Review Article

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A REVIEW ON ASHWAGANDHA (*WITHANIA SOMNIFERA*): MIND AND BODY REJUVENATOR

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ABSTRACT

Withania somnifera or "Ashwagandha" is generally utilized as a folk medicine to cure different diseases. According to Indian Traditional System (Ayurveda), Ashwagandha is considered as one of the most significant medicinal plant and the best adaptogenic. It is a primary source from where we get withanolides (steroidal lactones), a class of phytochemicals which are utilized as main constituent in numerous formulations endorsed for several ailments. It is referred as a sedative, diuretic, mitigating, mainly used for boosting up the energy, endurance and acts as an adaptogen that exerts a solid immune stimulatory system. It is specially used as nervine tonic. Ashwagandha is utilized for treating cold and cough, ulcers, gauntness, diabetes, conjunctivitis, epilepsy, a sleeping disorder, feeble dementia, sickness, Parkinson's illness, joint inflammation, intestinal contaminations, bronchitis, asthma, ineptitude and sexual problem in patients.

Keywords: Ashwagandha, Rasayana, Withaferin A, Anti-stress, Anti-Parkinson, Glycoside.

INTRODUCTION

In traditional medicinal system number of diseases has been cured by using plants or plant products. The interest has been developed to use herbal plants for their distinctive therapeutic properties because of their common cause, cost viability, and insignificant results[1]. *Withania somnifera* Dunal (Ashwagandha, WS) (Figure 1) is generally used in Ayurveda, the traditional medicinal system of India. It's another name is "Indian Winter Cherry" Or "Indian Ginseng". The roots of this plant are considered to be a rasayana, or best adaptogen. Rasayana means an herbal or metallic formation that promotes a stable state of mental and physical health. It has been a significant medical plant in indigenous clinical system for more than 3000 years. There are about 450 Ayurvedic medicinal plants in which 56 popular plant or one of their ingredients of Ayurvedic prescriptions are available for neurological disorders[2]. *Withania somnifera* (Linn) Dunal is specially used for neurotic action. It holds the most prominent place and also known as "Sattvic Kapha Rasayana" herb[3] in Ayurveda literature. The roots of the plant have a horsey smell (in Sanskrit, ashva means "horse" and gandha means "smell")[4,5]. *Withania* is accounted to have 23 species and out of which *Withania somnifera* (Linn) Dunal and *Withania coagulans* Dunal are of high restorative importance. In Ayurveda it is classified as rasayana and expected to advance physical and emotional health, re-establish the body and increase the life span. It is notable for its activities like Immuno-modulator[6]. The plant having various properties, for example, anti-oxidative[7], anti-stress[8], immunomodulatory[9], anti-diabetic[10], anti-inflammatory[11], anti-microbial[12] and cardio protective[13]. This may also enhance the endothelial function[14], reduced reactive oxygen species, effective to aging effects[15], anxiety and stress[16], arthritis[17], epilepsy[18], fatigue[19], neurodegenerative disease[20], thyroid[21] and skin diseases[22]. Ashwagandha is the main plant whose constituents are used in daily life as supplements for body and brain health[23,24]. In present review authors explained the details description of the plant and their phytochemicals and their numerous therapeutic uses from ayurvedic and modern prospective. Taxonomy and vernacular names of Ashwagandha are given in Table 1 and 2.

Figure 1. ***Withania somnifera***

Table 1: Taxonomy of Ashwagandha

Taxonomical Rank	Taxon
Kingdom	Plantae
Sub-kingdom	Tracheobionata
Super-Division	Spermatophyta
Division	Angiosperma
Class	Dicotyledons
Order	Tubiflorae (Solanales)
Family	Solanaceae
Genus	*Withania*
Species	*somnifera* (L.) Dunal[25]

Table 2: Vernacular names of Ashwagandha

Vernacular Names	
English	Winter cherry, Indian ginseng
Sanskrit	Ashvagandha (Horse smelling)
Hindi	Asgandh
Urdu	Asganda nagori
Punjabi	Aksan, Asgand
Haryanavi	Aksin
Gujarati	Ghodaakun, Asuth
Rajasthani	Sarvgandha
Marathi	Askandha, Kanchuki
Konkani	Fatarfoda
Bengali	Ashvaganda
Oriya	Asugandha
Assamese	Asgandhisrol
Kannada	Amangura, Sogadeberu
Malayalam	Amukkiram, Pevetti
Tamil	Amkulan-kalang, Achuvagandhi
Telugu	Penneru gaddalu
Chinese	Cui Mian Shui, Nan Fei Zui Qie
Danish	Withania
French	Ashwagandha, cerise d'hiver, coqueret somnifère, ginseng indien
German	Ashwagandha, Indischer Ginseng, Schlafbeere, Winterkirsche
Italian	Ashwagandha, ciliegia d'inverno, ginseng indiano
Nepalese	Aasoganda
Norwegian	Withania, indisk ginseng
Persian	Meheman
Sinhalese	Amukkara
Spanish	Ashwagandha, cerezo de invierno, ginseng indiano, oroval
Swedish	Withania, indisk ginseng
Tibetan	Ba-dzi-gandha[26,27]

Botanical description of Ashwagandha (*Withania somnifera*)

Ashwagandha is small, typically erect, woody shrub, unarmed bush belongs to Solanaceae family. The plant grows up to 2 feet of height. Roots are fleshy, whitish brown and bristly covered. The roots are the significant part of the plant and used therapeutically. Leaves are simple ovate, petiolate, smooth, smaller and opposite. flowers are undistinguished, greenish or yellow, in axillary, umbellate cymes; small berries, globose, orange-red when mature, enclosed in the persistent calyx; seeds yellow, reniform. The bright red fruit is collected in the late fall and seeds are dried for planting in the spring season[28].

Geographical distribution

Ashwagandha (*Withania somnifera* (Linn) Dunal) develops all through the drier parts and sub-tropical part of India. It is broadly found in North-Western India specially in Bombay, Gujarat, Rajasthan, Madhya Pradesh, Uttar Pradesh, Punjab and some mountain areas i.e., Himachal Pradesh and Jammu, rising to a height of 1500 meters[29]. The species is widely distributed in many other countries like Pakistan, Afghanistan, Israel, Egypt, Jordan, Morocco, Spain, Canary Island, Eastern Africa Congo, South Africa[30].

Phytochemical constituents of Ashwagandha (*Withania somnifera*)

The phytochemicals of *Withania somnifera* are always of an interest for the researchers. This species has been studied by various researcher and groups of chemicals such as steroidal lactones, alkaloids, flavonoids, tannin have been extracted and identified[31,32]. From the aerial parts, roots and berries of *Withania somnifera* more than 13 alkaloids, 138 withanolides, and several sitoindosides (a withanolide containing a glucose molecule at carbon 27) have been isolated[33-41]. The change in environment may produce a new or unexpected secondary metabolic profile[42].

Withanolides are the main chemical constituents of this plant mainly present in the leaves and roots. Their concentration of constituents falls between 0.001 to 0.5% of dry weight. These are group of C28-steroidal lactones raise on an ergostane structure in which C-22 and C-26 are oxidized to form a six membered lactone ring. A basic structure is designed as a 'withanolide skeleton'[43-45]. Withanolide skeleton described as a 22-hydroxyergostan-26-oic acid, 22-lactone. Tempering of the carbocyclic skeleton or the side chain arise to various novel structure variants with anolides. Reported studies of the plants accumulating that these polyoxygenated compound possess enzymes capable of oxidizing all carbon atoms in the steroid nucleus. Withanolides and ergostane-type steroids having same characteristic feature of C8 or C9 side chain with a lactone or lactol ring. The lactone ring is six-membered which is fused with carbocyclic part of the molecule though oxygen bridge or C-C bond. The oxygen side chain may lead to the bond scission, new bond formation, ring aromatization and many other kinds of arrangements resulting in the novel structures[46,47]. Major compound found in *Withania somnifera* is Withaferin A. whereas, *coagulin* L has been isolated in high amount in *W. coagulans.* Ashwagandhanolide is a unique thio-dimer of withanolide found in the plant[48]. There are 14,20-epoxide bridge specific to *W. coagulans* isolated from withanolides[49].

Recently a novel chlorinated withanolide, 6achloro-5b,17a-dihydroxywithaferin A isolated from *W. somnifera*[50]. Many other chemical constituents have been reported e.g. alkaloid in the roots, fruits and leaves, nicotine, somiferine, somniferinine, withanine, pseudowithanine, tropine, 3a-tigloyloxytropane, choline, cuscohygrine, dl-isopelletierine and new alkaloids anaferine and anhygrine in the medicinal plant[51,52]. The plant also consists of chemical constituents like acylsteryl glucosides, starch, hantreacotane, ducitol and a various of amino acids such as aspartic acid, proline, tyrosine, alanine, gkycine, cysteine, glutamic acid, tryptophan, and iron[53].

Folk view of Ashwagandha (*Withania somnifera*)

Ashwagandha (*Withania somnifera*) is consumed as a folk medicine for various ailments. *Somnifera* is a Latin word which means "sleep-inducer" thus it's specially used as neuroprotective since the ancient times[54]. It is consumed by folk in constipation and memory loss. The paste and powder prepared from the roots of ashwagandha is a great folk remedy for rheumatic pain, arthritis and heart disorders. Also useful in pulmonary tuberculosis, inflammation of joints, epilepsy, brain disorders and in several physiological ailments. Ashwagandha has role in the treatment of ulcers and tumors[55,56]. In the northern part of India *Withania somnifera* is known as "Asgandnagori" or "Ba-dzigandha" and mainly indicated for the treatment of respiratory disorder, hepatic disorders, body strengthening and maintaining the hemoglobin level[57,58]. In Africa, Ashwagandha (*Withania somnifera*) was considered as the weed of contaminated and waste areas. The leaves of the plant were used for skin infections and inflammations. The fine root powder mixed with the fat of animals (crocodile and python) for the treatment of sores and ulcers as an ointment[59]. In the Zulu tradition, roots of ashwagandha are used to protect people from black magic. It was also worked as boundaries for insects[60]. In China, ashwagandha was categorized as "Tonify qi" and "Tonify Blood and Essence"[61] which nourished the heart, kidney, spleen and some other organ of the body.

Ayurvedic view on Ashwagandha (*Withania somnifera*)

Ashwagandha (*Withania somnifera*) plays an important role in Ayurveda. It has been utilized for many years in Ayurvedic medication and categorized as Rasayana herb that maintains body's wellbeing by numerous ways[62,63]. Rasapanchaka of Ashwagandha as per ayurveda is shown

Table 3: Rasa Panchaka (Physical properties) of Ashwagandha

Sanskrit/English	Sanskrit/English
Vipaka/ Metabolic Property	Madhura/Sweet
Virya/ Potency	Ushna/ Hot
Guna/ Physical Property	Snigdha, Laghu/ Oily, light
Rasa/ Taste	Tikta, Kashaya, Madhura /Pungent, Astringent, Sweet[64]

Ashwagandha is Kapha (Water and earth component) and Vata (Air and space component) sedative. It is most commonly utilized restorative plant for the "Vata" constitution, which is related with air and space. It maintains the Vata energy and keeps up flexible skin and joints, a sound body weight, endurance, great mental capacity and a sound sensory system[65]. It is the rasayana herb which is utilized as a tonic for memory endurance and hormonal capacity. There are various therapeutic uses of this plant which is shown in curing Murchha (syncope), Apasmara (epilepsy), Shosha (cachexia), Unmada (craziness/psychosis), Karshya (weakening), Arsha (heaps), Prameha Pidika (diabetic carbuncle), Arbuda (tumor), Gandamala (cervical lymphadenitis), Bhagandara (fistula-in-ano), Guhya-vrana (ulcer in genitalia), Vatarakta (gout), Kushtha (illnesses of skin), Kilasa (vitiligo), Asthibhanga (bone break), Katigraha (stiffness in lumbo-sacral area), Gridhrasi (sciatica), Hanugraha (jaw spasming), Janu Stabdhata (firmness of the knee), Hrudgraha (cardiovascular disappointment), Yoni dosha (issues of female genital lot) and Vidradhi (ulcer)[66].

Some significant properties of Ashwagandha in Ayurveda

Vajikara - Increases sexual craving
Rasayani - Revitalizes the body
Balya - develops strength
Ati shukrala - Enhances quality and amount of semen
Shwitrapaha - Useful in treating of white staining of the skin
Shothahara - Useful in treating of edematous conditions and assists with clearing pollutants (Ama) from the different regions of the body.
Kshayapaha - Useful in treating thinness and under nutritive conditions[67,68]

Modern view on Ashwagandha (*Withania somnifera*)

Herbal plants and chemical constituents derived from the plants represent more than 50% of drugs in modern medication system. For the economic development of world, pharmaceutical industry plays a major role[69]. The process of drug discovery has been revolutionized the development of a novel medicine. When we talk about the development of herbal medication, there is a serious concern about their processing and adulteration. Isolated compounds from these Natural plants undergoes various chemical processes or synthesis which alters the natural plants[70]. Today 80% of antimicrobial, cardiovascular, immunosuppressive drugs are of plant origin. *Withania somnifera* has led the pharmaceuticals to manufactures different products with various therapeutic uses such as sports nutrition, memory, ageing, immune support and weight management. In the market it is introduced mostly into three main part i.e., dietary supplement, cosmetic and beverages. The demand of dietary supplements has also been raised in United states. Due to these business instigating reasons; manufacturer is constantly innovating new herbal products in the market in which adulteration rate has increased and quality of herbal formulation is compromised somewhere.

Reported therapeutic uses of Ashwagandha

Various studies have been conducted on this plant to know its pharmaceutical and therapeutical uses. Large scale clinical studies are still needed to prove the clinical efficacy of this herb, especially in stress related diseases, neuronal disorders and cancers. Some reported studies on *Withania somnifera* are shown in the Table 4.

CONCLUSION

Withania somnifera (Linn) Dunal is generally known as Ashwagandha in Ayurvedic system of medication. The plant has various pharmacological activities like Anti-stress, hepatoprotective, immunomodulatory, anti-arthritis, hostile to tumor, anti-ageing upheld by trial and clinical examinations. Further investigations will improve the support of its diverse activity on living beings. Although the review indicates that the Ashwagandha is a real potent agent which has a various traditional and modern uses.

Table 4: Reported studies on Ashwagandha (*Withania somnifera*)

Anti-inflammatory	It was reported that *Withania somnifera* possesses anti-inflammatory property when compared with a common anti-inflammatory drug, hydrocortisone. The root powder of *W. somnifera* was administrated orally up to 1000 mg kg-1W that decreased the glycosaminoglycan content by 92% which was very high than that of hydrocortisone and phenylbutazone medicine used for inflammation. This study was carried out in mice and it was found that the methanolic fraction of the isolates showed top anti-inflammatory activity as compared to that drug[71-73]
Anti-stress	It was reported that the metabolites extracted from *W. somnifera* have been effective in various brain disorders such as anxiety, epilepsy, catalepsy, depression, and sleep. In a study it was found that the extract worked as a suppressor of corticosterone activating choline acetyltransferase, which increases serotonin level in hippocampus. A rodents injected with Aβ 25-35 and withanolide A and withanoside IV from *W. somnifera* roots promoted neurite outgrowth in cultured neurons.Also, Withanoside IV, sominone, an aglycone of withanoside IV was proved as the main metabolite for the CNS activity[74,75]
Anti-microbial	The ethanolic extract of the leaves or whole plant of *W. somnifera* was used to isolate chemical constituents withanolides which demonstrated anti-microbial properties. The experimental study on mice showed antimicrobial activity of aqueous fruit extracts which were administrated orally against *salmonella* infection. It was also found that extract increased survival rate in mice as well as decreased the bacterial load in various vital organs[76-78].
Immunomodulatory	It was studied that ashwagandha showed important modulation of immune reactivity in animal models. In a study, a mouse was treated with three immunosuppressive drugs i.e., cyclophosphamide, azathioprine and prednisone and ashwagandha. It was found that ashwagandha significantly increase Hb concentration, RBC count, platelet count, and body weight in mice[79]. It was also reported that administration of Ashwagandha extract was found to significantly reduce the leucopenia induced by cyclops hosphamide (CTX) treatment and increased the number of α-esterase positive cells in the bone marrow of CTX treated animals as compared to the CTX alone treated group[80]. It is observed that withaferin A and withanolide E exhibited specific immunosuppressive effect on human B and T lymphocytes and on mice thymocytes too[81]. Withanolide E had specific effect on T lymphocytes whereas withaferin A affected both B and T lymphocytes[82-85].
Anti-cancer	*Withania* had been studied extensively for anticancer property[86-89] and it was studied that a treatment of skin cancer in mice with root extract of *W. somnifera* resulted in a significant decrease in the incidence and average number of skin lesions compared to control group[90,91]. In another study on male albino mice t *W. somnifera* was found to have the anti-tumor effect in urethane-induced lung. The extract of *W. somnifera* administrated and urethane reduced tumor incidence significantly[92,93]. Root extract possess' good anti-cancer properties. Withaferin A and Withanolide D showed significant anti-tumour activity. Steroidal lactone extracted from Ashwagandha was proved to be useful in treating pancreatic cancer [94,95].
Hepato-protective	Various studies showed that the extract of roots of *W. somnifera* have hepatoprotective activity. The extract influenced the levels of lipid peroxidation and therefore provided the hepatoprotection[96]. In another study it was reported that roots of *W. somnifera* consist of different flavonoids and neurotransmitters that activates the neuroendocrine system, resulting in hyperactivity of the endomembrane and exit out of molecules via exocytosis[97].
Antioxidant	In a clinical experiment on animal, it was reported that glycowithanolides extract of *W. somnifera* have antioxidant property. The equimolar concentration of sitoindosides VII-X and withaferin A isolated from *W. somnifera* increases superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) activity in rat brain frontal cortex and striatum in rat mind[98-100].
Anti-arthritic	*W. somnifera* calms the pain produced in nervous system[101]. It was studied and documented that *W. somnifera* possesses anti-arthritis properties[102]. It is widely known to be analgesic as well as antipyretic. A study was reported in which rat experiencing heat analgesia induced by hot plate method. It was observed after 2 hours that the administration analgesic effect of *W. somnifera* was 78.03 %. Whereas paracetamol failed to exhibit any changes[103].
Anti-ulcer	It was observed that *W. somnifera* significantly safeguard against 18 hours immobilization, cold, immobilization and aspirin induced gastric ulcer. Hence the plant was proved to possesses that anti-ulcer property[104]
Hypocholesterolemic and Hypolipidemic	A study was reported that root powder of *W. somnifera* decreases total lipid, cholesterol, and triglycerides in hypercholesterolemia animals. *W. somnifera* showed hypocholesterolemic activity in male albino rats and it could have also mediated through an increased bile acid synthesis for elimination of body[105].
Anti-ageing	A clinical trial study was carried out to observe the anti-ageing properties of *W. somnifera*. In the trial, root powder (0.5 g) was given orally to 101 normal healthy males (50-59 years) for three times in a day for a year. Results showed increase in Hb, RBC, hair melanin and seated stature in treated group in comparison to placebo group. So, after this study the plant is also known for anti-ageing effects[106].
Neurodegenerative diseases	Patients with Alzheimer's diseases having cognitive impairment caused by neuritic atrophy and synaptic loss[107] as per neuropathological post-mortem studies of the brain. The atrophy of neurites has also been observed as an important part of the etiology in the patients suffering with Parkinson's disease, Huntington's disease, and Creutzfeldt– Jakob disease. There are number of studies which showed that Ashwagandha slows, stops, reverses or removes neuritic atrophy and synaptic loss. Glycowithanolides withaferin- A and sitoindosides VII-X extracted from the roots of Ashwagandha significantly reversed ibotenic acid induced cognitive defects in Alzheimer's disease model[108,109].
Sexual behaviour	In rat model, methanolic root extract of *withania somnifera* were orally administered at dose 3000 mg/kg/day for 7 days regularly. In the results it was found that root extract of *withania somnifera* induced a market impairment in sexual vigour, penile erectile dysfunction, sexual performance. This ant masculine effect was attributed to hyperprolactinemic, GABAergic, serotonergic or sedative activities. The plant is mainly detrimental to male sexual problems[110].

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