

ANTISTRESS ACTIVITY OF ASHWAGANDHA (*Withania somnifera* Dunal)**- A REVIEW**

Gajarmal Amit Ashok Shende M.B. Chothe D.S.
 PG Department of Dravyaguna, Government Ayurveda College, Nanded, Maharashtra,
 India.

ABSTRACT

According to various surveys, the stress is the major problem for many diseases ranging from psychiatric disorders to endocrine disorders including diabetes mellitus, hypothyroidism, male sexual dysfunction, peptic ulcer, hypertension, ulcerative colitis etc. In Holy *Geeta*, it is seen that *Arjuna* was one of the sufferer from stress during *Mahabharata* war. At that time Lord *Krishna* takes responsibility to counsel him in *Geeta*. On the same mode, today's life style was very frustrated due to busy schedule of even school going child up to old aged people. That's why medicine related to stress and psychosis has a huge market in the world. As modern medicine can provide some benefits & results but they are mixed and unsatisfactory. So the answer is hidden in *Ayurveda* i.e. *Rasayana* (Rejuvenation therapy). It is one of the eight branches of *Ayurveda*. *Rasayana* drugs are claimed to contribute in revitalising the tissues and even the psyche thereby maintaining the health of the human being. These are stated to possess rejuvenation power which enhance the *Ojas* of the body i.e. vitality. [1] It is similar to the modern concept of adaptogenic agents which gives the protection to the human physiological system against diverse stressor. Recent studies shows that the *Ayurvedic* herbs having adaptogens which could induce a state of non-specific increase of resistance to affect internal homeostasis. The adaptogens improve the response to stress and help the body to adapt by normalizing physiological processes in times of increased stress. *Ashwagandha* is one of the best medicinal herbs for that purpose & is compared well with *Eleutherococcus senticosus* (Siberian Ginseng), *Panax Ginseng* (Chinese/ Korean Ginseng) in its adaptogenic & antistress activity, hence popularly known as Indian ginseng. That's why we take a review of antistress activity of *Ashwagandha* (*Withania somnifera* Dunal).

Keywords: *Ashwagandha*, *Withania somnifera*, Stress, Adaptogens, *Medhya Rasayana*

INTRODUCTION

Stress is simply a reaction to a stimulus that disturbs our physical or mental equilibrium. Acute stress can be exciting; it keeps us active & alert. But chronic stress can have detrimental effects on health. The Father of Stress Hans Selye made 2 observations, the body has a set of similar responses to a broad array of

stressors & under certain conditions, the stressors will make you sick. [2] Within seconds of an acutely stressful event, norepinephrine is released from nerve endings in preparation for a rapid response & the adrenal glands release epinephrine & norepinephrine into the blood stream, resulting in the familiar fight or flight response. Within minutes of a stressful event

(Possibly lasting for several hours) a much more complex interaction between the nervous & endocrine systems & other forms of internal communication occurs resulting in an intricate stress adaptation response. During this time the adrenal glands release extra cortisol into the circulation. A wide range of events or conditions is considered physiologically stressful because the adrenals are stimulated to release stress hormones. These occurrences include calorie restriction, surgery, sleep deprivation, excessive exercise & various mental states- all of which can result in elevated cortisol & catecholamine stress hormones. Under health consequences of chronic stress, the Natural Killer cell activity, Secretory IgA & Bifidobacteria +Lactobacilli were decrease while Enterobacteria, E. coli & risk of myocardial infraction were increases. [3] So the objective of this paper is to review the research regarding antistress activity of *Ashwagandha* (*Withania somnifera Dunal*), a commonly used herb in *Ayurvedic* medicine. All this review is limited to published articles & on net available articles in English language.

It is seen that *Ashwagandha*'s antistress & anabolic activity was similar to *Panax ginseng*, in an animal model of chronic stress. *Withania somnifera* & *Panax ginseng* extracts decreases the number & severity of stress induced ulcers, reversed stress induced inhibition of male sexual behaviour & inhibited the adverse effects of stress on retention of learned tasks. Both reversed stress induced immune suppression, only *Withania* increased peritoneal macrophage activity. But *Withania* has an advantage over *Panax ginseng* in that it does not appear to result in Ginseng abuse syndrome, a condition characterized by high blood pressure, water retention, muscle tension & insomnia

when excess amounts are consumed. Also *Withania* appearing to stimulate stem cell proliferation & improve red blood cell, white blood cell & platelet parameters. [4]

With an abundance of antioxidants, iron, amino acids & other phytochemicals, it's no surprise that studies suggest *Ashwagandha* has medicinal properties that can directly & indirectly prevent & treat a number of diseases. *Ashwagandha* in *Sanskrit* means 'smelling like a horse', probably originating from the odour of its fresh root which resembles that of a sweaty horse. It is well known antistress herb. The species name *somnifera* means 'sleep-bearing' in Latin, indicating that ash was considered a sedative which also contains flavonoids & active ingredients of the withanolide class. [5]

To evaluate the antistress effects of *Withania somnifera*, an alcoholic extract from roots & seeds dissolved in normal saline was given (100mg/kg intra peritoneal as a single dose) to 20-25 g mice in a swimming performance test in water at 28°-30° C. It is seen that the extracts approximately double the swimming time when compared to control. It suggested that *Withania somnifera* induced a stage of nonspecific increased resistance during stress. Glycosides of *Withania somnifera* exhibited significant antistress activity in forced swimming induced immobility in mice, restraint stress induced gastric ulcer & auto analgesia in rats. Further clinical studies should be conducted as well as studies in multiple animal based models using a variety of suitable biochemical markers to understand its mechanism of action. [6]

Researchers using *Withania somnifera*, discovered the animals given the herb an hour before the foot shock, experienced a significantly reduced level of

stress. This research confirms the theory that *Withania somnifera* has a significant antistress adaptogenic effect. Research conducted at the Department of Pharmacology, University of Texas health science centre indicated that extracts of *Ashwagandha* produce GABA-like activity which may account for the herbs anti-anxiety effects. Its function is to be decrease neuron activity & inhibit nerve cells from over firing. This produces calming effect. Excessive neuronal activity can lead to restlessness & insomnia, but GABA inhibits the number of nerves cells that the fire in brain & helps to induce sleep, uplift mood & reduce anxiety. [7]

The *Ayurvedic* text describe a set of rejuvenative measures to impart biological sustenance to the bodily tissues called ‘*Rasayana*’ act as micronutrients, specific to brain tissue are called ‘*Medhya Rasayana*’ which retard brain aging & help in regeneration of neural tissues besides producing antistress & memory enhancing effect.[8]

Stress, as a major cardiovascular risk factor leads activation of sympatho-adrenal & hypothalamic pituitary adrenal (HPA) axis & causes oxidative stress induced changes & provide cardio protection in ischemic rats similar to the properties ascribed to adaptogens. [9]

The extensive studies on the biological model of animals for the antistress properties of *Ashwagandha* have shown to be effective in increasing the stamina (physical endurance) & preventing stress induced gastric ulcer. It has similar anti stress activity in rats. An aqueous suspension of *Ashwagandha* root was used at 100mg/kg/oral dosage. The result prevents/ decreases adrenal cortisol & ascorbic acid which occurs due to swimming stress. In the rats pre-treated with the drug,

this parameter was near control values & on increase in the swimming time was observed. These results indicate that *Withania somnifera* used in the crude form is a potent anti-stress agent. This indicates clinical use of *Withania somnifera* in the prevention & treatment of many stress induced diseases like arteriosclerosis, premature ageing, arthritis, diabetes, hypertension & malignancy. [10]

Two new glycowithanolides, sitoindoside IX (1) & sitoindoside X (2), isolated from *Withania somnifera Dunal*, were evaluated for their immunomodulatory & CNS effects like antistress, memory & learning in laboratory animals, because the plant extract was used by practitioners of the Indian system of medicine for similar purpose. Both these compounds (50-200mg/kg) produced significant anti stress activity in albino mice & rats, augmented learning acquisition & memory retention in both young & old rats. These findings are consistent with the use of *Withania somnifera* in *Ayurveda* to attenuate cerebral function deficits in the geriatrics population & to provide nonspecific host defence. [11]

Anti-stress activity associated with glycosides (sitoindosides VII & VIII) present in this plant was reported to the usefulness of *Ashwagandha* as an anti-stress adaptogen. Administered orally (50-200mg/kg orally) both sitoindosides IX & X compounds also produced significant anti-stress activity in albino mice & rats. They also augmented learning, acquisition & memory retention in both young & old rats. [12]

The study conducted by Archana et al in 1998 for evaluating the anti-stressor properties using adult wistar strain albino rats & cold water swimming stress test. The results indicated that the drug treated

animals show better stress tolerance. Pre-treatment with this drug increased the swimming endurance in mice. It prevented gastric ulcers induced chemically or by stress in rats. The drug prevented increase in adrenal weight & decrease in ascorbic acid & cortisol content of adrenals during stress. They concluded that it appears so induced a state of non-specifically increased resistance (SNIR) during stress. [13]

The major biochemical constituents of *Ashwagandha* root are steroidal alkaloids & steroidal lactones in a class of constituents called Withanolides. At present near about 12 alkaloids, 35 Withanolides & several Withanolides from this plant has been isolated & studied. *Ashwagandha*'s pharmacological activity has been attributed to two main withanolides, withaniferin A & withanolide. The withanolides serve as important hormone precursors that can convert into human physiologic hormone as needed. When there is an excess of a certain hormone, the plant based hormone precursor occupies cell membrane receptor sites so the actual hormone can't attach & exert its effect as happened in stress with serum cortisol. On other hand if the hormone level is low, the plant based hormone exerts a small effect. They are the most important bioactive constituents of root of *Ashwagandha*, that's why modern herbalists classify *Ashwagandha* as an adaptogen, a substance said to increase the body's ability to withstand stress of all types. It also contains flavonoids & many active ingredients of the withanolide class. Numerous studies over the past two decades indicate that it has antistress & rejuvenating properties. [14]

Ashwagandha is an immunomodulatory agent & have been shown to possess antistress activity. One has con-

ducted research at BHU, Varanasi, India show *Withania somnifera* that many of the elements of *Ashwagandha* are antioxidants. These elements have effect on the brain test of animals & found that *Ashwagandha* led to larger amounts of three different natural antioxidants; superoxide dismutase, catalase & glutathione peroxidase. For years, Indians have prescribed *Ashwagandha* as a treatment for cerebral disorders in the elderly, including memory loss. A scholar from university of Leipzig looked at the effects of *Ashwagandha* on the neurotransmitters of the brain. *Ashwagandha* lead to more acetylcholine receptor activity concluded that the increase of activity in that particular neurotransmitter could account for the increase in cognitive ability & memory that is attributed to *Ashwagandha*. As scholar from University of Texas Health Science Centre found that extracts of the shrub has activity that was similar to GABA which could explain why the plant is effective in reducing anxiety & stress. Another study shows *Withania somnifera* that the plant can enhance memory which also reduced anxiety & depression in animals. [15]

Ashwagandha has been use within *Ayurvedic* & indigenous medical system for over 3000 years. Both preclinical & clinical studies demonstrate the use of *Ashwagandha* for anxiety, neurological disorders, therapeutically as an adaptogen in nervous exhaustion, insomnia, debility due to stress. Chronic stress induced hyperglycaemia, cognitive deficits, immunosuppression & depression was attenuated by *Ashwagandha*. Also studies have demonstrated that *Withania somnifera* possesses GABA – mimetic properties. Since GABA agonism has been linked to anxiety, the extracts of *Withania somnifera* may have beneficial effects in anxiety &

related disorders. A double blind placebo control study in patients with ICD-10 anxiety disorders, 6 weeks treatment with ethanolic extract of *Withania somnifera* showed anxiolytic activity over placebo. It concludes that *Withania somnifera* has useful anxiolytic potential. [16]

Withania somnifera has historically been used in Asia for treating stress related health conditions. One of the scholars was randomly assigned the participants to *Withania somnifera* extract (125mg QD, 125mg BID or 250mg BID) or placebo groups. He found that between days 0 & 60, the *Withania somnifera* extract 125mg QD group decreased significantly more than placebo for mean mHAM-A score, serum cortisol, serum C-reactive protein, pulse rate & blood pressure & increased significantly for mean serum DHEAS & haemoglobin. The *Withania somnifera* extract 125mg BID & 250mg BID dosage also improved the fasting blood glucose levels & lipid profiles for study participants. Participants & dropouts reported no adverse effects. Therefore it provides evidence that the consumption of *Withania somnifera* extract significantly reduces experiential & biochemical indicators of stress without adverse effects. [17]

'*Medhya Rasayanas*' retard brain aging & help in regeneration of neural tissues besides producing antistress, adaptogenic & memory enhancing effects. As *Ashwagandha* has this property, it can be used in both curative & promotive aspects in stress in '*Vardhaknya Chikitsa*'. Young can be advocated to use *Medhya Rasayana* regularly as the period for the administration of *Rasayana* is effectively in young & middle age groups. However *Medhya Rasayana* can be effectively used in stress, delaying the deteriorating aspects of '*Jara*'. [18]

It has been shown to slow, stop reverse & remove neurotic atrophy & synaptic loss, the main cause for neurodegenerative disorders including Alzheimer's & dementia as confirmed by several clinical studies. Glycowithanolides, withaferin-A & sitoindosides VII-X isolated from the root of *Withania somnifera*, have been shown to significantly reverse the ibotenic acid induced cognitive defects in Alzheimer's disease model. The experimental studies have revealed that after oral administration in mice, withanoside IV is metabolized into sominone, which induces marked recovery in neuritis & synapses & also enhance axonal & dendritic out growth & synaptogenesis. These effects maintain for at least 7 days after discontinuing withanoside IV administration which reflects the clinical usefulness of withanoside IV & its metabolite, sominone in the treatment & management of Alzheimer's & dementia. On the same way we can use this theory for stress induced diseases. [19]

Hypothalamic – Pituitary - Adrenal influences in neurological aging. This HPA axis is an endocrine closed loop system that controls the secretion of stress hormones (glucocorticoids). Aging is associated with a reduced ability to adopt to stress increased HPA activation & chronic elevations of glucocorticoids (e.g. cortisol). Animal & human data suggest that cumulative exposure to high levels of glucocorticoids can be particularly detrimental to the aged hippocampus (the brain structure involved in learning & memory). Due to the decreased ability to handle stress & increased activation of the HPA axis associated with adaptogenic properties may be beneficial. *Ayurvedic* herb *Ashwagandha* (*Withania somnifera*) has a posi-

tive influence on stress response, mental function & cognition. [20]

The anti-peroxidative & antioxidant action of *Withania somnifera* could be attributed to withanolides (sitoinosides VII-X) & withaferin-A (glycowithanolides) present in *Withania somnifera* extract. Besides the presence of other potential sources of antioxidant compound such as polyphenols, flavonoids & alkaloids, vitamin-C can attribute to the antioxidant efficacy of *Withania somnifera* as In-vitro exposure of goat blood to 1, 4-dioxane & TCE can alter the biochemical parameters, induce oxidative imbalance by reducing antioxidant dioxane / TCE induced oxidative stress. [21]

RESULTS & OBSERVATIONS

Studies indicate that the *Ashwagandha* (*Withania somnifera* Dunal) possess antistress property. It also appears to exert a positive influence on the endocrine, cardiopulmonary & CNS. Toxicity studies reveal that *Ashwagandha* appears to be a safe compound.

DISCUSSION & CONCLUSION

The results of research articles are very encouraging & indicate that this herb should be studied more extensively to confirm these results & reveal other potential therapeutic effects. According to *Guna Karma* of *Ashwagandha*, due to *Snigdha Guna* (Unctuous), *Balya* (Tonic) and *Vaya-Sthapana* (Anti-aging) properties of *Ashwagandha*, it directly acts as *Rasayana*. This along with *Tikta Rasa* (Bitter) and *Laghu Guna* (Light) acts on *Dhatwagni* for *Sukshma Pachana karma* (Metabolism) to produce *Prakrit Dhatu* (seven primitive matter). [22] It ultimately results in *Ojas Nirmiti* (governing the immune system). It will break the pathology and help to maintain the strength of the body to stand during stress. Also *Ashwa-*

gandha supports sound sleep and anti-stress effect due to alkaloids and glycosides which can affect elements of the central nervous system and immune system. [23] An important active principle of *Withania somnifera* is *Withaferin-A*, have been shown to possess a remarkable range of therapeutic properties i.e. antistress, antioxidant, immunomodulatory. [24] From this, it is seen that it will be used in *Vata Dosha Pradhana Samprapti*. Clinical trials using *Ashwagandha* for a variety of conditions should also be conducted.

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CORRESPONDING AUTHOR

Dr. Gajarmal Amit Ashok

PG Department of Dravyaguna,
Government Ayurveda College,
Nanded, Maharashtra, India

Email: dgalaxy78@gmail.com
