

A review on ashwagandha (*Withania Somnifera*): An Indian antiaging herb.

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Abstract

Introduction: As a Rasayana, Ashwagandha (*Withania somnifera*) is a highly praised plant in the Indian Ayurvedic healthcare system. It's used for a variety of ailments, but most notably as a nervine tonic. Many scientific researches were conducted in light of these facts, and its adaptogenic and anti-stress properties were thoroughly investigated.

Objective: To study and review the literature available about Ashwagandha.

Discussion and conclusion: Various studies have reported health benefits of Ashwagandha. The use of Ashwagandha as a pretreatment provided significant protection preventing stomach ulcers caused by stress. It has a Cognition Promoting Effect and has been found to be beneficial in youngsters with memory problems as well as elderly adults with memory loss. It's also been reported to help with neurological disorders including Parkinson's, Huntington's, and Alzheimer's. It has a GABA-mimetic action and has been proven to stimulate dendritic development. It has an anti-anxiety impact and boosts energy and mitochondrial health. It is an anti-inflammatory and anti-arthritis drug that has been proven to be beneficial in the treatment of Rheumatoid and Osteoarthritis patients. To show its therapeutic effectiveness in stress-related illnesses, neurological disorders, and malignancies, large-scale investigations are required.

Keywords: Rejuvenator, Adaptogen, neuro regeneration, Anti-tumor, Anti-arthritis, *Withania somnifera*, Ashwagandha.

Introduction

For millennia, Ashwagandha has been utilized as a Rasayana (anti-aging) herb in Ayurveda (India's traditional system of medicine) for its wide-ranging health effects. Rasayana is a herbal or metallic concoction that promotes a young physical and mental state of health as well as happiness. These treatments are given to middle-aged and elderly people to help them live longer. Ashwagandha is the most well-known of the Rasayana herbs in Ayurveda. Adaptogens and anti-stress compounds make up the majority of Rasayana herbs.

Ashwagandha powder is often administered with water, ghee (clarified butter), or honey. Ashwagandha (*Withania somnifera*) is a natural plant that has been studied for a variety of conditions, like fatigue, aches, muscle strain, rheumatoid joint inflammation, skin infections, and for its anticancer properties. Ashwagandha water extract (ASH-

WX) is a strong antioxidant that has been shown to prevent cancer cell proliferation in recent research. For its multimodal effects, *Withania somnifera* (L) is one of the most widely recommended herbs in Ayurvedic medicine. Researchers have studied a wide range of pharmacological actions, including immunomodulatory, antioxidant, anti-inflammatory, anti-stress, antidiabetic, and antihypertensive properties, as well as the organ-protective properties. The preventive action of Ashwagandha in maintaining immunological homeostasis in inflammatory and infectious diseases is supported by scientific research.

Previous studies have established the chemical composition of numerous Ashwagandha extracts and formulations. In a nutshell, withanolides (steroidal lactones), the primary phytochemical in Ashwagandha, play a key role in producing synergistic multimodal activities. The phytochemicals are a collection of C28-steroidal lactone triterpenoids. They

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mainly include with anolides A, B, and D, with a ferin A, with a somnifera A, with anoside IV and V, sitoindoside IX and X, with a none, 12-deoxywithastramonolide, etc. Besides, polyphenols including naringenin, catechin, syringic acid, and p-coumaric acid are found in significant amounts in Ashwagandha extracts. A blend of such phytochemicals makes Ashwagandha as a strong therapeutic herb [1]. This study aims to review the therapeutic uses of Ashwagandha documented in various trials as well as meta-analysis.

Material and Methods

This is a literature review, based on reported scientific studies preferably from PubMed database. The qualities obtained are described in accordance with Ayurvedic literature's traditional usage of Ashwagandha. The undergraduate students of DMAMCHRC, Wanadongri, and Nagpur have conducted this study under guidance of their teaching faculty.

Review of Literature

Ayurveda, India's ancient medical system has been practiced from 6000 BC. Ashwagandha has been administered as a Rasayana for the past 6000 years. Ashwagandha, Latin name, *Withania somnifera*, is known as winter cherry also, found in India in abundance. It is also found in Africa, in some parts of Europe and North America. Ashwagandha is used as a wonder herb of India. It has been used as a key ingredient in various Ayurvedic medicines for treating various health conditions. Ashwagandha root is used as an aphrodisiac, tonic, anthelmintic, diuretic, thermo genic, astringent, stimulant, and anthelmintic [2].

It is commonly administered in malnourished children. When added to milk, it serves as the best nourishment for children. It is also used in general debility in geriatrics. Other uses are in leucoderma, rheumatism, constipation, nervous breakdown, insomnia, goiter etc.

Ashwagandha has attracted the attention of researchers worldwide due its wonderful medicinal properties. Ashwagandha is compared with Panax Ginseng (Chinese/Korean Ginseng) and *Eleutherococcus senticosus* (Siberian Ginseng) for its adaptogenic action, and hence it is widely known as Indian Ginseng also. Many extensive studies on the animals for the adaptogenic (anti-stress) properties of Ashwagandha have shown it to be effective in increasing the stamina (physical endurance) and preventing stress induced gastric ulcer, carbon tetrachloride (CCl₄) induced hepatotoxicity and mortality [3].

The chemistry of Ashwagandha has been studied extensively and more than 35 chemical ingredients have been identified. These chemical constituents have been extracted, and isolated for medicinal purpose. The biologically active chemical constituents are steroidal lactones (withanolides, withaferins), alkaloids (isopelletierine, anaferine), withanolides, and Saponins. Ashwagandha is also rich in iron [4].

Ashwagandha showed anticancer activity in various studies. Previous work done on Ashwagandha leaves found that, water extract of the leaves was effective in various types of cancer. For instance, one study showed that tumour suppressor proteins

(p53 and pRB) were activated by Ashwagandha leaves and it increased the level of cyclin B1 in cancer cells. One more study found that Ashwagandha leaves have cytotoxic effect on MCF-7 breast cancer cells. This was stronger than that exerted on PA-1 and A-459 cancer cell lines [5].

A meta-analysis by Pérez-Gómez et al. showed that Ashwagandha supplements may improve maximum oxygen consumption (VO₂max) in athletes as well as in healthy adults [6]. In this meta-analysis, no article is found to report any related side effect that is attributable to the treatment. The study also reports a high compliance with the Ashwagandha supplements and very few numbers of dropouts. The hypothesis for the encouraging results of supplementation with Ashwagandha can be associated with levels of the physical activity of the participants that promotes and increases the physiological adaptations to exercise. VO₂ max is considered as the most valid parameter for cardiorespiratory fitness [7]. Ashwagandha increases resistance to chemical, biological, and physical stressors. It builds energy and overall strength. Hence, it is known as an “adaptogen.”

The other studies assessing cardiorespiratory and physical endurance of healthy adults have also reported parallel beneficial results with the usage of Ashwagandha, emphasizing the substantial increase in VO₂ max and strengthening of muscles [8,9].

Moreover, Ashwagandha has anti-stress [10,11] and anti-fatigue actions also. This could be the reason behind the significant enhancement in the time of exhaustion in the experimental group [12] Ashwagandha significantly increases red blood cell count and the hemoglobin percentage in animals and in humans also [13,14]. Subsequently it increases the capacity of oxygen transport to the tissues.

Anti-stress activity of Ashwagandha is found to have a significant effect in weight management. Stress causes a rise in serum cortisol levels, which results in increased visceral fat accumulation in humans. Prolonged stress also raises circulating glucocorticoid concentrations, which promotes carbohydrate and fat consumption and lowers energy expenditure by inhibiting corticotrophin-releasing hormone and increasing neuropeptide hypothalamic production. Low leptin levels have also been linked to an increase in anxiety and depression [15]. Leptin is a hormone that controls energy balance by decreasing food intake and, as a result, causes weight reduction. Stress reduction maintains normal leptin levels and aids in the management of obesity.

Ashwagandha is a common herbal medication used to treat infertility and sexual dysfunction. Extracts of Ashwagandha fruits, stems, leaves, and especially roots improve sperm quality indicators like count and motility in men and reduce the effects of toxic chemicals on the gonads in both males and females. Ashwagandha may increase gonadal weights in both sexes. It also promotes oogenesis and spermatogenesis, and balances the levels of testosterone and LH, FSH. Sexual behavior parameters such as the female sexual distress score and the female sexual function index show statistically significant improvement following administration of Ashwagandha extract.

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The exact mechanism of Ashwagandha's effect on the reproductive system is not clear, but it is thought to be related to its anti-oxidative properties and capacity to enhance the hormonal balance of LH, FSH, and testosterone as well as the detoxification process. Furthermore, the GABA mimic property of Ashwagandha extract is considered to play a key role in stimulating gonadotropin-releasing hormone production and restoring hormonal balance [16]. Some clinical trials showed significant anti stress and anti-anxiety activity of Ashwagandha when compared with the placebo group [17]. Besides anti stress and anti-anxiety activity the Ayurveda wonder herb is seen to be helpful in sleep disorders [18,19].

A meta-analysis of five studies found evidence for clinically positive results of Ashwagandha extract on sleep compared to placebo. These studies found a slight but substantial increase in total sleep. The seven-point scale, total sleep time, sleep onset latency, sleep efficiency, and waking time following sleep onset were all employed in these researches. The results were more prominently observed in adults with insomnia, with a therapeutic dosage of 600 mg/day for a treatment period of 8 weeks. The extract of ashwagandha considerably enhanced mental alertness upon awakening. In terms of safety, adverse effects reporting were restricted to mild side effects [20].

Recent clinical trials with randomized double-blind placebo control models with Ashwagandha extracts revealed that at specific doses ranging from 200 mg/kg to 1000 mg/kg WS was not only beneficial, but also safe and well tolerated. Furthermore, several researches have demonstrated anti-cancer activity of Ashwagandha or its main component WFA in human cancer cell lines and animal studies. The safety of Ashwagandha in humans, as well as its potential therapeutic efficacy demonstrated in pre-clinical trials with the underlying varied molecular pathways, implies that Ashwagandha and WFA might be used in patients with various cancers.

There are at least two ways Ashwagandha can be used to treat neoplastic disorders. First, having the Ashwagandha's safety record, it can be given as an adjuvant therapy to reduce the side effects of radiotherapy and chemotherapy owing to its anti-inflammatory properties. Second, because of its potential to aid in radio- and chemo sensitization, Ashwagandha can be used with other conventional medicines such as chemotherapies to synergize and amplify the effects of radiation and chemotherapy. All data so far suggests the potential of Ashwagandha or WFA in cancer treatment. However, this must be confirmed with clinical studies [21,22].

Ashwagandha showed a hopeful phototherapeutic intervention in cases of malignancies that are related to Neuroblastoma related. Neuroblastoma is a very aggressive disease in paediatric patients. It is a disease of the sympathetic nervous system. Treatments are frequently unsuccessful and have severe adverse effects. Differentiation agents are used in conventional neuroblastoma treatment. Normal non-malignant cells are already differentiated. Hence, differentiation treatment has less adverse effects on normal cells than chemo radiotherapy. In a study, it was found that Ashwagandha water extract significantly decrease cell proliferation. It also induces cell differentiation that is specified by morphological changes.

It is also indicated by NF200 expression in IMR-32 cell of neuroblastoma.

Ashwagandha water extract treatment arrested cell cycle at G0/G1 phase and it raised early apoptotic population. Marker of modulation of cell cycle, Cyclin D1, anti-apoptotic marker Akt-P and bcl-xl provide indication that Ashwagandha water extract may prove to be effective in neuroblastoma related malignancies [23].

Ashwagandha also improves the problems induced by (Bisphenol A) BPA which are mostly behavioral problems. BPA is used in production of polycarbonate plastics and epoxy resins. It is a recognized endocrine disruptor and has close similarity to the molecular structure of human oestrogen. The disruption leads to impairment of learning and memory. Along with that, Ashwagandha treatment restores the NMDA receptors in hippocampal region and demonstrated anti-oxidative property while improving the levels of endogenous anti-oxidants in the brain. N-methyl-aspartate-receptors (NMDARs) is a specific inotropic glutamate receptor which is found in the hippocampus of the mid brain are critical in regulating the synaptic plasticity and cognition. Ashwagandha significantly improve cognitive dysfunction which is the primary symptom in many neurodegenerative diseases [24].

Ashwagandha is a useful addition in the treatment of Parkinson's disease also. It is effective in autophagy activation, inhibition of oxidative stress, activation of pro-survival astroglia, and inhibition of pro-inflammatory microglia. Ashwagandha is well-tolerated natural compound to stop neuro degeneration. It could be an effective drug to cease the progression of Parkinson's disease. Ashwagandha root extract has the neuroprotective effect against β -amyloid and HIV-1Ba-L (clade B) induced neuro-pathogenesis.

Ashwagandha is studied extensively for its uses in COVID 19. One of the studies revealed that four constituents of Ashwagandha exhibited the maximum docking energy among the designated natural constituents. The constituents are Withanoside II, Withanoside IV, Withanoside V and Sitoindoside. Moreover, MD simulation (molecular dynamics simulation) study of 100 ns expects Withanoside V have strong binding affinity. It also has hydrogen-bonding interactions with the active site of protein and shows its stability in the active site. The binding free energy score is also the highest score in comparison with the other selected compounds. The study suggests that Withanoside V, the compound present in Ashwagandha might serve as a strong inhibitor against Mpro (main protease) of SARS-CoV-2 to battle COVID-19 and it may have an antiviral effect on nCoV.

A review article discusses about the potential of Ashwagandha for prophylaxis as well as management of COVID-19. The various experimental studies taken into account in this review. These studies indicate that Ashwagandha potentially maintain immune homeostasis, regulate inflammation. It also suppresses pro-inflammatory cytokines and provides organ protection (lung, liver, nervous system, heart and kidney) [25].

Discussion and Conclusion

With the review of the scientific data, we can conclude that Ashwagandha is a significantly potent regenerative drug (Rasayana of Ayurveda). It has multiple pharmacological actions like antitumor, anti-arthritis, anti-inflammatory, analgesic. It is anti-stress and neuroprotective also. It has been found useful in various conditions like Parkinson's disease, dementia, stress induced diseases and others. Apparently, Ashwagandha is found to be safe in various clinical studies. Hence, Ashwagandha provides a potent, safe natural alternative in various diseases. More clinical studies are required to prove Ashwagandha's benefits in various health conditions and rule out the side effects if any.

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