

AN REVIEW ON ASHWAGANDHA: A RASAYANA (REJUVENATOR) OF AYURVEDA

Prachi S. Shahane^{1*} and Chetan Ghulaxe²¹Assistant Professor M.S Ayurved College Gondia Maharashtra.²Assistant Professor P.R Patil Institute of Pharmacy Talegaon SP Dist. Wardha.

*Corresponding Author: Dr. Prachi S. Shahane

Assistant Professor, M.S Ayurved College Gondia Maharashtra.

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INTRODUCTION

Withania somnifera (Ashwagandha) is very revered herb of the Indian Ayurvedic system of medicine as a Rasayana (tonic). It is used for various kinds of disease processes and specially as a nervine tonic. Considering these facts many scientific studies were carried out and its adaptogenic / anti-stress activities were studied in detail. In experimental models it increases the stamina of rats during swimming endurance test and prevented adrenal gland changes of ascorbic acid and cortisol content produce by swimming stress. Pretreatment with *Withania somnifera* (WS) showed significance protection against stress induced gastric ulcers. WS have anti-tumor effect on Chinese Hamster Ovary (CHO) cell carcinoma. It was also found effective against urethane induced lung-adenoma in mice. In some cases of uterine fibroids, dermatosarcoma, long term treatment with WS controlled the condition. It has a Cognition Promoting Effect and was useful in children with memory deficit and in old age people loss of memory. It was also found useful in neuro degenerative diseases such as Parkinson's, Huntington's and Alzheimer's diseases. It has GABA mimetic effect and was shown to promote formation of dendrites. It has anxiolytic effect and improves energy levels and mitochondrial health. It is an anti-inflammatory and antiarthritic agent and was found useful in clinical cases of Rheumatoid and Osteoarthritis. Large scale studies are needed to prove its clinical efficacy in stress related disorders, neuronal disorders and cancers.

Scientific classification

Kingdom: Plantae, Plants;
Subkingdom: Tracheobionta, Vascular plants;
Super division: Spermatophyta, Seeds plants;
Division: Angiosperma
Class: Dicotyledons
Order: Tubiflorae
Family: Solanaceae
Genus: *Withania*
Species *somnifera* Dunal

AIM AND OBJECTIVE

- 1) To study the chemical composition of numerous Ashwagandha extracts.
- 2) To study various formulation

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.

Chemical composition

The biologically active chemical constituents of *Withania somnifera* (WS) include alkaloids (isopelletierine, anaferrine, cuseohygrine, anahygrine, etc.), steroidal lactones (withanolides, withaferins) and

saponins (Mishra, 2000 et al., 2000). Sitoindosides and acylsterylglucosides in Ashwagandha are anti-stress agents. Active principles of Ashwagandha, for instance the sitoindosides VII-X and Withaferin-A, have been shown to have significant anti-stress activity against acute models of experimental stress (Bhattacharya et al., 1987). Many of its constituents support immunomodulatory actions (Ghosal et al., 1989). The aerial parts of *Withania somnifera* yielded 5-dehydroxy withanolide-R and withasomniferin-A (Alta-urRahman et al., 1991).

**Scientific studies on ashwagandha
Adaptogenic / Anti-stress effect**

Ashwagandha is compared well with *Eleutherococcus senticosus* (Siberian Ginseng) and *Panax Ginseng* (Chinese / Korean Ginseng) in its adaptogenic properties, and hence it is popularly known as Indian Ginseng (Singh et al., 2010). The extensive studies on the biological model of animals for the adaptogenic / anti-stress properties of Ashwagandha (Abbas and Singh, 2006; Kalsi et al., 1987; Singh et al., 1976, 1977, 1981, 1982, 1993a, 1993b, 2003; (Singh, 1995a, 1995b, 2006, 2008) 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. Ashwagandha

have similar anti-stress activity in rats (Archana & Namasivayam, 1999). An aqueous suspension of Ashwagandha root was used at 100 mg/kg/oral dosage. The results indicate a significant increase in the plasma corticosterone level, phagocytic index and avidity index in rats subjected to cold swimming stress. In the rats pretreated with the drug, these parameters were near control values and an increase in the swimming time was observed. These results indicate that *Withania somnifera* used in the crude form is a potent anti-stress agent. The results of above studies lend support to the hypothesis of tonics, vitalizers and rejuvenators of Ayurveda which indicate clinical use of *Withania somnifera* in the prevention and treatment of many stress induced diseases like arteriosclerosis, premature ageing, arthritis, diabetes, hypertension and malignancy (Singh, 1986, 2005; Singh and Misra, 1993).

- i. Effect on cortisol and ascorbic acid contents of adrenals. The cortisol content of adrenals was reduced significantly in animals subjected to 5 h constant swimming as compared to non-swimmer group. Pretreatment with WS prevented reduction of the cortisol content of adrenals. The ascorbic acid content was also reduced significantly after 5 h of swimming as compared to the animal of non-swimmer group. Pretreatment with WS prevent reduction in ascorbic acid content which occurs after swimming stress. Thus, *Withania somnifera* treatment prevents, decrease of adrenal cortisol and ascorbic acid which occurs due to swimming stress.
- ii. Anti-ulcerogenic effect: Ashwagandha was found to be useful in the prevention of stress-induced ulcers of the gastrointestinal tract (Singh et al. 1982). It showed significant protection against 18 h immobilization, cold + immobilization (4h) and aspirin induced gastric ulcers and lowered the mean ulcer index in rats.
- iii. Effect on leucocytosis Ashwagandha given to a group of mice with milk injection produced reduction in leucocytosis.
- iv. Anabolic effects: There was a significant increase in the body weights of the Ashwagandha treated group as compared to control for a period of 3 months in rats. V Acute toxicity studies In acute toxicity studies the LD50 of *Withania somnifera* was found to be 1750 mg (p.o.) in albino mice

Effect on central nervous system

Cognition Promoting Effect Ashwagandha is a well known Ayurvedic Rasayana, and belongs to a sub-group of Rasayanas known as Medhyaraslāyanas. Medhya typically refers to the mind and mental/intellectual capacity. Thus, Medhya Rasayana like Ashwagandha, is used to promote intellect and memory. The cognition-promoting effect of Medhya Rasayanas is best seen in children with memory deficits, or when memory is compromised following head injury, or a prolonged illness and in old age (Singh and Udupa., 1993). Effect on neurodegenerative diseases such as Parkinson's, Huntington's and Alzheimer's diseases.^[1]

In patients with Alzheimer's disease, neuritic atrophy and synaptic loss (Dickon and Vicker, 2001) are considered the major causes of cognitive impairment, as based on the results of neuropathological post-mortem studies of the brain (Dekosky & Scheff, 1990). In the brains of patients suffering from other neurodegenerative diseases such as Parkinson's disease, Huntington's disease, and Creutzfeldt–Jakob disease, the atrophy of neurites has also been observed as a significant part of the etiology. There are dozens of studies that show that Ashwagandha slows, stops, reverses or removes neuritic atrophy and synaptic loss. Therefore Ashwagandha can be used to treat Alzheimer's, Parkinson's, Huntington's and other neurodegenerative diseases at any stage of the disease, even before a person has been diagnosed and is still in the state of mild forgetfulness, etc. Glycowithanolides withaferin- A and sitoindosides VII-X isolated from the roots of Ashwagandha significantly reversed ibotenic acid induced cognitive defects in Alzheimer's disease model (Bhattacharya et al., 1995). Ashwagandha has been described as a nervine tonic (Singh et al., 1988, 1993) in Ayurveda and that is why it is a common ingredient of Ayurvedic tonic. Tonics, rejuvenators and vitalizers of Ayurveda appear to allay disease and induce immunity (Singh et al., 1986) and longevity in the users. Pretreatment with Ashwagandha extract was found to prevent all the changes in antioxidant enzyme activities, catecholamine content, dopaminergic D2 receptor binding and tyrosine hydroxylase expression induced by 6-hydroxydopamine (6-OHDA) in rats (an animal model of Parkinson's disease) in a dose-dependent manner. Thus, these results suggest that Ashwagandha may be helpful in protecting the neuronal injury in Parkinson's disease (Nagashyana et al., 2000).

GABA-mimetic effect on neurodegeneration and neuroregenerative potential Behavioral experiments have lent support to the GABA-mimetic activity of Ashwagandha root extract. GABAergic neurodegeneration due to neuroleptic-induced excitotoxicity and oxidative stress is one of the etiopathological mechanisms in the pathophysiology of tardive dyskinesia (Gunne et al., 1993) and GABA agonists are shown to be effective in ameliorating the symptoms of tardive dyskinesia. The beneficial effect of Ashwagandha root extract might be due to its GABA mimetic activity. Ashwagandha, its constituents and the metabolites of its constituents promote the growth of nerves after taking it for 7 days. An intriguing study demonstrated that chronic oral administration of withanoside IV attenuated the axonal, dendritic and synaptic losses and memory deficits induced by amyloid peptide Aβ(25-35) in mice (Kuboyama et al, 2006). After oral administration in mice, withanoside IV was metabolized into sominone, which induced marked recovery in neurites and synapses and also enhanced axonal and dendritic outgrowth and synaptogenesis. These effects were maintained for at least 7 days after discontinuing withanoside IV administration. These data

suggest that withanoside IV, and its metabolite, sominone, may have clinical usefulness as antidementia drugs. Another team found that the methanol extract of Ashwagandha (5 mg/ml) significantly increased the percentage.

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 adjunct 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

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.

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 disrupt or 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 hippo campal region and demonstrated antioxidative property while improving the levels of endogenous antioxidants 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 neuro degenerative diseases.

DISCUSSION AND CONCLUSION

Withania somnifera (Ashwagandha) is a plant used in medicine from the time of Ayurveda, the ancient system of Indian medicine. The plant has also been widely

studied for their various pharmacological activities like antioxidant, anxiolytic, adaptogen, memory enhancing, antiparkinsonian, antiinflammatory, antitumor properties. Various other effects like immunomodulation, hypolipidemic, antibacterial, cardiovascular protection, sexual behaviour, have also been studied. While *Withania somnifera* has been used successfully in Ayurvedic medicine for centuries, more clinical trials should be conducted to support its therapeutic use.

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