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Major Therapeutic Activity of Withania

Key Points at a Glance

Withania

- traditionally (in Ayurvedic medicine) a tonic and *rasayana* herb
- confirmed as an adaptogen
- clinically demonstrated:
  - as a tonic for children and the elderly
  - as beneficial in chronic stress (high dose of withanolides)
  - as beneficial in male infertility (also reduced stress)
  - as an adaptogen for athletes and improved muscle strength in elderly
  - to improve immune function in volunteers and as adjunctive treatment in cancer
  - to reduce anxiety in generalised anxiety disorder
  - to improve mental function in healthy volunteers and the elderly
  - to possibly reduce blood sugar and cholesterol
  - as beneficial for arthritis
- contains steroidal compounds including withanolides (also quality markers)

Traditional Use

Withania somnifera root has been used in Ayurvedic medicine for general debility, nervous exhaustion, fatigue, wasting in children, anaemia, loss of memory, loss of muscular energy, convalescence, insomnia, dementia, impotence, spermatorrhoea, inflammatory conditions such as, bronchitis, asthma, psoriasis, arthritis; as an aphrodisiac and a nutrient and tonic for pregnant women and the elderly. The plant has the Sanskrit common name of ashwagandha.[1-3]

Withania is said to provide fresh energy and vigour for a system worn out by any constitutional disease.[1] As a *rasayana* herb, it promotes physical and mental health, augments resistance of the body against disease and adverse environmental factors, revitalises the body in debilitated conditions and increases longevity.[4] *Rasayanas* (restorative tonics) are regarded almost as nutrients in their effect on the body. These herbs can be age specific in their effect on the losses that occur naturally during human life span. For example, an ancient Ayurvedic text notes the use of Withania as a restorative *rasayana* for loss of virility in 61- to 70-year olds, and for loss of locomotive ability (91–100 years).[5]

It has also been noted that the properties of Ayurvedic *rasayanas* (also known as vitalisers) were similar to those of adaptogen herbs. Indeed the rejuvenators, tonics and vitalisers described in another ancient Ayurvedic text (Carak Samhita) are likely to be adaptogens.[6-8] Research with experimental models have confirmed this and Withania was found to have some adaptogenic properties.[6-11] Withania has been called Indian Ginseng, perhaps because of the similarity of the pharmacological properties.[10]

In Ayurveda, Withania is also regarded as a *medhya rasayana* – a promoter of learning and memory retrieval. The *medhya rasayana* herbs may provide a therapeutic effect by reducing stress, facilitating mental health and reducing anxiety and tension.[12,13]

Other traditional uses of Withania root include:

- general tonic in seminal diseases and as a nervine tonic (Tibet),[14]
- premature ejaculation (Uganda),[15]
- as a sedative and hypnotic; and taken for rheumatic pains (Middle East),[16]
- tonic (South Africa).[17]

An antistress (adaptogenic) activity is suggested by the traditional use of Withania by healers of Ethiopia to treat 'evil eye'.[18]

Constituents

Withania root contains steroidal compounds including withanolides which are regarded as quality markers.[19]

Clinical Studies

Tonic and Adaptogenic Activity

In randomised, double-blind, placebo-controlled trials Withania root powder:

- increased haemoglobin, serum iron, **body weight** and strength of hand grip in children aged 8–12 years (dosage: 2 g/day, in milk);[20]
- **improved haemoglobin**, red blood cell count, serum cholesterol, nail calcium, seated stature, and sexual performance in healthy male patients aged 50 to 59 years (dosage: 3 g/day).[21]

In a trial of the same design, Withania was evaluated in those with **chronic stress**. Three groups were treated with varying dosage regimes for 60 days and compared to a placebo group. Treatment with Withania resulted in significantly improved well being (as evidenced by reduced total stress and anxiety scores). Additional findings are outlined in the following table.[22] The proprietary extract was manufactured from Withania root and leaf, and standardised for withanolides to a minimum of 8%, and withaferin A to a maximum of 2%.[22] Testing indicates the extract to be approximately 8:1, with a phytochemical profile similar to extracts manufactured from Withania root.[23] Using this information, the three groups received Withania extract equivalent to about: 1 g dried root, 4 times/day (providing at least 40 mg/day of withanolides); 1 g dried root, 2 times/day (providing at least 20 mg/day of withanolides) or 2 g dried root, 2 times/day (providing at least 40 mg/day of withanolides).

Compared to baseline, Withania produced the following effects which were significant in comparison to the changes found for the placebo group: • decrease in serum cortisol (measured in the morning), • **increase in serum DHEAS** (dehydroepiandrosterone sulphate), • decrease in serum C-reactive protein, • increase in serum haemoglobin, • decrease in pulse rate and blood pressure.
Dose-dependent results were obtained.
Two of the Withania treatment groups also had significantly greater improvements compared to placebo in mean fasting blood glucose and lipid profiles.

Two trials have assessed the effect of Withania in **male infertility**. The trials can be described as preliminary, due to a lack of control for treatment effects. (A 'control' group was included in each trial to establish normal levels for the parameters tested.) In both trials Withania root (5 g/day, with skimmed milk) was administered for 3 months. In both trials treatment with Withania significantly improved sperm quality, improved semen antioxidant parameters and increased serum luteinising hormone and testosterone. After treatment with Withania, both morning and afternoon **serum cortisol** levels significantly decreased from baseline values.[24,25] One trial included a subgroup of heavy smokers and those under psychological stress.[24]

Withania root (0.5 g/day of powder, for 40 days) improved **cognitive function** in healthy volunteers. The controlled trial was conducted in India.[26]

In uncontrolled trials, Withania:

- improved sleep patterns, responsiveness, alertness, state of awareness and **physical capability** in trainee mountaineers (dosage: 1 g/day);[27]
- improved **muscle strength** and muscle functional performance in healthy elderly men and women aged 60–75 years (dosage: dried herb equivalent undefined).[28]

Immune Function, Cancer

In an uncontrolled study, Withania root increased the population of CD4+ T cells and activation of CD56+ **natural killer cells** in a small number of healthy volunteers (dosage: dried herb equivalent undefined).[29]

Withania root powder or extract has been used in preliminary and uncontrolled settings with **cancer** patients in India, although details are limited. An encouraging response was observed in advanced oral carcinoma (Withania extract and radiotherapy): tumours disappeared in 3 patients and the response in the other 3 patients was good. Blood glutathione levels decreased.[30,31] Treatment with Withania powder improved the life status of neuroblastoma patients (after surgery) and some laryngeal carcinoma patients (who received radiotherapy). It was also beneficial for recovery of neural deficit after encephalitis.[6]

Anxiety

There have been several preliminary or uncontrolled trials in which Withania has shown an anxiolytic effect.[32,33] In addition to this effect, **memory function** improved in these elderly patients with psychiatric symptoms. Withania root (10 g/day) was taken for 3 months).[33]

More rigorous trials have been conducted.

- Double-blind, crossover study. Withania (dried herb equivalent unknown) reduced tension and anxiety in volunteers. Unlike diazepam, the **anxiolytic effect** occurred without producing drowsiness.[34]
- Randomised, double-blind, placebo-controlled trial. Treatment with Withania (dried herb equivalent undefined) for 6 weeks reduced anxiety in patients diagnosed with **generalised anxiety disorder** according to the ICD-10.[35]
- Randomised, controlled trial. Withania (extract providing 9 mg/day of withanolides) combined with a standard multivitamin for 12 weeks produced a

greater decrease in anxiety than those who received psychotherapy and a placebo. The Withania and multivitamin treatment had other benefits, such as improved concentration and less fatigue, in these volunteers who had moderate to severe anxiety.[36]

Other Conditions

Withania root (3 g/day for 30 days) decreased blood sugar levels from baseline in six **type 2 diabetics**. The hypoglycaemic effect was similar to that obtained in the control group treated with glibenclamide. In a group of six **hypercholesterolaemic patients** Withania (same dosage) significantly decreased serum total cholesterol, triglycerides, LDL- and VLDL-cholesterol compared to baseline values. Lipid profiles remained largely unchanged in the untreated control group. The mean calorie and fat intakes of the treatment groups were higher than that of the control groups.[37]

Withania root powder (4–9 g/day, uncontrolled trial) was beneficial for patients with acute **rheumatoid arthritis** and some cases of nonarticular rheumatism and chronic rheumatoid arthritis with acute exacerbations.[38]

Actions

Tonic, adaptogenic, immune modulating, mild sedative, anti-inflammatory, antianaemic, anxiolytic.

Indications

- Debility, fatigue, convalescence, nervous exhaustion, anxiety.
- Stress (especially if chronic).
- May modulate cortisol and DHEAS (high doses).
- Reduced mental or physical performance, insomnia.
- Fatigue, postviral syndromes, poor immune function; adjunctive treatment for cancer.
- Poor growth and anaemia, especially in children.
- Impotence, male infertility.
- Chronic diseases especially those marked by inflammation such as arthritis.
- As a general tonic for disease prevention and for the elderly.

Cautions and Contraindications

Few adverse effects are expected. Because Withania contains steroidal compounds, large doses of liquid extract or powder (mixed in water or milk) may cause mild nausea.

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