axis and the neuroendocrine system (Khare, 2007).
3. Several people also use Ashwagandha for improving thinking ability, decreasing pain and swelling (inflammation), and preventing the effects of aging (Ali, 1997).
4. Ashwagandha is applied to the skin for treating wounds, backache, and one-sided paralysis (hemiplegia) (Kirtikar et al., 1980).
5. Useful in treatment of arthritis, which involves joints that are painful, dry, swollen and inflamed, Ashwagandha would be the herb of choice (Khare, 2007).
6. It is said to impact sexual health—increasing fertility and even sperm count. It has also been traditionally used as an aphrodisiac. However, the roots may actually decrease fertility for women, so be forewarned (Nadkarni, 1982).
7. For wound care, the leaves of the plant are said to provide a therapeutic poultice. In addition, the roots have antifungal and antibacterial properties— well for warding off infection.
8. Some other benefits are: Diuretic, Galactogogue, Anti-epileptic, Combats stress, Fights cognitive decline due to brain cell degeneration.
9. One of the special properties of Ashwagandha is that it will enhance Ojas. Ojas is the most subtle, refined level of the physical body and is the end result of healthy food which is properly digested. It is responsible for a healthy immune system, physical strength and lustrous complexion, clarity of mind and sense of well being. It allows consciousness to flow within the body. With decreased Ojas, we are less in touch with ourselves and more prone to diseases and having a feeling of disharmony. 'Ojakshaya' (decreased Ojas) is a condition similar to AIDS/HIV (Anonymous, 2007).
10. Ashwagandha operates at the level of the overall body system by maintaining balance in the substances and processes running in the human body. For instance, if some hormones are lower than they should be, Ashwagandha increases them. On the other hand, if some hormones are higher than they should be, Ashwagandha decreases them (Khare, 2007).
11. Ashwagandha is a revitalizing herb that maintains proper nourishment of tisuues, particularly muscle and bones (Jain et al. 2001).
12. According to animal trials Ashwagandha expands the lifespan.
13. Ashwagandha helps to manage body weight problems for a lean and healthy body.
14. It is good hypnotic in Alcoholism, It is bitter in taste and hot in potency, it alleviates vata and kapha; it stimulates thyroid activity and Enhances anti-peroxidation of liver (Kuttan, 1996)

Table 1: Taxonomic Position of *Withania somnifera*

Kingdom	**Plantae**
Division	Angiosperms
Class	Dicotiledoneae
Order	Tubiflorae
Family	Solanaceae
Genus	*Withania*
Species	*Somnifera*

Table 2: Vernacular Names of *Withania somnifera*

Sanskrit	Ashwagandha, Ashvakandika, Gandhapatri, Palashaparni
Hindi	Asgandh, Punir
English	Winter cherry
Bengali	Ashwaganda, Asvagandha
Telugu	Asvagandhi, Penneru, Pennerugadda, Dommadolu
Gujrati	Asan, Asana, Asoda, Asundha,Ghodaasoda
Malayalam	Amukkiram, Pevetti
Tamil	Amukkira, Asubam, Asuvagandi
Marathi	Askandha, Kanchuki, Tilli
Urdu	Asgand, Asgand Nagori
Odiya	Asugandha
Persian	Kaknaj-e-Hindi, Asgand Nagaori
Arabic	Kaknaj-e-Hindi

Table 3: Unani Description of *Withania somnifera*

Unani name	Asgand
Botanical name	*Withania somnifera* (Family: Solanaceae)
Synonyms	*Withania ashwagandha* Kau, *Physalis flexuosa* Linn
Properties	*Mizaj* Hot 1^0, Dry 1^0
Maza	Mucilaginous, bitter and acrid
Boo	Pungent odor, smell of horse's urine
Muzir	Mehrooreen (for persons with hottemperament)
Mukhrij	Expels Balgham (Phlegm) and Sauda (Black Bile)
Nafa-e-Khas	Muqawwi-e-Bah (Aphrodisiac)

Table 4: Ayurvedic Pharmacodynamic Properties of *Withania Somnifera*

Rasa	Tikta (Bitter), Katu (Pungent), Madhura (Sweet)
Guna	Laghu (Light), Snigdha (Oily)
Virya	Ushna (Hot)
Vipaka	Madhura (Sweet)
Doshakarma	Kapha-Vatashamak (Alleviates K and V Dosha)

Table 5: Phytoconstituents of *Withania Somnifera*

Leaves	The leaves of the plant are reported to contain 12 withanolides, 5 unidentified alkaloids, glycosides, chlorogenic acid, many free amino acids, glucose, condensed tannins and flavonoids (Khare, 2007). Withaferin A, a steroidal lactone is the most significant withanolide isolated from the extract of the leaves and dried roots of *Withania somnifera*. (Anonymous, 1982).
Fruit	The green berries contain proteolytic enzyme, amino acids, condensed tannins, and flavonoids. They contain a high fraction of free amino acids which include alanine, proline, glycine, tyrosine, hydroxyproline, valine, aspartic acid, glutamic acid, cystine and cysteine. The occurrence of a proteolytic enzyme, chamase in the berries may be responsible for the high content of the amino acid (Qamar et al., 2012).
Root	The roots are reported to contain amino acids, alkaloids, volatile oil, steroids, starch, reducing sugars, hentriacontane, dulcitol, glycosides, withaniol, an acid, and a neutral compound. Basic alkaloids include pseudotropine, anahygrine, cuscohygrine, tropine, anaferine, withananine, isopelletierine, pseudo-withanine, withananinine, somnine, somniferine, somniferinine. Neutral alkaloids include 3- tropyltigloate and an unidentified alkaloid. Other alkaloids include withanine, withasomnine, and visamine (Khare, 2007). The free amino acids identified in the root include aspartic acid, glycine, tyrosine, alanine, proline, tryptophan, glutamic acid, and cystine (Khare, 2007).
Stem	The stem of the plant contains condensed tannins and flavonoids (Qamar et al., 2012).
Bark	The bark contains a number of free amino acids (Anonymous, 1982).
Shoot	The tender shoots are rich in crude protein, calcium and phosphorous, and are not fibrous. They are reported to contain scopoletin (Qamar et al., 2012).

Pharmacological activities

Anti-inflammatory and Anti-arthritic activity

Ashwagandha has confirmed some very efficient anti-inflammatory activity. In fact, in one study its anti-inflammatory activity was comparable to that of a 5 mg/kg dose of hydrocortisone (Dhuley, 2007). In another study, five plants were assessed for their anti-inflammatory activity. Results showed that while each of the plants possessed varying degrees of anti-inflammatory activity, Ashwagandha possessed the greatest (Bone, 1996). Perhaps the anti-inflammatory activity of Ashwagandha explains its efficacy in arthritis. In a one-month study, a combination of Ashwagandha, Boswellia serrata, Tumeric, and zinc were given to 42 patients with osteoarthritis. At the end of the study, there was a considerable drop in severity of pain and disability (Ichikawa, 2006).

Immunomodulatory Activity

Ashwagandha showed a considerable modulation of immune reactivity in animal models. Administration of Ashwagandha was found to prevent myelo-suppression in mice treated with three immunosuppressive drugs viz. cyclophosphamide, azathioprin, and prednisolone. Treatment with Ashwagandha was found to significantly increase Hb concentration, RBC count, platelet count, and body weight in mice (Ziauddin *et al*., 1996). Administration of Ashwagandha extract was found to significantly reduce leucopenia induced by cyclophosphamide (CTX) treatment. Administration of Ashwagandha extract increased the number of esterase positive cells in the bone marrow of CTX treated animals, compared to the CTX alone treated group (Davis *et al*., 1998). Administration of Ashwagandha extract was found to significantly decrease leucopenia induced by sub-lethal dose of gamma radiation (Kuttan, 1996). Withaferin A and Withanolide E exhibited specific immunosuppressive consequence on human B and T lymphocytes and on mice thymocytes. Withanolide E had specific effect on T lymphocytes whereas Withaferin A affected both B and T lymphocytes (Aggarwal *et al*., 1999; Davis *et al*., 2000, Gautam *et al*., 2004; Rasool *et al*., 2006; Rastogi *et al*., 1998).

Anti-oxidant activity

Researchers from Banaras Hindu University in Varanasi, India, have discovered that some of the chemicals found in *Withania somnifera* are influential 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 (Dhuley, 2007). These findings are reliable with the therapeutic use of *Withania somnifera* as an Ayurvedic rasayana. The antioxidant effect of active principles of *Withania 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 (Bone, 1996).

Anti-stress and Anabolic activity

Given their relative similarities in function, a comparative study was performed on Ginseng (*Panax ginseng*), and Ashwagandha (*Withania somnifera*). Using aqueous suspensions of the powdered root, each herb was tested in mice: (1) for anti-stress activity (by the swimming endurance test); and (2) anabolic activity (by the weight measurement of body weight and levator ani muscle). In the swimming endurance test, Ashwagandha and Ginseng each showed anti-stress activity as compared to the control group, although the activity was higher with Ginseng. In the anabolic study, the mice treated with Ashwagandha showed a greater gain in body weight than those treated with Ginseng, although significant anabolic activity was observed for both herbs (Grandhi, 1994).

Neuropharmacological Activity

Total alkaloidal fraction of root extract showed prolonged hypotensive, bradycardiac and respiratory stimulant activities in dogs. Hypotensive effect was mainly due to autonomic ganglion blocking action and was augmented by the depressant action on higher cerebral centres. The total alkaloids produced a taming and a mild depressant effect (tranquillizer-sedative type) on the CNS in several experimental animals (Rastogi et al., 1998). Systemic administration of Asgand root extract led to differential effects on acetylcholinesterase (ACHE) activity in basal forebrain nuclei. Slightly enhanced ACHE activity was found in the lateral septum and globus pallidus. Asgand root extract affects preferentially events in the cortical and basal forebrain cholinergic signal transduction cascade. The drug induced increase in cortical muscarinic acetylcholine receptor capacity might partly explain the cognition-enhancing and memory-improving effects of extract from *Withania somnifera* observed in animals and humans (Schliebs et al., 1997).

Hypothyroid activity

Animal studies have shown that Ashwaganda may have an effect on thyroid activity. An aqueous extract of dried Withania root was given to mice daily for 20 days. Significant increases in serumT4 were observed, indicating the plant has a stimulating effect at the glandular level. *Withania somnifera* may also stimulate thyroid activity indirectly, via its effect on cellular antioxidant systems. These results indicate Ashwaganda may be a useful botanical in treating hypothyroidism (Panda, 1996; Panda, 1998).

Anti-carcinogenic activity

Ashwagandha is reported to have anti-carcinogenic effects. Research on animal cell cultures has shown that the herb decreases the levels of the nuclear factor kappaB, suppresses the intercellular tumor necrosis factor, and potentiates apoptotic signaling in cancerous cell lines (Ichikawa et al., 2006). One of the most exciting of the possible uses of Ashwagandha is its capacity to fight cancers by reducing tumor size (Prakash et al., 2002; Jayaprakasam et al., 2003). To investigate its use in treating various forms of cancer, the antitumor effects of *Withania somnifera* have been studied by researchers. In one study, the herb was evaluated for its anti-tumor effect in urethane-induced lung tumors in adult male mice (Singh et al., 1986). Following administration of Ashwagandha over a period of seven months, the histological appearance of the lungs of animals which received the herb was similar to those observed in the lungs of control animals.

Anti-hyperglycemic Effect

Ashwagandha along with other ingredients of a composite formulation (Transina) have been reported to decrease streptozocin (STZ)-induced hyperglycemia in rats. This anti-hyperglycemic effect may be due to pancreatic islet free radical scavenging activity because the hyperglycemic activity of STZ is a consequence of decrease in pancreatic islet cell superoxide dismutase (SOD)

activity leading to the accumulation of degenerative oxidative free radicals in islet-beta cells (Bhattacharaya et al., 1997).

Anti-aging 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 (Bone, 1996).

Musculotropic Activity

The total alkaloids of Asgand 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 (Anonymous, 1982).

Macrophage-Activating Effect

The chemotactic activity of macrophages and production of interleukin-1 (IL-1) and tumour necrosis factor (TNF) were significantly reduced in mice treated with the carcinogen ochratoxin A (OTA). Administration of Asgand with other drugs was found to significantly inhibit OTA-induced suppression of macrophage chemotaxis and production of IL-1 and TNF by macrophages (Dhuley, 1997).

Morphine Tolerance and Dependence-Inhibiting Effect

Repeated administration of Asgand in mice attenuated the development of tolerance to the analgesic effect of morphine. Asgand also suppressed morphine-withdrawal jumps, a sign of the development of morphine dependence (Kulkarni et al., 1997). Administration of glycowithanolides of *Withania somnifera* was found to suppress morphine- induced inhibition of intestinal motility and to attenuate the development of tolerance to the analgesic effect of morphine in mice (Rao et al., 1995).

Anticonvulsant Activity

Administration of Asgand root extract was found to reduce jerks and clonus in 70% and 10% animals respectively with dose of 100mg/kg and reduction in the severity of pentylene tetrazole (PTZ)-induced convulsions was evident from EEG wave pattern (Kulkarni et al., 1996). Asgand root extract showed reduction in severity of motor seizures induced by electrical stimulation in right basilateral amygdaloid nuclear complex through bipolar electrodes. The protective effect of Asgand extract in convulsions has been reported to involve GABAergic mediation (Kulkarni et al., 1993).

Hepatoprotective Activity

Withaferin A at 10mg/kg dose showed significantly protective effect against CCl4-induced hepatotoxicity in rats. It was as effective as hydrocortisone dose for dose (Khare, 2007, Rastogi et al., 1998).

Cardio protective activity

Ashwagandha has been evaluated in clinical studies with human subjects for its diuretic, hypoglycemic, and hypocholesterolemic effects (Andallu and Radhika, 2000). Six type 2 diabetes mellitus subjects and six mildly hypercholesterolemic subjects were treated with a powder extract of the herb for 30 days. A decrease in blood glucose comparable to that which would be caused by administration of a hypoglycemic drug was observed. Significant increases in urine sodium, urine volume, and decreases in serum cholesterol, triglycerides, and low-density lipoproteins were also seen.

Conclusion

Indigenous herbal medicines have been popular since time immemorial and recently have also commanded major attention worldwide due to their potential neutraceutical values. Herbs are the likely drugs used to regain the alterations made in normal physiological system by foreign organisms or by any malfunctioning of the body. A comprehensive and organized study is required for recognition, cataloguing and documentation of plants, which may provide a significant way for the encouragement of the traditional knowledge of the herbal medicinal plants. The present literature survey revealed that the plant *Withania somnifera* is a foundation of pharmacologically and medicinally

vital chemicals such as withanolides, hentriacontane, dulcitol, withaniol, amino acids, choline, beta-sitosterol, chlorogenic acid, scopoletin and other useful constituents. With an abundance of antioxidants, iron, amino acids and other phytochemicals it's no surprise that studies suggest Ashwagandha has medicinal properties that can directly and indirectly prevent and treat a number of diseases.

Clinical trials must be conducted to support its therapeutic use. It is also significant to recognize that its extract may be effective not only in the isolation but may have modulating effect when used in combination with other drug.

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