

A Review on Therapeutic Use of *Withania Somnifera* (Ashwagandha)

Yogita Ale¹, Shivani Sharma¹, Ashutosh Chaudhary^{2*}, Amandeep Singh³

¹Assistant Professor, Dev Bhoomi Institute of Pharmacy & Research, Dehradun.

²Research Scholar, Dev Bhoomi Institute of Pharmacy & Research, Dehradun

³Professor, Dev Bhoomi Institute of Pharmacy & Research, Dehradun

ABSTRACT

Withania somnifera (Ashwagandha) is a highly esteemed medicine of the Indian Ayurvedic medicine system as Rasayana (tonic). It is used in a variety of disease procedures and especially as a tonic for nervine. Based on these facts many scientific studies were conducted and its apoptogenic / anti-stress activities were studied in detail. In experimental models it increases the rats' strength during endurance testing and inhibits changes in the adrenal gland of ascorbic acid and the cortisol content produced by swimming pressure. Preparations with *Withania somnifera* (WS) have shown significant protection against stomach ulcers caused by stress. WS has anti-tumor effect on Chinese Hamster Ovary (CHO) cell carcinoma. It has also been found to be effective against urethane-induced lung-adenoma in mice. In some cases of uterine fibroids, dermatosarcoma, long-term treatment with WS controls the condition. It has a Cognitive Impact Effect and has been helpful for children with memory impairment and aging. It has also been found to be effective in non-neurodegenerative diseases such as Parkinson's, Huntington's and Alzheimer's diseases. It has an imitation effect of GABA and has been shown to promote the formation of dendrites. It has a stressful effect and improves energy levels and mitochondrial health. An anti-inflammatory and anti-arthritic agent and found to be effective in the treatment of Rheumatoid and Osteoarthritis. Extensive studies are needed to prove its clinical effectiveness in stress-related disorders, neuronal disorders and cancer.

Keywords: *Withania somnifera*, rejuvenator, adaptogen / anti-stress, anti-tumor, neuroregenerative, anti-arthritic .

INTRODUCTION

Ashwagandha (*Withania somniferous*, fam. Solanaceae) is best known as "Indian Winter cherry" or "Indian Ginseng". It is one of the most important herbs of Ayurveda (traditional Indian medicine) used for thousands of years as Rasayana for its extensive health benefits. Rasayana is described as a herbal remedy or substance that promotes youthful physical and mental health and enhances happiness. These types of herbs are given to young children as tonics, and are taken by middle-aged and adults to prolong life. Among the ayurvedic herbs in Rasayana, Ashwagandha occupies the most prominent place. Known as "Sattvic Kapha Rasayana" Herb (Changhadi, 1938). Most Rasayana remedies are adaptogen / anti-stress agents.

Ashwagandha is commonly found as churna, fine ground flour that can be mixed with water, ghee (refined butter) or honey. It improves brain function and nervous system and improves memory. It improves the functioning of the reproductive system which promotes healthy sexual and reproductive balance. Being a powerful adaptogen, it improves the body's resilience to stress. Ashwagandha

improves the immune system by improving the immune system between cells. It also has powerful antioxidant properties that help protect against cell damage caused by free radicals.

CHEMICAL COMPOSITION

Chemical agents that act in terms of *Withania somnifera* (WS) include alkaloids (isopelletierine, anaferine, cuseohygrine, anahygrine, etc.), steroidal lactones (withanolides, withaferins) and saponins (Mishra, 2000 et al., 2000). Ashwagandha Sитоindosides and acylsterylglucosides are anti-depressant substances. The active principles of Ashwagandha, for example sитоindosides VII-X and Withaferin-A, have been shown to have significant anti-depressant functions against severe forms of experimental stress (Bhattacharya et al., 1987). Most of its components support the immune action (Ghosal et al., 1989). The aerial components of *Andania somnifera* produced 5-dehydroxy with gold-R and andasomniferin-A (Atta-ur-Rahman et al., 1991).

ANCIENT USE OF ASHWAGANDHA

Ayurveda, a traditional medical system practiced in India can be traced back to 6000 BC (Charak Samhita, 1949). For 6000 years Ashwagandha has been used as a Rasayana. Ashwagandha root is considered a tonic, aphrodisiac, narcotic, diuretic, anthelmintic, astringent, thermogenic and stimulant. The root smells like a horse ("ashwa"), which is why it is called Ashwagandha (when eaten it gives the horse strength). It is widely used in pediatric weight loss (when given milk, it is the best tonic for babies), weakness from old age, arthritis, vata regenerative conditions, leucoderma, constipation, insomnia, mood disorders, goiter etc. (Sharma, 1999). Attachments formed when roots are crushed with water are used to reduce inflammation in the joints (Bandar, 1970). It is also used locally for carbuncles, ulcers and painful inflammation (Kritikar and Basu, 1935). The root combined with other drugs is limited to snake venom and scorpion-sting. It is also useful for leucorrhoea, abscesses, acne, flatulent colic, worms and fungi (Misra, 2004). Nagori Ashwagandha is the highest of all Ashwagandha species. Great benefits come from the use of the new Ashwagandha powder (Singh, 1983).

The leaves are bitter and are prone to fever, painful inflammation. The flowers are astringent, depurative, diuretic and aphrodisiac. The seeds are anthelmintic and mixed with astringent salt and rock removes white spots on the cornea. Ashwagandha Rishta prepared from it is used in hysteria, anxiety, memory loss, syncope, etc. It also acts as a stimulant and increases sperm count (Sharma, 1938).

SCIENTIFIC RESEARCH ON ASHWAGANDHA ADAPTOGENIC / ANTI-STRESS EFFECT

Ashwagandha is well compared to *Eleutherococcus senticosus* (Siberian Ginseng) and Panax Ginseng (Chinese / Korean Ginseng) in its adaptogenic areas, hence it is widely known as Indian Ginseng (Singh et al., 2010). Extensive studies of the animal model of apoptogenic / anti-stress properties of Ashwagandha. has been shown to be effective in increasing energy (physical endurance) and preventing the stress caused by a stomach ulcer, carbon tetrachloride (CCl₄) causing hepatotoxicity and death. Ashwagandha has a similar anti-stress function in mice (Archana and Namasivayam, 1999). The aqueous suspension of Ashwagandha roots was applied at 100 mg / kg / oral dose. The results show a significant increase in plasma corticosterone levels, a phagocytic index and an avidity index in mice exposed to cold swimming pressure. In tree-lined mice, these limits were close to control values and an increase in swimming time was observed. These results indicate that *Withania somnifera* used raw has been a powerful anti-depressant drug. The results of the above

studies support the thinking of tonics, vitalisers and rejuvenators in Ayurveda that show the clinical use of *Andania somnifera* in the prevention and treatment of many depressive disorders such as arteriosclerosis, premature aging, arthritis, diabetes, high blood pressure, and high blood pressure. and risk (Singh, 1986, 2005; Singh and Misra, 1993).

I. EFFECT ON SWIMMING PERFORMANCE

Ashwagandha has been shown to increase swimming performance in mice as judged by the increase in swimming time during physical endurance testing. Ashwagandha antistress properties have been investigated in all of these studies using adult mice undergoing a placebo-controlled test. Animals treated with Ashwagandha have shown a significant increase in swimming time compared to controls. The rat control team swam for a total of 385 minutes, and the drug-addicted animals continued to swim for an average of 740 minutes. Therefore, swimming time was almost doubled after treatment with *Withania somnifera* (WS).

II. EFFECT OF CORTISOL AND ASCORBIC ACID CONTENT ON THE ADRENALS

The cortisol content of the adrenals is significantly reduced in animals less than 5 h swimming each time compared to the non-swimming group. Pre-treatment with WS prevented the reduction of the cortisol content of the adrenals. The ascorbic acid content was also significantly reduced after 5 h of swimming compared to the non-swimming group animal. Re-treatment with WS prevents a decrease in the ascorbic acid content that occurs after swimming pressure. Therefore, treatment with *Andania somnifera* prevents, decreased adrenal cortisol and ascorbic acid occurring due to swimming pressure.

III. ANTI-ULCEROGENIC EFFECT

Ashwagandha has been found to be effective in preventing ulcers caused by pressure on the intestinal tract (Singh et al. 1982). It has shown significant protection against extinction of 18 h, cold + immobilization (4h) and aspirin which has caused stomach ulcers and reduced the mean of the mean wound in mice.

IV. EFFECT OF LEUCOCYTOSIS

Ashwagandha given to a group of rats by milk injection produced a reduction in leucocytosis.

V. ANABOLIC EFFECTS:

There was a significant increase in the body mass index of the Ashwagandha-treated group compared with the 3-month control in mice.

TOXICOLOGICAL STUDIES

In toxic studies the LD50 of *Andania somnifera* was found to be 1750 mg (poo) in albino mice.

ANTI-TUMOR EFFECT ON CHINESE HAMSTER OVARY (CHO) CARCINOMA CELLS

The roots of *Withania* have created a barrier effect of about 49% on the colonial function of CHO cells. It inhibits cell growth and inhibits cell attachment. It caused the inhibition of long-term growth of CHO cells which was dependent on cell density and the duration of Ashwagandha exposure (Sumantran et al., 2007). This information will also help oncologists who plan to use Ashwagandha as synergizers with conventional chemotherapy or radiation therapy.

EFFECTS OF URETHANE ON LUNG-ADENOMA IN MICE AND OTHER SUBJECTS:

Ashwagandha has been found to be very useful in the detection of carcinogenesis in a crude way. Prevents urethane-induced lung-adenomas in mice. Other urethane effects such as leucopenia are also banned. Urethane, a chemical antagonist, causes various side effects, all of which Ashwagandha has blocked. The drug can be used as a combination of chemical cancer or radiotherapy. Apart from having an anti-cancer effect it will also reduce the side effects of anti-cancer agents, which consistently reduces insecurity and quality of life. WS also acts as an immunomodulator and therefore can extend the life expectancy of cancer patients, where the patient's immune system is depleted which is a cause for concern. Our results suggest its use as an anti-tumor (Singh et al. 1979, 1981, 1986, 2010) and as an immunomodulator agent.

Studies and studies of Ashwagandha's activities in preventing and reducing tumor growth have shown encouraging evidence that these highly specific herbs can be very effective in treating plant-related diseases including cancer (Singh and Gilca, 2010). It also improves white blood cell count (WBC) and function, which is limited to chemotherapy for cancer treatment. Ashwagandha in the treatment of uterine fibroids has been shown to reduce the tendency of uterine bleeding and the disappearance of fibroids after long-term treatment.

EFFECT ON THE CENTRAL NERVOUS SYSTEM COGNITION PROMOTING THE EFFECT

Ashwagandha is a well-known Ayurvedic Rasayana, and belongs to a small group of Rasayana known as the Medhyarasayanas. Media often refers to power and mind / mind. Media Rasayana, like Ashwagandha, therefore, is used to promote intelligence and memory. The effect of promoting Medya Rasayanas' understanding is best seen in children with memory deficits, or when memory is at risk following head injuries, or chronic illness and aging (Singh and Udupa., 1993).

EFFECT OF NEURODEGENERATIVE DISEASES SUCH AS PARKINSON'S, HUNTINGTON'S DISEASE AND ALZHEIMER'S DISEASE

In patients with Alzheimer's disease, neuritic atrophy and synaptic loss (Dickon and Vicker, 2001) are considered to be major causes of mental retardation, based on the results of post-mortem brain studies (DeKosky & Scheff, 1990). In the brains of patients suffering from other non-neurodegenerative diseases such as Parkinson's disease, Huntington's disease, and Creutzfeldt-Jakob disease, atrophy of neurites is also considered an important part of etiology. There are many studies showing that Ashwagandha decreases, stops, reverses or eliminates neuritic atrophy and synaptic loss. Ashwagandha can therefore be used to treat Alzheimer's, Parkinson's, Huntington's and other non-neurodegenerative diseases in any stage of the disease, even before a person is diagnosed and is in a state of paralysis, etc. X-rays away from Ashwagandha roots significantly altered the botenic acid that has caused mental retardation in the Alzheimer's disease model (Bhattacharya et al., 1995).

Ashwagandha has been described as a nervine tonic (Singh et al., 1988, 1993) in Ayurveda and hence it is a common ingredient in Ayurvedic tonic. Tonics, rejuvenators and vitalizers of Ayurveda have been shown to reduce disease and cause immunity (Singh et al., 1986) and longevity for users.

Ashwagandha regimens have been found to prevent all changes in antioxidant enzyme activity, catecholamine content, binding of dopaminergic D2 receptor and tyrosine hydroxylase expression induced by 6-hydroxydopamine (6-OHDA) in mice (animal model). of Parkinson's disease) in

dosage - a reliable method. Therefore, these results suggest that Ashwagandha may help prevent neuronal damage in Parkinson's disease (Nagashyana et al., 2000).

GABA-MIMETIC EFFECT ON NEURODEGENERATION AND NEUROREGENERATIVE POWER

Behavioral tests have supported the GABA-mimetic function of Ashwagandha root extraction. GABAergic neurodegeneration due to neuroleptic-induced excitotoxicity and oxidative stress is one of the etiopathological approaches to the pathophysiology of tardive dyskinesia (Gunne et al., 1993) and GABA agonists have been shown to be effective in reducing the symptoms of tardive dyskinesia. The beneficial effect of Ashwagandha root extraction may be due to its GABA simulation function. Ashwagandha, its nutrients and metabolites of its properties promote nerve growth after taking it for 7 days.

Interesting studies have shown that chronic oral administration of withanoside IV reduced axonal, dendritic and synaptic loss and memory loss caused by amyloid peptide A β (25-35) in mice (Kuboyama et al, 2006). After oral administration in mice, withanoside IV was synthesized into sominone, which restored significant recovery in neurites and synapses and promoted axonal and dendritic uptake and synaptogenesis. These effects were maintained for at least 7 days after discontinuation of anesthetic IV administration. These data suggest that andanoside IV, along with its metabolite, sominone, may have clinical use as an anti-antementementia drug.

One group found that the release of Ashwagandha methanol (5 mg / ml) significantly increased the percentage of neurites in human neuroblastoma cells SK-N-SH. The outcome of the discharge depends on the dose and time. The mRNA levels of dendritic markers MAP2 and PSD-95 by RT-PCR have been found to be significantly increased therapeutically by this release. Immunocytochemistry has shown some expression of MAP2 in extracted neurites. These results suggest that the methanol extraction of Ashwagandha improves the formation of dendrites (Kulkarni et al., 1993).

ANXIOLYTIC EFFECT:

Ashwagandha created a anxiety-finding effect similar to the drug Lorazepam in all three common anxiety tests: high-maze, social interaction and latency feeding in an unfamiliar environment. In addition, both Ashwagandha and Lorazepam, reduced rat brain levels of tribulin, the last sign of clinical anxiety, when levels were increased after administration of an anxiogenic agent, pentylenetetrazol.

Ashwagandha also showed an antidepressant effect, similar to that of imipramine, in two standardized tests, a mandatory 'behavioural test' and 'learning to be weak'. Research supports the use of Ashwagandha as a mood enhancer in clinical situations of anxiety and depression.

EFFECT ON MITOCHONDRIAL ENERGY LEVELS AND HEALTH:

The effect of Ashwagandha on glycosaminoglycan synthesis in tissue granulation carrageenin-in dosed air pouch granuloma was studied. Ashwagandha has been shown to have great potential to prevent the insertion of ribosome -35S into granulation tissues. The effect of constipation on oxidative phosphorylation (reduction of ADP / O ratio) was also observed in mitochondria of granulation tissue. In addition, ATPase's reliable Mg²⁺ activity was found to be influenced by Ashwagandha. Ashwagandha also reduces the activity of succinate dehydrogenase enzyme in mitochondria of granulation tissues (Begum & Sadique, 1987).

THE ANTI-INFLAMMATORY EFFECT OF WITHAFERIN:

Withaferin A and 3-b-hydroxy-2,3-dihydrowithanolide F isolated from *Andania somnifera* show promising anti-bacterial, antitumoral, immunomodulating and anti-inflammatory properties (Budhiraja and Sudhir, 1987).

ANTI-ARTHRITIC EFFECT:

Ashwagandha is an analgesic that relaxes the nervous system in response to pain (Twajj et al., 1989). The powerful anti-arthritis properties (Singh et al. 1984, 1986) of Ashwagandha are now widely accepted and documented; it is also found to act as an antipyretic and analgesic as well. Ashwagandha (1000 mg / kg / oral) produced significant analgesic activity in rats exposed to heat analgesia caused by the hot plate method. The analgesic effect of Ashwagandha was recorded as 78.03 percent in the second hour of administration. Involvement of pain mediators; Prostaglandin and 5-hydroxytryptamine in the analgesic activity of Ashwagandha were studied with treatment with paracetamol (100 mg / kg, ip) and cyproheptadine (10 mg / kg, ip). Ashwagandha's analgesic activity was potent with cyproheptadine, however, paracetamol failed to show any significant change in its activity, elevating serotonin involvement, but not prostaglandins in Ashwagandha analgesic activity (Mazen et al. , 1990).

CONCLUSION

The available scientific data supports the conclusion that Ashwagandha is a powerful rejuvenating tonic (Rasayana of Ayurveda), due to its many medicinal actions such as anti-stress, neuroprotective, antitumor, anti-arthritis, analgesic and anti-inflammatory etc. with various types of diseases such as Parkinson's, dementia, memory loss, depressive disorders, malignoma and others. Ashwagandha is used as a home remedy by the Indians, taking it as the best tone for adults and children, and as an aphrodisiac for young people. It is one of the best tonic tonics of Ayurveda, the most ancient system of Medical Science. Our clinical experience has shown that in addition to the listed neurological conditions, brain damage that causes paralysis and neuronal deficits also improves with long-term treatment with Ashwagandha. We also use it for all types of cancer including bladder and lung cancer, especially in the later stages, giving patients many health benefits. We have some cases of lung cancer that have rejected modern treatment and recovered clinically and radiologically with our Ashwagandha treatment. (Singh N., 2010- unpublished data). In a recent conference (Singh, 2005) on an important drug concept, it was considered as one of six important therapeutic remedies.

Therefore, the findings clearly show that the traditional use of Ashwagandha has a sound and scientific basis. Major clinical studies are needed to confirm the clinical effectiveness of this remedy, especially for stress-related disorders, neuronal disorders and cancer.

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