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Ashwagandha, A rejuvenator of Ayurveda: An overview

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Abstract

Withania somnifera (Ashwagandha) is an immunomodulating herb, used in Ayurvedic medicine as a rasayana (tonic). It has a cognition promoting effect and also useful in children with memory deficit and in old age people to increase the memory. It is useful in neurodegenerative diseases such as Parkinson's, Huntington's and Alzheimer's diseases. The herb and enhance the energy levels and mitochondrial health. It is an anti-inflammatory and anti-arthritis agent and 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.

Key words: *Withania somnifera*, rejuvenator, anti-stress, anti-tumor, neurodegenerative, anti-arthritis

Introduction

Ashwagandha (*Withania somnifera*, Solanaceae) is commonly known as “Indian winter cherry” or “Indian Ginseng”. It is one of the most important herb used for millennia as a rasayana for its wide ranging health benefits. Rejuvenator is also names as rasayana. It is described as an herbal or metallic preparation that promotes a youthful state of physical and mental health and expands happiness. These types of remedies are given to small children as tonics, and are also taken by the middle-aged and elderly to increase longevity. Among the ayurvedic Rasayana herbs, Ashwagandha holds the most prominent place. It is known as “Sattvic Kapha Rasayana” herb . Most of the rasayana herbs are adaptogen / anti-stress agents.(Changhadi, 1938)

Ashwagandha is commonly available as a churna, a fine sieved powder that can be mixed with water, ghee (clarified butter) or honey. It enhances the function of the brain and nervous system and improves the memory. Also used as a good supplement for promoting a healthy sexual and reproductive balance. Being a powerful adaptogen, it enhances the body's resilience to stress. Ashwagandha improves the body's defense against disease by improving the cell-mediated immunity. It also possesses potent antioxidant properties that help protect against cellular damage caused by free radicals.

The biologically active chemical constituents of *Withania somnifera* (WS) include alkaloids (isopelletierine, anaferine, cuseohygrine, anahygrine, etc.), steroidal lactones (withanolides, withaferins) and saponins (Mishra *et al.*, 2000, Mishra, 2004). Sitoindosides and acylsterylglucosides in ashwagandha are anti-stress agents. Active principles of herb, 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 (Atta-ur-Rahman *et al.*, 1991).

Ayurveda, the traditional system of medicine practiced in India can be traced back to 6000 BC (Charak Samhita, 1949). For most of these 6000 years ashwagandha has been used as a rasayana. The root of ashwagandha is regarded as tonic, aphrodisiac, narcotic, diuretic, anthelmintic, astringent, thermogenic and stimulant. The root smells like horse (“ashwa”), that is why it is called ashwagandha (on consuming it gives the power of a horse). It is commonly used in emaciation of children (when given with milk, it is the best tonic for children), debility from old age, rheumatism, vitiated conditions of vata, leucoderma, constipation, insomnia, nervous breakdown, goiter etc. (Sharma, 1999). The roots are crushed with water and formed into a paste. It is applied to reduce the inflammation at the joints (Bhandari, 1970). It is also locally applied in carbuncles, ulcers and painful swellings (Kritikar and Basu, 1935). The root in

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combination with other drugs is prescribed for snake venom as well as in scorpion-sting. It also helps in leucorrhoea, boils, pimples, flatulent colic, worms and piles (Mishra, 2004).

The leaves are bitter and are recommended in fever, painful swellings. The flowers are astringent, depurative, diuretic and aphrodisiac. The seeds are anthelmintic and combined with astringent and rock salt remove white spots from the cornea. Ashwagandharishta prepared from it is used in hysteria, anxiety, memory loss, syncope, etc. It also acts as a stimulant and increases the sperm count (Sharma, 1938).

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., 1997). The extensive studies on the biological model of 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 (Kalsi et al. 1987; Singh et al. 1977). Ashwagandha have similar anti-stress activity in rats. 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.

Effect on swimming performance

Ashwagandha was shown to increase swimming performance in rats as judged by increase in swimming time during physical endurance test. Ashwagandha's antistress properties have been investigated in all these studies using adult rats were carried out by swimming endurance stress test. Ashwagandha treated animals showed a significant increase in the duration of swimming time as compared to control. The control group of mice swam for a mean time of 385 minutes, whereas the drug-treated animals continued to swim for

a mean duration of 740 minutes. Thus, the swimming time was approximately doubled after *Withania somnifera* (WS) treatment.

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.

Anti-ulcerogenic effect

Ashwagandha was found to be useful in the prevention of stress-induced ulcers of the gastrointestinal tract. It showed significant protection against 18h immobilization, cold + immobilization (4h) and aspirin induced gastric ulcers and lowered the mean ulcer index in rats.

Effect on leucocytosis

Ashwagandha given to a group of mice with milk injection produced reduction in leucocytosis.

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.

Acute toxicity studies

In acute toxicity studies the LD50 of *Withania somnifera* was found to be 1750 mg (p.o.) in albino mice.

Anti-tumor effect (Effect on Chinese Hamster Ovary (CHO) cells carcinoma)

Withania roots caused the inhibitory effect of about 49% on colony forming efficiency of CHO cells. It inhibits the cell growth and prevents the cell attachment. It induced long term growth inhibition of CHO cells which was dependent on the cell density and duration of ashwagandha exposure. This knowledge in turn will assist oncologists who plan to use the ashwagandha as 'synergizers' with conventional chemotherapy or radiation therapy.

Effect on Urethane induced lung-adenoma in mice and other studies:

Ashwagandha was found to be very useful in experimental carcinogenesis in the crude form. It prevented urethane-induced lung-adenomas in mice. The other effects of urethane like leucopenia were also prevented. Urethane, which is a chemical stressor,

causes variety of ill effects, all of which were prevented by *Withania*. The drug can be used as an adjunct to cancer chemotherapy or radiotherapy. Besides having an anti-cancer effect it will also reduce the side effects of anti-cancer agents, which invariably reduce immunity and quality of life. WS also acts as an immunomodulator and hence can enhance life span of cancer patients, where lowered immunity states of the patient are the cause of concern. Our results suggest its use as anti-tumor and immunomodulator agent (Dixit *et al.*, 1995).

The research and studies of Ashwagandha's activities in the inhibition and reduction of tumour growth have shown encouraging evidence that this remarkable herb may prove to be extremely effective in the treatment of tumor type diseases including cancer. It also improves the white cell count (WBC) and function, which are depleted in the chemotherapeutic treatment of cancer. Ashwagandha in the treatment of fibroid tumors of the uterus showed reduction of uterine bleeding tendencies and disappearance of fibroids after long treatment (Abbas *et al.* 2004, 2005).

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 Medhyarasayanas. 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.

Effect on neurodegenerative diseases such as Parkinson's, Huntington's and Alzheimer's diseases

In patients with Alzheimer's disease, neuritic atrophy and synaptic loss (Dickon & 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 it 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 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 and longevity in the users.

Pretreatment with ashwaganda 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 & Andren, 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 A β (25-35) in mice (Kuboyam *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 of cells with neurites in human neuroblastoma SK-N-SH cells. The effect of the extract was dose- and time-dependent. mRNA levels of the dendritic markers MAP2 and PSD-95 by RT-PCR were found to be markedly increased by treatment with the extract. Immunocytochemistry demonstrated the specific expression of MAP2 in neurites extended by

the extract. These results suggest that the methanol extract of ashwagandha promotes the formation of dendrites (Kulkarni *et al.*, 1993).

Anxiolytic effect

Ashwagandha induced a calming anxiolytic effect that was comparable to the drug lorazepam in all three standard anxiety tests: the elevated plus-maze, social interaction and the feeding latency in an unfamiliar environment. Further, both ashwagandha and lorazepam, reduced rat brain levels of tribulin, an endocoid marker of clinical anxiety, when the levels were increased following administration of the anxiogenic agent, pentylenetetrazole.

Ashwagandha also exhibited an antidepressant effect, comparable with that induced by imipramine, in two standard tests, the forced swim-induced 'behavioral despair' and 'learned helplessness' tests. The investigations support the use of ashwagandha as a mood stabilizer in clinical conditions of anxiety and depression. (Abdel-Magied *et al.*, 2001)

Effect on energy levels and mitochondrial health

The effect of ashwagandha on glycosaminoglycan synthesis in the granulation tissue of carrageenin-induced air pouch granuloma was studied. Ashwagandha is shown to exert significant inhibitory effect on incorporation of ribosome -35S into the granulation tissue. The uncoupling effect on oxidative phosphorylation (ADP/O ratio reduction) was also observed in the mitochondria of granulation tissue. Further, Mg²⁺ dependent ATPase activity was found to be influenced by ashwagandha. It also reduced the succinate dehydrogenase enzyme activity in the mitochondria of granulation tissue (Begum & Sadique, 1987).

Anti-inflammatory effect due to withaferin

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

Anti-arthritis effect

Ashwagandha is an analgesic that soothes nervous system from pain response. The powerful anti-arthritis properties of ashwagandha are now widely accepted and documented; it is furthermore found to be effective as antipyretic as well as analgesic also.

Ashwagandha (1000 mg/kg/oral) produced significant analgesic activity for a rat experiencing heat analgesia induced by hot plate method. The peak analgesic effect of ashwagandha was recorded as 78.03 percent at 2nd hour of administration. The involvement of pain mediators; prostaglandin and 5-hydroxytryptamine in analgesic activity of ashwagandha was studied by pretreatment with paracetamol (100 mg/kg, ip) and

cyproheptadine (10 mg/kg, ip). The analgesic activity of ashwagandha was potentiated significantly by cyproheptadine. However, paracetamol failed to exhibit any significant change in its activity, suggesting the involvement of serotonin, but not prostaglandins in the analgesic activity of ashwagandha (Mazen *et al.*, 1990).

Conclusion

The available scientific data reveals that ashwagandha is a real potent regenerative tonic (Rasayana of Ayurveda), due to its multiple pharmacological actions like anti-stress, neuroprotective, antitumor, anti-arthritis, analgesic and anti-inflammatory etc. It is useful for different types of diseases like Parkinson, dementia, memory loss, stress induced diseases, malignoma and others.

Ashwagandha is used as a household remedy by Indians, who consider it as the best tonic for old people and children, and as aphrodisiac by young people. It is one of the best nerve tonics of Ayurveda, the most ancient system of Medical Sciences. Our clinical experience showed that besides the enumerated neurological conditions, brain strokes causing paralysis and neuronal deficit also improve in the long term treatment with ashwagandha. We are also using it in all forms of cancer including prostate and lung cancers, especially in last stages, giving the patients lot of health benefits. We have some cases of lung cancer who have refused modern therapy and recovered clinically and radiologically with our therapy of ashwagandha.

Thus, the above findings clearly indicate that the traditional use of Ashwagandha has a logical and scientific basis. Large scale clinical studies are needed to prove the clinical efficacy of this herb, specially in stress related diseases, neuronal disorders and cancers.

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