



**A REVIEW ON ADAPTOGENIC ACTIVITY OF ASHWAGANDHA (*WITHANIA SOMNIFERA*): AN AYURVEDIC APPRAISAL**

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**ABSTRACT**

Stress is a state of mental or emotional strain resulting from demanding circumstances. It's a universal experience, which has an important defensive function towards harmful psychological stimuli. Owing to this there are various pharmacological and non-pharmacological treatments with fatal adverse reaction. The need of hour is to have a cost-effective adaptogenic drug. Adaptogens are compounds that increase the ability of an organism to adapt to environmental factors and avoid damage. Ayurveda explains these qualities under concepts of vyadhikshamatva (immunity). Ashwagandha is considered to be the best adaptogenic drug among shankhapushpi (*Clitoria ternatea*), yashtimadhu (*Glycyrrhiza glabra*), brahmi (*Bacopa monnieri*), guduchi (*Tinospora cordifolia*), mandookaparni (*Centella asiatica*), etc medhya dravya (cognitive enhancers). This study reviews the Ayurvedic and modern literature related to stress and its management as adaptogens through Ayurveda. Ayurveda is the traditional system of medicine of India and contains a very scientific description of stress and general manovikaras (psychiatric illness). Ayurveda has been a great potential in the field of rasayana (rejuvenation) as there are lots of single herbs and preparations which possess adaptogenic properties and strengthens the physiological adaptation.

**Keywords:** Ashwagandha, Stress, Vyadhikshamatva, Adaptogens, Ayurveda.

**INTRODUCTION**

The present society demands physical, social and psychic excellence, consequently practicing unwholesome life style. The contribution of this life style, is stress and psychological problems, which can lead to various psychiatric disorders. Stress is a state of mental or emotional strain resulting from demanding circumstances. It's a universal experience, which has an important defensive function towards harmful psychological stimuli. Stress acts through the autonomic nervous system, produces some physical and psychological symptoms like cognitive deficit, immune suppression, sexual dysfunction, gastric ulceration, irregularities in glucose homeostasis, and changes in plasma corticosterone levels, arteriosclerosis, premature ageing, arthritis, diabetes, hypertension and malignancy<sup>1</sup>. Stress management is a wide topic of interest in this era. Owing to this there are various pharmacological and non-pharmacological treatments in contemporary medicine with drawback of fatal adverse reaction. Hence the entire globe is in pursuit of stress management. The need of hour is to have a cost-effective adaptogenic drug.

Adaptogens are compounds that increase the ability of an organism to adapt to environmental factors and avoid damage<sup>2</sup>. Adaptogens are effective in the reduction of stress reactions in the alarm phase, thereby avoiding the exhaustion stage and providing a certain protection against stress. Adaptogenic effect

can also be described as a strengthening of the physiological adaptation<sup>3</sup>. Ayurveda explains these qualities under concepts of vydhikshamatva (immunity)<sup>4</sup>.

**Stress in Ayurveda**

According to Ayurveda, body is not static, it continuously undergoes changes to adapt itself to the environmental activities<sup>5</sup>. Such a continuous activity of the body and its psychosomatic constitution is brought about by three essential humors of life known as vata, pitta and kapha<sup>6</sup>. Vata helps in jnanotpatti(cognition) in the existence of manas(mind). It receives and transmit messages from environment to different centres of brain and also to other parts of the body. Interesting phenomenon here is physiology of manas. Proper channeling occurs only in the presence and normal functioning of manas. Manas through its anutwa (atomic) and ekatwa (unitary) coordinates with vata to bring physiological processes<sup>7</sup>. If the organism fails to adjust or adapt to environment, it succumbs to disease. It mainly depends on shareerika prakruthi (constitution) and manasika prakrithi (mental disposition) of the individual<sup>8</sup>.

The phenomena of stress can be better understood through trisutra (tripod theory) i.e. Hetu (cause), linga(symptoms) and oushadha(therapeutics)<sup>9</sup>. Hetu being improper utilization of sensory faculties, mental faculty and its artha(object). Linga emerges as a result of hetu i.e., depending on amount of

imbalance in dosha (humors) and duration of changes. In short term duration, dosha (humors) get vitiated and results in derangement at the level of manas and buddhi (intellect). Here ahita mano artha (unpleasant object of mind) is identified as stressor. Practice of ahita mano artha develops various lakshana (symptoms) like fear, agitation, irritability, anger, grief, dryness of body, debility, palpitation, sleep disturbances etc<sup>10</sup>.

Aushadha is held responsible for the mitigation of diseases as well as maintenance and promotion of health. Main three treatment modalities are daiva vyapashraya (psycho spiritual healing), yuktivyapashraya (rationale therapy), satvavajaya (psychic intervention)<sup>11</sup>. Major concept of rational therapy are Medhya therapy and cognitive enhancing drugs. They have an effective action over mind and have the property of anti-stress and promote mental health. It is also mentioned in the classics that one who uses Medhya Dravyas would attain longevity, memory, intellect, youth, excellence of lustre, complexion and voice, excellent potentiality to all the body and sense organs. It also enumerates effective management of stress through rational treatment modality. The drugs like ashwagandha (*Withania somnifera*), shankhapushpi (*Clitoria ternatea*),

yasthimadhu (*Glycyrrhiza glabra*), brahmi (*Bacopa monnieri*), guduchi (*Tinospora cordifolia*), mandookaparni (*Centella asiatica*), jyotishmati (*Celastrus paniculata*), vacha (*Acorus calamus*), jatamamsi (*Valeriana jatamansi*) are widely used in the management of stress for its anxiolytic property. Among these ashwagandha is considered to be the best adaptogenic drug among medhya dravya (cognitive enhancers)<sup>12</sup>.

### Ashwagandha

The plant *Withania somnifera* (L.) Dunal, commonly known as "Ashwagandha" is known for its therapeutic use in the ayurvedic system of traditional medicine. "Ashwa" means horse and "gandha" means smell, hence the name Ashwagandha comes from smell of horses. The plant is commonly known as "Indian Ginseng". The drug has been mentioned in ancient literatures like Charaka samhita, Sushruta samhita, Bhava Prakasha etc. (Table 1)<sup>13,14,15</sup>. Ashwagandha is known in herbal medicine as an "adaptogen", which means it can help restore overall health, as well as help the body acclimate to stress<sup>16</sup>.

Table 1 Pharmacological properties<sup>13,14,15</sup>

Properties	Kaiyadeva Nighantu	Raja Nighantu	Bhava Prakasha Nighantu	API
Rasa (taste)	Kashaya (astringent) Tikta (bitter)	Katu (pungent) Tikta	Tikta Kashaya	Tikta Kashaya
Guna (property)	-	-	-	Laghu
Veerya (potency)	Ushna (hot)	Ushna	Ushna	Ushna
Vipaka (post digestion effect)	-	-	-	Madhura (sweet)
Karma (pharmacological activity)	Vata Kapha Shamana (alleviating vata, kapha humor)	Vata Kapha Shamana	Vata Kapha Shamana	Vata Kapha Shamana

### Chemical constituents

Chemical analysis has revealed over 35 chemical constituents contained in the roots of *Withania somnifera* (WS)<sup>17</sup> shows its main constituents as alkaloids and steroidal lactones, among alkaloids withanine is the main constituent. Other alkaloids are Anaferine, Anahygrine, Beta-Sisterol, Cuseohygrine, Iron, Isopelletierine Pseudotropine, Pseudo-withanine, Scopoletin, Somniferinine, Somniferine, Somnine, Tropanol, Tropine, Withanine, Withanane Withanolides A-Y (Steroidal lactones)<sup>18,19</sup> and 3-a-glyoxytropine. There are two acyl steryl glucoside viz. sitoindoside VII and sitoindoside VIII. A withanolide named sitoindoside contains a glucose molecule at carbon 27. The roots of *Withania somnifera* consists of a compound known as withanolide as primary compound and is identified as amphoteric; i.e., it regulates important physiologic processes<sup>20</sup>. Steroidal lactones are present in leaves, commonly called withanolides with C28 steroidal nucleus and C9 side chain, with a six membered lactone ring<sup>21</sup>. Withaferin A and withanolide D which are two main withanolides, attributes to have much pharmacological action.

### Research work

#### Animal study

**Adaptogenic activity:** The extensive studies on the biological model of animals for the adaptogenic / anti-stress properties of Ashwagandha have shown its efficacy in preventing stress induced gastric ulcer, increasing the physical endurance and carbon tetrachloride (CCl<sub>4</sub>) induced hepatotoxicity and mortality. When aqueous suspension of Ashwagandha root at 100 mg/kg/oral dosage was used, it showed significant result in increasing the plasma corticosterone level, phagocytic index and

avidity index in rats subjected to cold swimming stress. Increase in the swimming time was observed in rats pre-treated with the drug<sup>22,23</sup>. Another study showed that sitoindoside produced anti-stress activity, potentiated by Withaferin-A. It was also observed from preliminary acute toxicity studies that the compounds have a low order of toxicity<sup>24</sup>.

**Antioxidant effect:** Antioxidant activity of sitoindosides VII-X and withaferin A (glycowithanolides), was tested using the major free-radical scavenging enzymes, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX) levels in the rat brain frontal cortex and striatum. Increased antioxidant activity was inferred with increase in these enzymes and a protective effect on neuronal tissue. oral administration of glycol withanolides were given once daily for 21 days, dose-related increased in all enzymes were observed; effectiveness of deprenyl (a known antioxidant) administration was compared. This proved antioxidant effect of WS in the brain<sup>25</sup>. In another study, an aqueous suspension of WS root extract was evaluated for its effect on stress-induced lipid peroxidation (LPO) in mice and rabbits. LPO blood levels were increased by lipopolysaccharides (LPS) from *Klebsiella pneumoniae* and peptidoglycans (PGN) from *Staphylococcus aureus*. Simultaneous oral administration of WS extract prevented an increase in LPO<sup>26</sup>.

**Anti-stress effect on chronic stress (CS):** When *Withania somnifera* and *Panax ginseng* extracts were compared for their ability to attenuate some effects of chronic stress, they reversed CS-induced immunosuppression, but only the *Withania* extract increased peritoneal macrophage activity in the rats.<sup>27</sup> In another study, WS methanolic extract for 15 days significantly reduced the stress induced gastric ulcer, volume of gastric secretion, free

acidity, and total acidity. WS inhibited stress-induced gastric ulcer more effectively as compared to the standard drug ranitidine<sup>28</sup>. In a study EuMil, a polyherbal formulation consisting WS as one of its ingredients for 14 days treatment normalized the perturbed regional nor-adrenaline (NA), dopamine (DA), 5-hydroxytryptamine (5HT) concentrations, induced by chronic stress. EuMil also significantly attenuated the stress-induced increase in the rat brain tribulin activity<sup>29</sup>.

**Antidepressant activity:** Ashwagandha exhibited an antidepressant effect comparable to that induced by imipramine (10 mg/kg, i.p.), in the forced swim-induced “behavioural despair” and “learned helplessness” tests. Other similar studies confirm these results, lending support to the use of Ashwagandha as an antistress adaptogen<sup>30,31</sup>.

**Effect on Central Nervous System:** Neuritic regeneration and synaptic reconstruction activity is seen in withanolide-A<sup>32</sup>. Animal study with ashwagandholine (AG) exhibited a taming effect and a mild depressant (tranquilizer) effect on the central nervous system. Effects of isolated sitoindosides VII-X and withaferin were identified to have brain cholinergic, glutamatergic and GABAergic receptors in male Wistar rats. Ashwagandholine, total alkaloids extracted from extract of WS roots, caused relaxant and antispasmodic effects against various agents that produce smooth muscle contractions in intestinal, uterine, tracheal, and vascular muscle. These results were consistent with the use of WS to produce relaxation<sup>33,34,35</sup>.

**Anxiolytic effect:** The bioactive glycol withanolides (WSG), isolated from WS roots investigated the anxiolytic and antidepressant actions in rats. Oral administration of WSG (20 and 50 mg/kg) for 5 days were compared to benzodiazepine lorazepam (0.5 mg/kg, i.p.) for anxiolytic action. An anxiolytic effect was seen in the elevated plus-maze, social interaction and feeding latency in an unfamiliar environment, tests in WSG, comparable to that produced by lorazepam<sup>36</sup>.

**Nootropic effect:** Animal study on rat showed acetylcholinesterase (AChE) activity in the lateral septum and globus pallidus, and decreased AChE activity in the vertical diagonal band was seen in sitoindosides VII-X and withaferin. The compounds preferentially affect events in the cortical and basal forebrain cholinergic-signal transduction cascade. The drug-induced increase in cortical muscarinic acetylcholine receptor capacity might partly elucidate the cognition enhancing and memory-improving effects of WS extracts in animals and in humans<sup>37</sup>. Neurite outgrowth, cortical neurons noted in Withanoside IV in cultured rat<sup>38</sup>. Withanoside IV is linked to have an effect on memory deficits, loss of axons, dendrites, synapses and restructure neuronal dysfunction of Alzheimer's disease in Abeta-injected mice. Reserpine induced retention deficit was significantly reversed by chronic WS administration<sup>39</sup>. WS root extract improved retention of a passive avoidance task in a step-down paradigm in mice, also reversed the scopolamine-induced disruption of acquisition and retention and attenuated the amnesia produced by acute treatment with electroconvulsive shock (ECS), immediately after training. Oral administration of WS for 6 days significantly improved memory consolidation in mice receiving ECS treatment. WS reversed the scopolamine-induced delay in transfer latency on the elevated plus-maze, on day 1. On the basis of above findings, it is suggested that WS exhibits a nootropic-like effect in naive and amnesic mice<sup>40</sup>.

**Effects on the Endocrine System:** Studies were conducted to determine the efficacy of WS in regulating thyroid function based on the observations that WS provides protection from free

radical damage in the mouse liver. Mice were given WS root extract (1.4 g/kg by gavage, daily for 20 days). The treatment significantly increased the serum levels of 3,3',5-triiodothyronine (T3) and tetraiodothyronine (T4). WS significantly reduced hepatic lipid peroxidation and increased the activity of superoxide dismutase and catalase. The results suggest WS stimulates thyroidal activity and also promotes hepatic antioxidant activity<sup>41,42,43</sup>.

## Human study

**Cognitive enhancing effect:** A prospective, double-blind, multi-dose, placebo-controlled, crossover study with 26 healthy males, aged 20–35 years old given 2 caps twice a day, morning and evening, to evaluate effect of standardized aqueous extract of *Withania somnifera* on tests of cognitive and psychomotor performance in healthy human participants. The study showed significantly improved reaction time in 5 of the 6 psychomotor performance tests. *Withania somnifera* brings significant changes in neurological baseline functions as Sitoindosides VII-X and Withaferin A (glycowithanolides) increase cortical muscarinic acetylcholine capacity, with a modulation of cholinergic neurotransmission<sup>44</sup>. A double-blind, placebo-controlled comparative clinical study of effects of *Withania somnifera*, *Panax ginseng*, and placebo on psychomotor performance in 30 healthy participants concluded that there was significant improvement in sensorimotor function, auditory reaction time, and mental arithmetic ability<sup>45</sup>.

## DISCUSSION

Adaptogenic activity can be understood by understanding concepts of rasyana and vyadhikshamtva. Ashwagandha by its prabhava (idiosyncrasy) and karma (action) acts as rasayana. Ashwagandha promotes nutrition by direct enrichment of nutritional quality of rasa (nutritional blood), improving Agni (digestion), metabolism and promotes the competence of srotas (microcirculatory channels in body), thereby acts as adaptogen<sup>46</sup>. It also has antagonistic actions on the oxidative stressors there by strengthening physiological adaptation<sup>47</sup>.

As per to guna karma (properties) of Ashwagandha, due to snigdha guna (unctuous), balya (physical and mental endurance) property and rasayana karma it promotes physiology of the body. This along with tikta rasa (bitter) and laghu Guna (light) acts through sookshma srotas and reach target tissue to have expected medhya acton<sup>48</sup>. It ultimately results in ojas (governing the immune system). Ojas is the end product of physiological kapha and is the source of energy. It will overcome the samprapthi (pathology) and help to maintain the strength of the body to adapt during stress. From this, it can be inferred that it will be used in vata dosha pradhana samprapti<sup>49</sup>. These indicate that the Ashwagandha with madhur vipaka (post digestion effect being sweet) possibly can be advocated as adaptogens in Ayurveda<sup>50</sup>.

The rasayana herbs exert their effect through vyaadhikshamatvam (immunosuppressant), vyadhibala virodhitvam (immunostimulant) and vyadhiutpad akapratibandhakam (immuno-adjutant) activities<sup>51</sup>. It has been found that there is link between nervous, endocrine and immune systems. Ashwagandha known to stimulate cytokines which stimulates the hypothalamus-pituitary-adrenal axis and corticotrophin release factor (CRF), which ultimately enhances the production of adrenal corticotropic hormone (ACTH) resulting into increased secretion of glucocorticoids which have an overall suppressive effect on the immune system. The same

phenomenon is understood as vyadhiutpadakapratibandhakam meaning adaptogen<sup>52</sup>.

## CONCLUSION

The various research works show that stress is the cause of many life threatening diseases. Hence with the support of different studies mentioned above, Ashwaganda can be effectively utilized in preventing the complications of stress reactions through its adaptogenic activity. The scope of effectiveness of Ashwaganda can be extended to many stress induced diseases like menstrual mood disorders, autoimmune diseases, lifestyle disorders, endocrine disorders and even malignancy.

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