



Mills and Bone Academy

Educational Article

The Growing Clinical Reach of Withania – Kerry Bone

When considering the impact of herbal prescribing, there is probably no area more important in modern times than facilitating an optimal stress response with adaptogenic herbs. One of our best adaptogenic herbs comes from India, where its tonic effects have been recognised for thousands of years. This is of course the root of *Withania somnifera* (ashwagandha). But even in ancient texts this wonderful plant was known to have other related benefits, especially as a male tonic, for antiageing and to boost body strength. Based on modern research we can add other assets for *Withania*, especially in brain health.

Grasping these relevant and evidence-based insights into how *Withania* can not only optimise and conserve our stress response, but also help with sleep, anxiety, cognition and male fertility (to name a few) will further support your patients' health and well-being, and underpin your success as clinicians.

As noted above, *Withania somnifera* is an important herb from the Ayurvedic medical system used for the treatment of debility, emaciation, impotence and premature ageing. Not surprisingly, it has been dubbed the 'Indian ginseng'. Its Indian name, ashwagandha, is said

to refer to the 'smell and strength of a horse' and possibly alludes to its reputed aphrodisiac properties, although it could also relate to the smell of the root. Pharmacological research on *Withania* has stressed its anti-tumour, neuroprotective, antiaddictive and adaptogenic actions, reinforcing its comparison with Asian ginseng (*Panax ginseng*). However, *Withania* occupies an important place in the herbal materia medica because, while it is not as potent as ginseng, it lacks the potential stimulating effects of the latter. In fact, it has a mild sedative action as indicated by its specific name 'somnifera'. It is therefore ideally suited to the treatment of overactive but debilitated patients, in whom ginseng might tend to aggravate the overstimulation.

Before this century there were few clinical trials on *Withania*, but this has changed dramatically in recent times, with now around 30 trials published in peer review journals. Some of the key findings from these trials, which greatly extend the clinical reach of this important herb, are reviewed below.

Effects on stressed people

In early research, Withania (1 g/day) was administered to trainee mountaineers over 29 days in an uncontrolled trial that included a 5200 m altitude gain through trekking, and 6 days' training at that height, including a climb to 6400 m and subsequent descent. Psychological and physiological parameters were tested at various altitudes. Withania improved sleep patterns, responsiveness, alertness and state of awareness, together with physical capabilities.

More recently in an 8-week double blind, placebo-controlled, randomised clinical trial (DBPCRT) in 50 people under chronic stress, Withania (600 mg/day extract) significantly reduced perceived stress, food craving, serum cortisol and body weight.

In a 60-day DBPCRT, the stress-relieving and pharmacological activities of a Withania extract (240 mg/day) were investigated in 60 stressed, healthy adults. All participants completed the trial with no adverse events reported. In comparison with the placebo, Withania treatment was associated with a statistically significant reduction in the Hamilton anxiety scale ($p = 0.040$) (see below for more trials on anxiety). Withania intake was also associated with greater reductions in morning cortisol ($p < 0.001$), and DHEA-S ($P = 0.004$) compared with the placebo. Testosterone levels increased in men ($p = 0.038$) but not women ($p = 0.989$) over time, although this change was not statistically significant compared with the placebo ($p = 0.158$).

In another 8-week DBPCRT ($n = 60$), significant reductions in perceived stress were observed for Withania extract at intakes of 250 mg/day ($p < 0.05$) and 600 mg/day ($p < 0.001$); serum cortisol levels reduced with both treatment groups and there were significant improvements in sleep quality from taking the herb (see more on sleep below).

Male tonic and fertility activity

Early research (two open label clinical trials from the same research group in India) suggested that Withania might exert beneficial effects in male fertility. The first trial investigated the impact of Withania (5 g/day of root powder in milk) for 3 months in 75 infertile men. The trial assigned 3 subgroups: 25 men with relatively normal semen profile (although much poorer than a control group), 25 with low sperm concentration and 25 men with low sperm motility. The herbal treatment resulted in significant increases from baseline for sperm motility and concentration in all 3 subgroups ($p < 0.01$), although values were still substantially lower than normal. Interestingly, serum LH and testosterone increased in all subgroups ($p < 0.01$) while a fall in FSH and prolactin ($p < 0.01$) was most marked in the subgroup with low sperm count.

In the other trial, 60 apparently infertile men with normal sperm parameters received the above dose of Withania for 3 months. The men were again classified into 3 subgroups: 20 heavy smokers, 20 under psychological stress and 20 with infertility of unknown aetiology. Compared with baseline, significant improvements were noted for sperm liquefaction and concentration in all 3 subgroups ($p < 0.01$ to $p < 0.05$). Semen volume was not changed in any subgroup and sperm

motility improved only in the smokers and stressed men. Morning (8 am) and afternoon (4 pm) serum cortisol levels were significantly lower in all subgroups following Withania treatment (results were quite marked for the afternoon readings, with 36 to 48% reductions, indicating less stress on the body). Antioxidant parameters in semen were generally improved. LH and testosterone were significantly higher in all subgroups and FSH and prolactin were lower (except for prolactin in the subgroup with unknown aetiology).

Exercise and anabolic effects

In an 8-week DBPCRT in 57 men starting resistance training, Withania (600 mg/day extract) caused significant improvements in muscle strength and size, and testosterone. Specifically, the men had significantly greater increases in muscle strength on the bench-press exercise (placebo: 26.4 kg vs. Withania: 46.0 kg; $p = 0.001$) and the leg-extension exercise (9.8 kg vs. 14.5 kg; $p = 0.04$), and significantly greater muscle size increase at the arms (5.3 cm² vs 8.6 cm²; $p = 0.01$) and chest (1.4 cm vs. 3.3 cm; $p < 0.001$).

From a DBPCRT in active young men ($n = 38$) over 12 weeks: compared to placebo, Withania (500 mg/day dried extract) improved upper and lower-body strength, supported a favourable distribution of body mass, and was well tolerated clinically in men doing resistance training. No other between-group differences were found for body composition, visual analogue scales for recovery and affect, or systemic haemodynamics. However, only the Withania group experienced statistically significant improvements from baseline in average squat power, peak bench press power,

7.5 km time trial performance, and perceived recovery scores.

Meta-analysis (4 clinical trials) of the effect of Withania on maximum oxygen consumption (VO₂max) in men and women performing exercise found a significant enhancement in both healthy adults and athletes ($p = 0.04$). VO₂ max, also known as maximal oxygen uptake, is the measure of the maximum amount of oxygen a person can utilise during intense exercise. It commonly used to assess aerobic endurance.

Anxiety

A 2014 systematic review located five clinical trials. All trials gave positive results in anxiety and used varying methods of assessment (against placebo mainly). The authors concluded Withania improved anxiety and stress in all studies undertaken to date. Results from a recent trial found that Withania (1 g/day of a dried extract) is a safe and effective adjunctive therapy to with selective serotonin reuptake inhibitors (SSRIs) in generalised anxiety disorder, conferring a benefit over and above the drug therapy.

Sleep

Several recent RCTs provide evidence that the 'somnifera' in Withania's botanical name is well chosen. Positive trials for sleep improvement have been recorded in healthy volunteers, insomnia patients and the elderly.

One DBPCRT was conducted over 8 weeks in a mixed cohort of 80 healthy volunteers and insomnia patients. There were significant improvements with Withania treatment (600 mg/day dried extract) in sleep onset latency ($p = 0.013$), anxiety ($p < 0.05$), mental alertness ($p = 0.01$) and sleep quality ($p < 0.05$) for the insomnia patients. Further analysis confirmed

that sleep onset latency ($p < 0.0001$) and sleep efficiency ($p < 0.0001$) were the most improved parameters.

Cognition

Most adaptogenic herbs have been shown to benefit cognition in clinical trials. The data for *Withania* is now accumulating for this important application: two recent RCTs evaluated its clinical efficacy for improving memory and cognitive functioning in adults with mild cognitive impairment (MCI). A pilot trial over 8 weeks ($n = 50$) demonstrated significant improvements (compared with the placebo) in immediate and general memory, executive function, sustained attention and information-processing speed. In a second small crossover RCT ($n = 15$), *Withania* combined (surprisingly) with *Andrographis* improved cognitive performance in a test for attention and concentration after 4 weeks, which was positively correlated with electroencephalogram (EEG) changes.

Thyroid function

In an 8-week prospective DBPCRT in 50 people with subclinical hypothyroidism and elevated serum thyroid stimulating hormone (TSH) levels (4.5-10 $\mu\text{IU/L}$), *Withania* root dried extract (600 mg/day) improved serum TSH ($p < 0.001$), T3 ($p = 0.0031$), and T4 ($p = 0.0096$) levels significantly, compared to the placebo. Only one person taking *Withania* reported mild and temporary adverse effects, compared to 3 in the placebo group.

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