

ASHWAGANDHA

(Withania Somnifera)

An overview of the research and
clinical indications



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Ashwagandha: An Overview of the Research and Clinical Indications

BACKGROUND AND USES

Withania somnifera, also commonly known as Ashwagandha, is a small evergreen shrub that grows to roughly four to five feet tall. It is also called Ayurvedic ginseng or Indian ginseng, and is used in a manner similar to *Panax ginseng*'s profile. Ashwagandha grows prolifically in dry regions of South Asia, Central Asia and Africa, particularly in India, Pakistan, Bangladesh, Sri Lanka, Afghanistan, South Africa, Egypt, Morocco, Congo and Jordan¹⁷. In India, it is cultivated, on a commercial scale, in the states of Madhya Pradesh, Uttar Pradesh, Punjab, Gujarat and Rajasthan.¹⁷

The name ashwagandha is a combination of the Sanskrit word *ashva*, meaning horse, and *gandha*, meaning smell. The root has been described as having a strong "horselike" aroma, although some experts note that the origin of the name suggests that one who ingests it can attain the strength and vitality of a horse. This botanical is associated with stamina and re-invigoration, and increasing strength and energy.

In Ayurveda, the ancient Hindu system of medicine, *Withania somnifera* is classified as a *rasayana*, a group of plant-derived drugs reputed to promote physical and mental health, augment resistance of the body against disease and diverse adverse environmental factors, revitalize the body in debilitated conditions, and increase longevity.

As a part of the Ayurvedic herbal tradition, Ashwagandha has been used as an adaptogenic botanical medicine for hundreds of years. In botanical medicine traditions from around the world, certain herbs are in a category of functional use called "adaptogenic", meaning that the herb has the reputation of helping the body to resist damage from physical and mental stressors. In clinical and healing settings, Ashwagandha is used for both preventing harm from stress and for treating the consequences of stress, as part of an overall rejuvenation therapy to revitalize bodily functions.

ACTIVE CONSTITUENTS

Ashwagandha contains potentially active constituents of alkaloids and steroidal lactones that together are called withanolides (particularly withaferin A). Preparations are often standardized to their percentage content of withanolides.

MECHANISM OF ACTION

The withanolides constituents are what are thought to possess physiological activity and possible benefits. Plants that are more mature show a higher concentration of the constituent withaferin A. The withanolides are reported to show anti-oxidant properties, including the prevention of lipid peroxidation in animal studies. If this same benefit occurs in humans, it is really good news, as it means this herb helps prevent a fundamental process that is at the core of most heart disease and other cardiovascular complications. Preventing blood lipids from becoming inflamed is always good news for the maintenance of health and the prevention of heart attacks and strokes.

A number of studies point to clinical benefit in promoting improved function of the central nervous system (CNS). In clinical study, following 12 weeks of treatment with ashwagandha, circulating levels of monoamine oxidase (MAO) and GABA levels have decreased, while levels of 5-hydroxytryptophan and glutamic acid decreased.¹ Ashwagandha demonstrated GABA-like properties and enhanced diazepam effects in animals.² Rodent studies have shown it also appears to have anti-depressant effects.³ Ashwagandha has demonstrated an enhanced stress response^{4,5,6}, such as the response to swimming in cold water.^{7,8} In human neuroblastoma cells, its extract is reported to promote the formation of dendrites, which is a marker of increased connectivity in the brain.^{9,10}

RESEARCH SUMMARY

Optimal Aging

Ashwagandha's traditional use in Ayurvedic medicine includes its use as an optimal aging herb that increases longevity, promotes resistance to disease, and improves both mental and physical health. Culturally it is considered a strong tonic. Anti-oxidant properties are suggested by animal research, and this is a viable explanation of anti-aging effects.^{11,12,13,14,15} Based on today's research base, more clinical studies are needed to reach a firm conclusion from the point of view of Western medicine.

Improve generalized weakness, speed, lower limb strength and neuro-muscular coordination

This study had 40 healthy young adult participants, and the group who took the standardized root extract of *Withania somnifera* experienced increased velocity, power and VO2 max.²¹ Study participants' measures of balance and diastolic blood pressure

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remained unchanged. The conclusion was that this botanical agent might be useful for generalized weakness, to improve speed, lower limb muscular strength and neuromuscular co-ordination. It appears to be safe for young adults when given for the study's dosage of 500 mg in a capsule form, for 30 days duration.

Anxiety

This study used a randomized trial to explore the effectiveness of Naturopathic care on anxiety.²² Anxiety can be a debilitating condition, resulting in a person who is incapacitated to perform their activities of daily living, including performing well in the workplace. Employees (81 subjects) reporting moderate to severe anxiety of longer than 6 weeks duration were randomized according to age and gender, and put on either Naturopathic care (41 subjects) or on psychotherapy intervention (40 subjects). Naturopathic care included a standardized extract of *Withania somnifera* (300 mg b.i.d. standardized to 1.5% with anolides, prepared from the root). Both groups received deep breathing relaxation techniques. Both groups reported significant improvement in their anxiety. Significant improvements in secondary quality of life measures were also observed in the Naturopathic care group as compared to psychotherapy intervention.

Chronic Stress

A study employed a rat model of chronic stress, and investigated the result of using a standardized extract of *Withania somnifera* roots to assess the adaptogenic activity of the *Withania*.²⁴ The stress procedure was mild, unpredictable foot shock, administered once daily for 21 days to adult male rats. The chronic stress induced significant hyperglycemia, glucose intolerance, increase in plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression and mental depression. These chronic stress induced perturbations were attenuated by *Withania somnifera* (25 and 50 mg/kg), administered by mouth 1 hour before foot shock for 21 days. The results indicate that *Withania somnifera* has significant anti-stress adaptogenic activity, confirming the clinical use of the plant in Ayurveda. This is similar to findings that employ *Panax ginseng* as an adaptogenic botanical agent.

Integrative Oncology

This published literature review²³ across a number of animal studies concludes that *Withania somnifera* Dunal, commonly known as ashwagandha, presents itself as a novel complementary therapy for integrative oncology care. This botanical agent has been used for centuries in Ayurvedic medicine to increase longevity and vitality. Published research supports multiple uses, confirming antioxidant, anti-inflammatory, immune-

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modulating, and anti-stress properties found in the whole plant extract and several separate constituents. The article reviews the literature pertaining to *Withania somnifera* and its botanical constituents as antitumor agents and in conjunction with radiation and chemotherapy treatment. As a result of a search of MEDLINE and EBSCO

databases, it was concluded that *Withania somnifera* reduces tumor cell proliferation while increasing overall animal survival time. Furthermore, it has been shown to enhance the effectiveness of radiation therapy while potentially mitigating undesirable side effects. *Withania somnifera* also reduces the side effects of chemotherapeutic agents, cyclophosphamide and paclitaxel, without interfering with the tumor-reducing actions of the drugs. These effects have been demonstrated in vitro on human cancer cell lines, and in vivo on animal subjects, but there have been no human trials to date. Given its broad spectrum of cytotoxic and tumor-sensitizing actions, *Withania somnifera* warrants a human trial as a novel complementary therapy for integrative oncology care.

Alzheimer's disease

More research is needed in this area, but a new study shows some promising results. A just released study done on mice demonstrated the benefit of a 30 day course of oral administration of a semi-purified extract of the root of *Withania somnifera*, which consisted predominantly of withanolides and withanosides to reverse behavioral deficits, plaque pathology, accumulation of β -amyloid peptides ($A\beta$) and oligomers in the brains of middle-aged and old APP/PS1 Alzheimer's disease transgenic mice.¹⁶ This study showed a decrease in brain levels of β -amyloid peptides, which is represented by an increase in the transport of β -amyloid peptides out of the brain and into the periphery.¹⁶ At this time, one of the principal mechanisms by which Alzheimer's disease is thought to occur is the accumulation of these β -amyloid peptides in the brain. The effect of the *Withania somnifera* in enhancing the low-density lipoprotein receptor-related protein (LRP) in brain microvessels and the β -amyloid-degrading protease neprilysin (NEP) is what appears to promote the removal of these troublesome β -amyloid peptides from the brain and allow for better processing of these substances in the liver.¹⁶ This study showed reversal of behavioral deficits and plaque formation in the mice in the study.¹⁶ This finding deserves a human trial to determine if the same benefits can be obtained for people who have Alzheimer's disease, representing a welcome breakthrough in this debilitating illness.

CLINICAL INDICATIONS, PRACTITIONER DOSING, CONTRAINDICATIONS AND TOXICITY

Clinical Indications

- Promote protection from effects of stress
- Improve resilience to and recovery from stress
- Improve removal of β -amyloid peptides from brain in patients with Alzheimer's disease
- Generalized weakness
- Poor stamina
- Low energy and vitality
- Low immune function
- Hypercholesterolemia
- Chronic stress recovery
- Anxiety
- Integrative oncology – human studies and trials warranted

Dosage range

The dosage range recommended in review literature is 500 mg – 3 g Ashwagandha extract per day. Reviewed research did not provide clear dosage forms and amounts. Ashwagandha tablets may be standardized to 4.5mg withanolides. A typical daily dose of the dried root is 3-6 g a day. For standardized extracts containing 1.5% withanolides, a suggested daily dose range is 300-500 mg. For a 1:2 fluid extract, 6-12 ml is the suggested daily dose range.²⁵

Contraindications

Literature review reveals no adverse events were reported for the use of up to 3g of Withania extract tablets for a period of one year.¹⁸ There is very limited data available concerning contraindications for using Ashwagandha in humans.

Monitor patients with diabetes, or those using hypoglycemic agents, as Withania is associated with glucose-lowering effects, based on limited human and animal study.^{19,20}

Patients with known allergies/hypersensitivities to Ashwagandha, or to members of the Solonaceae family, should avoid using this botanical agent.

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Use cautiously in women who are pregnant or lactating, due to the lack of data to show clear safety for use during these phases of life. Large doses may possess abortifacient properties.

Alcohol, sedatives and anxiolytics should be avoided while taking *Withania somnifera*, as it is a mild central nervous system depressant.²⁵

Based on *animal* studies, use cautiously in:

- Patients with hypotension or those using anti-hypertensive drugs
- Patients with bleeding disorders or those taking anti-coagulant or anti-platelet drugs
- Patients taking sedative agents
- Patients taking inotropic or chronotropic agents
- Children, due to lack of data to show clear safety in this population
- Patients with thyroid disorders, to avoid hyper-stimulation
- Large doses for patients taking respiratory depressants

Toxicity

There are no reports to date of toxicity with the use of *Withania*. There are limited safety studies on the toxicity of *Withania* using human subjects.¹⁸ One trial, using 101 human male subjects, administered treatment of 3g of *Withania* by mouth with milk, daily, for one year, with no adverse events reported.¹⁸ Another study administered powdered *Withania* root daily for 30 days to 12 patients; no adverse events were reported.¹⁹

CONCLUSIONS

The overall botanical medicine benefit profile for Ashwagandha makes it a viable botanical agent for promoting overall improved stamina, vitality, strength and mental vigor. *Withania somnifera* is a strong adaptogen and helps to restore resilience in people who show signs of depletion. It is shown to offer clinical benefits for addressing anxiety, depression, neurodegenerative disorders and stress of both chronic and acute duration.

The most recent research, using mice as the study subjects, shows benefit with reversing some Alzheimer's disease symptoms, including promoting the removal of β -amyloid peptides from the brain.

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It appears to be a safe herb for medicinal use, as it has been used for hundreds of years without major incident.

This botanical agent would benefit from further study in human trials to better understand its mechanisms of action, to assess its drug/botanical agent interactions and further explore any toxicity in humans. Particular areas of research focus include integrative oncology and dementia of the Alzheimer's disease type.

ABOUT THE AUTHOR

Dr. Beverly Yates, Naturopathic Physician, graduated from the National College of Naturopathic Medicine in 1994. She is also a graduate of the Massachusetts Institute of Technology with a B. S. degree in Electrical Engineering. Dr. Yates served as the lead supervising doctor for the first ever fully accredited Naturopathic and Integrative medical residency in the state of California. Dr. Yates was a Featured Speaker for the California Naturopathic Doctors Association Integrative Medicine conference on Cardiology, presenting continuing medical education on Women and Cardiovascular Disorders.

Dr. Yates serves as a National Media Representative for the American Association of Naturopathic Physicians, appearing as an expert in natural medicine on TV shows in select metropolitan areas. She is a member of the Medical Advisory Board for Schwabe North America, and is on the Scientific Advisory Board for Gaia Herbs, Inc. and BSP Pharma, Inc. Recently, in response to Dr. Yates' contributions to community health, she provided testimony for the Tri-Caucus of the California legislature concerning the growing impact of obesity and diabetes in communities of color around the state and the country.

Sought after for her ability to provide concise, clear explanations about medical processes and natural medicine, Dr. Yates has appeared on numerous TV broadcast networks including ABC, CBS, CNN, CW, Fox, NBC, and PBS; her radio interviews include NPR, CNN Radio, Sirius International Satellite; and her print interviews include Essence Magazine, Good Housekeeping Magazine and Women's World newspaper. She presents continuing medical education (CME) to physicians and other health professionals all over the country.

Dr. Yates is a nationally recognized author [book: Heart Health for Black Women: A Natural Approach to Healing and Preventing Heart Disease, Marlowe & Co., 2000] and contributing author [medical textbook: Maternal Newborn and Child Nursing: Family Centered Care, Prentice Hall, 2003].

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