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A Brief Review On Ashwagandha

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Abstract

Withania somnifera (Linn) Dunal, better known by her popular name, Ashwagandha, is a member of the Solanaceae (nightshade) family, which has 1250 species that are extensively dispersed throughout the world's warmer regions. There are reportedly 23 species in the genus *Withania*, two of which have significant therapeutic value: *Withania somnifera* Linn Dunal and *Withania coagulans* Dunal. Ashwagandha, *Withania somnifera* (Linn) Dunal, is available in a variety of forms and formulations, including powder, decoction, oil, smoke, poultice, etc. This significant medication, sometimes referred to as Asgard, has been utilised for ages in both the Unani and Ayurvedic medical systems, either alone or in conjunction with other medications. The medicinal use of ashwagandha for anxiety, neurological and cognitive problems, inflammation, and Parkinson's disease is supported by clinical studies and animal research. Because of its chemopreventive qualities, ashwagandha may be a helpful addition for people receiving chemotherapy and radiation treatment. Additionally, ashwagandha is used medicinally as an immunological stimulant in patients with low blood counts of white blood cells and as an adaptogen for patients suffering from nervous weariness, sleeplessness, and debility as a result of stress. Within the family of substances known as withanolides, steroidal lactones and steroidal alkaloids make up the majority of the biochemical components of ashwagandha root.

Keywords: Ashwagandha, *Withania somnifera*, Withanolide, Medicinal plant, Neurological disorder

INTRODUCTION

Ashwagandha (*Withania somnifera*, fam. Solanaceae) is best known as "Indian Winter cherry" or "Indian Ginseng". (1,2) In Sanskrit, Ashwagandha means odor of the horse, originating from the aroma of the roots which resembles that of horse sweat, while the name "somnifera" in Latin means "sleep-inducer" which refers to its extensive use as an anti-stress remedy. (3) 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.(4)

Ashwagandha is a shrub found throughout the semi-arid region of India and other Southeast Asian countries. The plant is also available in African regions such as Congo, South Africa, Egypt, Morocco, and Middle-Eastern countries.(5,6) The extract of the Ashwagandha root has many biological implications due to its diverse phytochemicals, so it has been used, singly or in combination with other natural plants, in many research studies for its properties: anti-diabetic, anti-inflammatory, anti-microbial, anti-tumor, anti-stress, cardioprotective, or neuroprotective. (7,8) Traditionally, WS preparations are used for conditions such as arthritis, asthma, goiter, and ulcers, as well as anxiety, insomnia, and neurological disorders. These uses are linked to the botanical's reputed adaptogenic, anti-stress, and anti-inflammatory properties. (9)

Withania extract administration was found to increase the haemoglobin level, RBCs and decrease serum cholesterol, ESR etc. (Ziauddin et al., 1996). Administration of *W. somnifera* could reduce the leucopenia, enhanced the bone marrow cellularity and the ratio of normochromatic to polychromatic



erythrocytes in mice treated with nonlethal dose of gamma radiation (Kuttan, 1996). Administration of *Withania* could also enhance the total WBC count, bone marrow cellularity as well as esterase positive cells in mice treated with cyclophosphamide (Davis and Kuttan, 1998).(10)

Historical background of Ashwagandha

The prospective treatment alternative of traditional medicine can treat a wide range of problems with minimal side effects, enhanced efficacy, and the ability to control the disease at various stages, including prevention and cure. In many traditional medical systems, including Ayurveda, Unani, Siddha, homeopathy, Chinese, Tibetan, African, etc., ashwagandha is a key plant. The oldest medical systems include the Chinese medical system and the traditional Indian medical system, or Ayurveda. Further evidence and study grounded in science were needed for Ayurveda. Because its roots resemble sweating horses, Ashwagandha, which means "odour of the horse," is the name given to it in Ayurveda. It has been widely utilized to cure a variety of ailments for the past thousand years. Traditionally, Ayurvedic practitioners would boil the fresh roots in milk. Another way to administer it is to grind the roots into a fine powder known as "churna" and mix it with liquids, primarily milk, honey, and water. It is categorized as "Rasayana" in the Ayurvedic system, which means "tonic" and primarily functions as a body rejuvenator, disease prevention, aging slowing agent, and memory booster. In the Unani system, *Withania somnifera* is referred to as Asgand and is discussed in the book "Kitab-ul-Hashaish." Literature claims that Asgand Nagori and Asgand Dakani are the two types recognized in the Unani system; nevertheless, Asgand Nagori is the more recommended variety in terms of medicine. China has been more successful in promoting the usage of many herbs, including *Withania somnifera*, based on scientific research and proof. *Withania somnifera* is a native plant to Africa and is primarily thought of as a weed of garbage and contaminated regions. Leaves are applied as bandages to wounds and illnesses (11).

In India, the wild variety of *W. somnifera* is found in three forms.

- i. Sandy desert soil of Pilani, Marwar, and some parts of Rajasthan. Root: Straight, thick, unbranched, thick, fleshy, and distinctly fusiform.
- ii. Chandigarh and some mountainous areas of Punjab and Uttar Pradesh. Root: A straight unbranched tap root, tapering gradually from the crown, comparable in size and texture to form 1 thick and unbranched.
- iii. Near Delhi and Ahmedabad along hedges and shady habitats. Root: branched, light, and woody.(12)

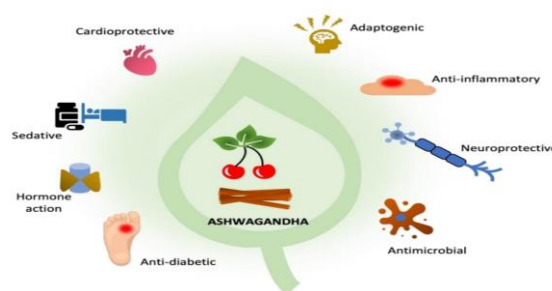


Figure 1: The comprehensive health benefit of Ashwagandha(13)

Vernacular names

Arabic: Kakanj Hindi

Bengali: Ashvagandha, Asvagandha

English: Winter cherry Gujrati : Asgandha, Asundha, Asana

Hindi: Asgandh, Punir

Kannada: Angaberu, Hirenaddina-Hire-gadday

Marathi: Asgandha, Askagandha, Askandhatilli Oriyan : Asugandha

Persian: Asgandh Nagori, Kakanjae Hindi

Sanskrit: Ashvagandha, Gandhrapatri, Palashparni, Varahapatri, Turangi-gandh

Telgu: Pennerugadda, Asvagandhi, panneru

Tamil: Amukkaram, Kizargu Amukkuram Urdu : Asgand Nagori (14)

Scientific classification

Kingdom : Plantae

Division : Angiosperms

Class : Dicotyledon Order : Tubiflorae Family : Solanaceae

Genus : *Withania*

Species : *somnifera* (14)

Phytochemical Studies

A review of literature reveals the presence of various chemical constituents in the different parts of the plant which are as follows:

Root

The roots are reported to contain alkaloids, amino acids, steroids, volatile oil, starch, reducing sugars, glycosides, hentriacontane, dulcitol, withaniol, an acid (m.p. 280-283°decomp.), and a neutral compound (m.p. 294-296°). The total alkaloidal content of the Indian roots has been reported to vary between 0.13 and 0.31 percent, though much higher yields (up to 4.3%) have been recorded elsewhere (Anonymous, 1982, Anonymous, 2007). Identity, purity, strength and assay of the dried roots of the plant are given in (Table)

Table : Identity, purity, strength and assay.

Foreign organic matter	Not more than 2%
Physicochemical constants	
<i>Ash values (%)</i>	
Total ash	6.0
Acid insoluble ash	1.5
Water soluble ash	3.0
<i>pH values</i>	
1% solution	5.5
10% solution	5.5
Loss on drying at 105 °C	8.7%
Solid contents	91.3%
<i>Successive extractive values (%)</i>	
Pet. Ether	0.348
Chloroform	0.304
Acetone	0.305
Alcohol	0.184

Many biochemically heterogeneous alkaloids have been reported in the roots. Basic alkaloids include cuscohygrine, anahygrine, tropine, pseudotropine, anaferrine, isopelletierine, withanane, withananine, pseudo-withanine, somnine, somniferine, somniferinine. Neutral alkaloids include 3-tropyltigloate and an unidentified alkaloid. Other alkaloids include withanine, withasomnine, and visamine. Withanine is sedative and hypnotic (Khare, 2007). Withasomnine has been separated from the roots of the plant grown in West Germany. Visamine is a new alkaloid which has been separated from the roots of the plant grown in Soviet Union. It prolonged hexanal-induced sleeping time and showed hypothermic and nicotinolytic effects in mice (Rastogi et al., 1998). The free amino acids identified in the root include aspartic acid, glycine, tyrosine, alanine, proline, tryptophan, glutamic acid, and cystine (Khare, 2007).



Leaf

The leaves of the plant (Indian chemotype) are reported to contain 12 withanolides, 5 unidentified alkaloids (yield, 0.09%), many free amino acids, chlorogenic acid, glycosides, glucose, condensed tannins, and flavonoids (Khare, 2007). The leaves of the plant from different habitats contain different withanolides—a group of C28 steroids characterized by a 6-membered lactone ring in the 9-carbon atom side chain.

Withaferin A, a steroidal lactone is the most important withanolide isolated from the extract of the leaves and dried roots of *Withania somnifera*. It is thermostable and slowly inactivated at pH 7.2. It is insoluble in water and is administered in the form of suspension. For its separation, the leaves are extracted with cold alcohol; the extract is purified and dried, and finally crystallized from aqueous alcohol (yield, 0.18% air dry basis). The yield of this compound from the South-African plants is reported to be as high as 0.86

percent. The curative properties of the leaves and roots are attributed to Withaferin A (Anonymous, 1982).



Fruit

The green berries contain amino acids, a proteolytic enzyme, condensed tannins, and flavonoids. They contain a high proportion of free amino acids which include proline, valine, tyrosine, alanine, glycine, hydroxyproline, aspartic acid, glutamic acid, cystine and cysteine. The presence of a proteolytic enzyme, chymase, in the berries may be responsible for the high content of the amino acid.



Stem

The stem of the plant contains condensed tannins and flavonoids.



Bark

The bark contains a number of free amino acids (Anonymous, 1982). (15,16,17 18,19,20)



Withania somnifera in ayurveda

Although *W. somnifera* is more frequently employed in conventional medicine, *W. coagulans* is also used in some particular preparations (Upadhyay and Gupta, 2011). In more than 200 Ayurvedic compositions, *W. somnifera* roots are used. The powdered root of the *W. somnifera* plant known as ashwagandha is frequently used to cure several diseases. It is additionally combined with other compounds. The main ingredient in Saraswati churna, an herbal powder mixture intended to treat neurological problems, is *W. somnifera*. Another product that contains *W. somnifera* is ashwagandhadhi lehyam, which is generally used as an energy booster, a cure for male impotence, and a supplement for general rejuvenation (Rasheed et al., 2013). Even while these applications may appear to be very different, it's conceivable that certain ratios and combinations with the other substances could provide very different results. It's interesting to note that traditional medical treatments only use the plant's root. Researchers in alternative medicine have lately examined the use of *W. somnifera* in Ayurvedic formulations and found that standardization, phytochemical screens, and testing for pathogen/heavy metal contamination can considerably enhance the effects of Ashwagandhadhi lehyam. *W. somnifera* containing ayurvedic preparations are used as analgesics for a variety of musculoskeletal disorders (including arthritis and rheumatism), some types of hypertension, for inducing sex and boosting sperm counts, in gynecological practice for vaginitis, and during pregnancy for the development of the breasts (Mishra et al., 2000). (21)

Conventional approaches in cultivation

W. somnifera is cultivated for food-supplement, herbal and medicine industries. With growing laboratory evidence of its medicinal value for a variety of ailments, sustained supply of active ingredient-enriched plants is desirable.

1. Climate required for growing Ashwagandha
2. Land preparation for Ashwagandha plantation:
3. Propagation, nursery raising and planting in Ashwagandha cultivation:
4. Manures and fertilizers of Ashwagandha crop:
5. Pests and diseases of Ashwagandha crop:
6. Good harvesting practices (22)

Plant distribution and morphology

Withania somnifera is commonly called Ashwagandha, Indian ginseng, or winter cherry, it is a well-known herb, used for centuries in Ayurvedic medicines for increasing longevity, vitality, and as a health-promoting tonic (rasayana) to boost body's resistance against diseases (Bhattacharya & Muruganandam, 2003). *Withania somnifera* is an erect, grayish, slightly hairy evergreen shrub with fairly long tuberous roots and short stem, stem and branches covered with minute star-shaped hairs, leaves simple, up to 10 cm long, ovate, petiolate, and alternate. The flowers are small and greenish or yellow, single or in small clusters in the leaf axils, flowering nearly throughout the year. The fruit is smooth, globose, fleshy, having many seeds, orange-red when ripe, enclosed in a membranous covering. This small, woody shrub grows to about 2 ft. in height and found in Africa, India, Mediterranean area, and also grown in United States (Khazal et al., 2013). Different chemotypes of *W. somnifera* are widely grown in India for its medicinal use (Kaul et al., 2005; Kulkarni & Dhir, 2008). The genus *Withania* includes 26 species of which only two are found in India, *W. somnifera* and *W. coagulans* Dunal (Barche et al., 2014; Chadha, 1976; Kulkarni & Dhir, 2008). A third species that is *W. obtusifolia* (Tackh) was reported from South India but Sundari et al. (1999) found that it was only a cytotype (2n ¼ 24) of *W. somnifera* (2n ¼ 48). Recently, Mir et al. (2010) and Kumar et al. (2011) have reported a third species from Indian germplasm, namely *W. ashwagandha* by using multi-disciplinary approaches. A metabolic profiling of crude extracts of leaves and roots of *W. somnifera* reported a total of 62 different major and minor primary and secondary metabolites from leaves and 48 from roots. Out of these, 29 metabolites were common to both leaves and roots which include fatty acids, organic acids, amino acids, sugars, flavones, and sterol derivatives and quantitative differences were also noticed between the leaf and root Tissue.



Figure . *Withania somnifera* (a) complete plant, (b) leaves, (c) fruits, and (d) roots. (23)

Description of the plant

A small or middle-sized under shrub, erect, grayish, branched, 30–150 cm high, with greenish or lurid yellow flowers. Fruits are a berry enclosed in the green persistent calyx, green when unripe, turns to orange red when mature. The fruit contains numerous small capsicums like seeds. Flowering occurs nearly throughout the year.

The shoots specially stem, veins and the calyx are covered with minute star-shaped hairs. Leaves are simple, ovate, petiolate, entire, exstipulate, acute, glabrous and up to 10 cm long and petioles are around 1.25 cm long. On vegetative shoots, the leaves are alternatively arranged and large while on floral branches, they are oppositely arranged in pairs of one large and one small leaf and arranged somewhat parallel, having a cymose cluster of 5–25 inconspicuous pale green flowers in their axil.

The roots are fairly long and tuberous (*20–30 cms and 6–12 mm in diameter) with a short stem and with few (2–3) lateral roots of slightly smaller size, straight, unbranched. They have buff to grayishyellow outer surface with longitudinal wrinkles and soft, solid mass with scattered pores in the center. The roots taste bitter and acrid. (24)



Chemical Composition

The biologically active chemical constituents of Withania somnifera (WS) include alkaloids (isopelletierine, anaferine, cuseohygrine, anahygrine, etc.), steroidal lactones (withanolides, withaferins) and saponins (Mishra, 2000 et al., 2000). Saponins and acylsterylglucosides in Ashwagandha are anti-stress agents. Active principles of Ashwagandha, for instance the saponins 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-urRahman et al., 1991). (26)

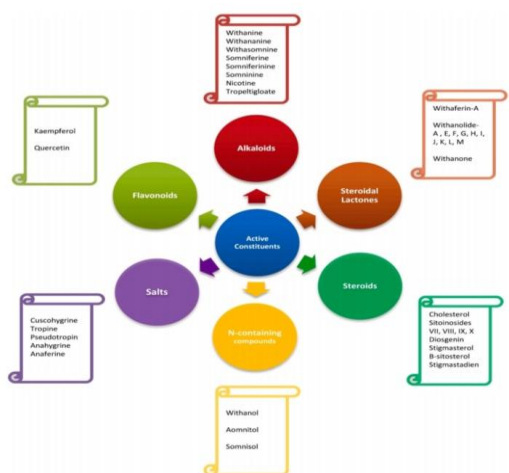


Fig . Different classes of phytochemicals present in Withania somnifera. (25)

Potential therapeutic effects of some active substances found in Ashwagandha.(27)

Active Substance	Potential Effects
Anaferine	anti-tuberculous, neuroprotective
Anahygrine	anti-tuberculous, neuroprotective
Withaferin A	anti-inflammatory, anti-cancer, anti-diabetic, cardioprotective, neuroprotective, antibacterial, anti-SARS-CoV-2, in dermatological diseases
Withanolide D	neuroprotective, anti-cancer
Withanone	antibacterial, anti-SARS-CoV-2, anti-cancer

Therapeutic uses of Withania somnifera

Withania somnifera is one of the major herbal components of geriatric tonics mentioned in Indian systems of medicine. In the traditional system of medicine Ayurveda, this plant is claimed to have potent aphrodisiac rejuvenative and life prolonging properties. It has general animating and regenerative qualities and is used among others for the treatment of nervous exhaustion, memory related conditions, insomnia, tiredness potency issues, skin problems and coughing. It improves learning ability and memory capacity.

The traditional use of ‘Ashwagandha’ was to increase energy, youthful vigour, endurance, strength, health, nurture the time elements of the body, increase vital fluids, muscle fat, blood, lymph, semen and cell production. It helps counteract chronic fatigue, weakness, dehydration, bone weakness, loose teeth, thirst, impotency, premature aging emaciation, debility, convalescence and muscle tension. It helps invigorate the body by rejuvenating the reproductive organs, just as a tree is invigorated by feeding the roots .(28)

The species’ root and root powder and paste are beneficial.23 The pulverized leaves of WS are used to treat exterior pain, inflammatory processes, and pubonic pains.(29)

Pharmacological Activities of Ashwagandha

1. Anti-ischemic and anti-hypoxic effect of W. somnifera

W. somnifera have demonstrated protective effect against middle cerebral artery occlusion induced injury in rats by dropping oxidative stress, reduction in lesion area and balancing the neurological functions (Chaudhary et al. 2003). The root extract of W. somnifera and withanolide-A protected against hypobaric hypoxia induced memory and hippocampal neurodegeneration in rats by improving reduced glutathione levels via the activation of glutathione biosynthesis pathway in isolated hippocampal cells. These effects were mediated by the activation of nuclear factor erythroid 2-related factor two

pathways and NO in a corticosterone-dependent manner (Baitharu et al. 2013, 2014)

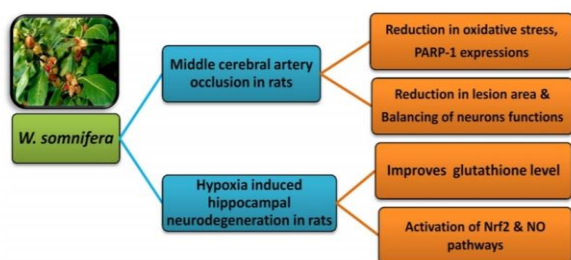


Figure . Anti-ischemic and anti-hypoxic effect of *W. somnifera*.(30)

2. Anti-cancer effect of *W. somnifera*

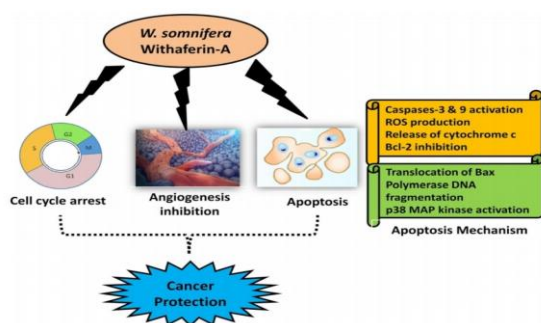


Figure . Anti-cancerous activity of *W. somnifera*. (30)

3. Anticonvulsant Activity

Administration of *W. somnifera* root extract was found to reduce jerks and clonus in 70% and 10% animals respectively with dose of 100mg/kg and reduction in the severity of pentylenetetrazole (PTZ)-induced convulsions was evident from EEG wave pattern (Kulkarni et al., 1996). *W. somnifera* root extract showed reduction in severity of motor seizures induced by electrical stimulation in right basilateral amygdaloid nuclear complex through bipolar electrodes. The protective effect of *W. somnifera* extract in convulsions has been reported to involve GABAergic mediation (Kulkarni et al., 1993).(15)

4. Cardioprotective activity

W. somnifera has been evaluated in clinical studies with human subjects for its diuretic, hypoglycemic, and hypocholesterolemic effects . Six type 2 diabetes mellitus subjects and six mildly hypercholesterolemic subjects were treated with a powder extract of the herb for 30 days. A decrease in blood glucose comparable to that which would be caused by administration of a hypoglycemic drug was observed. Significant increases in urine sodium, urine volume, and decreases in serum cholesterol, triglycerides, and low-density lipoproteins were also seen. (31)

5. Antidepressant and anti-anxiety activity

The roots of *W. somnifera* are used extensively in Ayurveda for the treatment of anxiety and depression. Earlier it was reported that, anxiolytic-antidepressant potential of *W. somnifera* and its glycowithanolides (Bhattacharya et al., 2000). Recent study reports also support the use of *W. somnifera* for depression and anxiety disorders. In a very

recent study, it is found that *W. somnifera* at 40 mg/kg significantly reduces the depression in various experimental models (Jayanthi et al., 2012). Clinical trials with healthy volunteers also revealed that aqueous extracts of *W. somnifera* improve the psychomotor performances in anxiety and depression (Pingali et al., 2014). It was assumed that *W. somnifera* reduces the production of nitric oxide in the brain tissues, resulting in its anxiolytic activity (Khan and Ghosh, 2011; Maity et al., 2011). Study findings explained that *W. somnifera* and its bioactive withanolides possess antidepressant and anti-anxiety potential and are useful in treating various types of mental disorders.(32)

6. Anti-diabetic activity

Various polyherbal formulations (Dianix, Trasina) of Indian Systems of Medicine showed strong anti-diabetic activity in human subjects . In patients, *W. somnifera* root powder stabilized blood glucose that was comparable to that of an oral hypoglycemic drug daonil, when treated orally for 30 days . Additionally, *W. somnifera* treatment significantly improved insulin sensitivity index and blocked the rise in homeostasis model assessment of insulin resistance in non-insulin-dependent diabetes mellitus in rats . In agreement with these studies, *W. somnifera* leaf and root extracts improved glucose uptake in skeletal myotubes and adipocytes in a dose-dependent manner, with the leaf extract demonstrating more pronounced effects than the root extract . Root and leaf extracts significantly normalized the levels of urine sugar, blood glucose, glucose-6-phosphatase, and tissue glycogen levels in alloxan-induced diabetes mellitus in rats. Additionally, attenuation of improving the nonenzymatic and enzymatic anti-oxidant defenses was also observed . Withaferin-A blocks inflammatory response in cytokine-induced damage to islets in culture and following transplantation and exhibits potent anti-glycating activity . (33)

7. Anti-microbial activities

The antibacterial properties of this multipronged medicinal plant were for the first time reported by Kurup (1956) against *Salmonella aurens*. In past one decade, antimicrobial activity against a range of bacteria and fungi ascribed to withanolide were reported (Dhuley, 1998, Ziauddin et al., 1996; Dhuley, 1998; Mishra et al., 2000; Owais et al., 2005). However, the existing literature shows that this herb should be studied more extensively to explore its potential in the treatment of other infectious diseases as well.(34)

8. Adaptogenic activity and anti-stress activity

Withania somnifera roots were investigated against a rat model of chronic stress (CS). The stress procedure was mild, unpredictable footshock, administered once daily for 21 days to adult male Wistar rats. CS induced significant hyperglycaemia, glucose intolerance and increase in plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression and mental depression. These CS induced perturbations were attenuated by *Withania somnifera* (25 and 50 mg/kg po) and by panax ginseng (PG) (100 mg/kg po), administered 1 h before footshock for 21 days. The results indicate that

Withania somnifera, like *Panax ginseng* (PG), has significant antistress adaptogenic activity, confirming the clinical use of the plant in Ayurveda. (14)

9. Anti ageing effect:

Double blind clinical trial carried out to study the effect of plant on prevention of ageing in 101 normal healthy males in 50-59 years age group. Root powder (0.5gm) was given orally three times a day for 1 year. Results showed statistically significant increase in Hb%, RBC, hair melanin, and seated stature in treated group in comparison to placebo group. Decrease in serum cholesterol was more in treated group than in placebo group. (35)

10. Hypothyroidism

Animal studies reveal ashwaganda has a thyrotropic effect. No changes in T3 levels were observed. *Withania* may also stimulate thyroid activity indirectly, via its effect on cellular antioxidant systems. *Withania* extract significantly decreased lipid peroxidation in the liver homogenate and significantly increased catalase activity, promoting scavenging of free radicals that can cause cellular damage. These results indicate ashwaganda may be a useful botanical in treating hypothyroidism. An aqueous extract of dried *Withania* root was given to mice via gastric intubation at a dose of 1.4 g/kg body weight daily for 20 days. Serum was collected at the end of the 20-day period and analyzed for T3 and T4 concentrations and lipid peroxidation was measured in liver homogenate via antioxidant enzyme activity. Significant increases in serum T4 were observed, indicating the plant has a stimulatory effect at the glandular level. (12)

11. Effect on leucocytosis

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

12. 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. (23)

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