An alternative treatment for anxiety: a systematic review of human trial results reported for the Ayurvedic herb ashwagandha (Withania somnifera).

Pratte MA¹, Nanavati KB, Young V, Morley CP.

Abstract

OBJECTIVE:
To assess existing reported human trials of Withania somnifera (WS; common name, ashwagandha) for the treatment of anxiety.

DESIGN:
Systematic review of the literature, with searches conducted in PubMed, SCOPUS, CINAHL, and Google Scholar by a medical librarian. Additionally, the reference lists of studies identified in these databases were searched by a research assistant, and queries were conducted in the AYUSH Research Portal. Search terms included "ashwagandha," "Withania somnifera," and terms related to anxiety and stress. Inclusion criteria were human randomized controlled trials with a treatment arm that included WS as a remedy for anxiety or stress. The study team members applied inclusion criteria while screening the records by abstract review.

INTERVENTION:
Treatment with any regimen of WS.

OUTCOME MEASURES:
Number and results of studies identified in the review.

RESULTS:
Sixty-two abstracts were screened; five human trials met inclusion criteria. Three studies compared several dosage levels of WS extract with placebos using versions of the Hamilton Anxiety Scale, with two demonstrating significant benefit of WS versus placebo, and the third demonstrating beneficial effects that approached but did not achieve significance (p=0.05). A fourth study compared naturopathic care with WS versus psychotherapy by using Beck Anxiety Inventory (BAI) scores as an outcome; BAI scores decreased by 56.5% in the WS group and decreased 30.5% for psychotherapy (p<0.0001). A fifth study measured changes in Perceived Stress Scale (PSS) scores in WS group versus placebo; there was a 44.0% reduction in PSS scores in the WS group and a 5.5% reduction in the placebo group (p<0.0001). All studies exhibited unclear or high risk of bias, and heterogenous design and reporting prevented the possibility of meta-analysis.

CONCLUSIONS:
All five studies concluded that WS intervention resulted in greater score improvements (significantly in most cases) than placebo in outcomes on anxiety or stress scales. Current evidence should be received with caution because of an assortment of study methods and cases of potential bias.

Chandrasekhar K, Kapoor J, Anishetty S.

Abstract

**CONTEXT:**
Stress is a state of mental or emotional strain or tension, which can lead to underperformance and adverse clinical conditions. Adaptogens are herbs that help in combating stress. Ayurvedic classical texts, animal studies and clinical studies describe Ashwagandha as a safe and effective adaptogen.

**AIMS:**
The aim of the study was to evaluate the safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha roots in reducing stress and anxiety and in improving the general well-being of adults who were under stress.

**SETTINGS AND DESIGN:**
Single center, prospective, double-blind, randomized, placebo-controlled trial.

**MATERIALS AND METHODS:**
A total of 64 subjects with a history of chronic stress were enrolled into the study after performing relevant clinical examinations and laboratory tests. These included a measurement of serum cortisol, and assessing their scores on standard stress-assessment questionnaires. They were randomized to either the placebo control group or the study drug treatment group, and were asked to take one capsule twice a day for a period of 60 days. In the study drug treatment group, each capsule contained 300 mg of high-concentration full-spectrum extract from the root of the Ashwagandha plant. During the treatment period (on Day 15, Day 30 and Day 45), a follow-up telephone call was made to all subjects to check for treatment compliance and to note any adverse reactions. Final safety and efficacy assessments were done on Day 60.

**STATISTICAL ANALYSIS:**
t-test, Mann-Whitney test.

**RESULTS:**
The treatment group that was given the high-concentration full-spectrum Ashwagandha root extract exhibited a significant reduction (P<0.0001) in scores on all the stress-assessment scales on Day 60, relative to the placebo group. The serum cortisol levels were substantially reduced (P=0.0006) in the Ashwagandha group, relative to the placebo group. The adverse effects were mild
in nature and were comparable in both the groups. No serious adverse events were reported.

**CONCLUSION:**
The findings of this study suggest that a high-concentration full-spectrum Ashwagandha root extract safely and effectively improves an individual's resistance towards stress and thereby improves self-assessed quality of life.

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A double-blind, placebo-controlled evaluation of the anxiolytic efficacy of an ethanolic extract of withania somnifera.

Andrade C¹, Aswath A, Chaturvedi SK, Srinivasa M, Raguram R.

**Abstract**
A double-blind, placebo-controlled study was conducted to evaluate the efficacy of an ethanolic extract of Aswagandha (Withania somnifera), in patients with ICD-10 anxiety disorders. The sample comprised 39 subjects, of whom 20 received the drug and 19 received placebo. The two groups were sociodemographically and clinically similar at baseline. At 2 and 6 weeks follow-up, data from approximately 85% of patients in each group were available for analysis. Statistical trends favouring the drug were observed at both time points. At 6 weeks, significantly more patients met a priori response criteria in the drug group (88.2%) as compared with the placebo group (50%). The drug was well-tolerated and did not occasion more adverse effects than did placebo. It is concluded that this ethanolic extract of Withania somnifera has useful anxiolytic potential and merits further investigation.

**KEYWORDS:**
Anxiety disorder; Aswagandha; Ayurvedic treatment; adjustment disorder with anxiety; clinical trial; generalized anxiety disorder; herbal therapy; panic disorder


Effect of standardized aqueous extract of Withania somnifera on tests of cognitive and psychomotor performance in healthy human participants.

Pingali U¹, Pilli R¹, Fatima N¹.

**Abstract**
**BACKGROUND:**
Withania somnifera is an herbal medicine that has been known to possess memory-enhancing properties. The current study involved an assessment of cognitive and psychomotor effects of Withania somnifera extract in healthy human participants.
MATERIALS AND METHODS:
In this prospective, double-blind, multi-dose, placebo-controlled, crossover study, 20 healthy male participants were randomized to receive 250 mg two capsules twice daily of an encapsulated dried aqueous extract of roots and leaves of Withania somnifera or a matching placebo for a period of 14 days. Cognitive and psychomotor performance was assessed pre-dose (day 1) and at 3 hrs post-dose on day 15 using a battery of computerized psychometric tests. After a washout period of 14 days, the subjects crossed-over to receive the other treatment for a further period of 14 days as per prior randomization schedule. Same battery of test procedures were performed to assess cognitive and psychomotor performance.

RESULTS:
Significant improvements were observed in reaction times with simple reaction, choice discrimination, digit symbol substitution, digit vigilance, and card sorting tests with Withania somnifera extract compared to placebo. However, no effect can be seen with the finger tapping test.

CONCLUSION:
These results suggest that Withania somnifera extract can improve cognitive and psychomotor performance and may, therefore, be a valuable adjunct in the treatment of diseases associated with cognitive impairment.

KEYWORDS:
Central nervous system; Withania somnifera extract; psychometric tests


Efficacy and Safety of Ashwagandha (Withania somnifera) Root Extract in Improving Sexual Function in Women: A Pilot Study.
Dongre S1, Langade D2, Bhattacharyya S3.

Abstract
Background. Many women experience sexual dysfunction where there are orgasm disorders and sexual difficulties. Ashwagandha (Withania somnifera) is a herb known to improve the body's physical and psychological condition. Objective. The purpose of the study was to determine the efficacy and safety of a high-concentration ashwagandha root extract (HCARE) supplementation for improving sexual function in healthy females. Methods. In this pilot study, 50 study subjects were randomized to either (i) HCARE-treated group or (ii) placebo- (starch-) treated group. The subjects consumed either HCARE or placebo capsules of 300mg twice daily for 8 weeks. Sexual function was assessed using two psychometric scales, the Female Sexual Function Index (FSFI) Questionnaire and the Female Sexual Distress Scale (FSDS), and by the number of total and successful sexual encounters. Results. The analysis indicates that treatment with HCARE leads to significantly higher improvement, relative to placebo, in the FSFI Total score (p < 0.001), FSFI domain score for "arousal"
(p < 0.001), "lubrication" (p < 0.001), "orgasm" (p = 0.004), and "satisfaction" (p < 0.001), and also FSDS score (p < 0.001) and the number of successful sexual encounters (p < 0.001) at the end of the treatment. Conclusions. This study demonstrated that oral administration of HCARE may improve sexual function in healthy women. The present study is registered in the Clinical Trial Registry, Government of India, with a number CTRI/2015/07/006045.


Nootropic potential of Ashwagandha leaves: Beyond traditional root extracts.
Wadhwa R¹, Konar A¹, Kaul SC².

Abstract
Rapidly increasing aging population and environmental stressors are the two main global concerns of the modern society. These have brought in light rapidly increasing incidence of a variety of pathological conditions including brain tumors, neurodegenerative & neuropsychiatric disorders, and new challenges for their treatment. The overlapping symptoms, complex etiology and lack of full understanding of the brain structure and function to-date further complicate these tasks. On the other hand, several herbal reagents with a long history of their use have been asserted to possess neurodifferentiation, neuroregenerative and neuroprotective potentials, and hence been recommended as supplement to enhance and maintain brain health and function. Although they have been claimed to function by holistic approach resulting in maintaining body homeostasis and brain health, there are not enough laboratory studies in support to these and mechanism(s) of such beneficial activities remain largely undefined. One such herb is Ashwagandha, also called "Queen of Ayurveda" for its popular use in Indian traditional home medicine because of its extensive benefits including anticancer, anti-stress and remedial potential for aging and neurodegenerative pathologies. However, active principles and underlying mechanism(s) of action remain largely unknown. Here we provide a review on the effects of Ashwagandha extracts and active principles, and underlying molecular mechanism(s) for brain pathologies. We highlight our findings on the nootropic potential of Ashwagandha leaves. The effects of Ashwagandha leaf extracts are multidimensional ranging from differentiation of neuroblastoma and glioma cells, reversal of Alzheimer and Parkinson's pathologies, protection against environmental neurotoxins and enhancement of memory.


Randomized placebo-controlled adjunctive study of an extract of withania somnifera for cognitive dysfunction in bipolar disorder.
Abstract

OBJECTIVE:
Cognitive impairments contribute significantly to inadequate functional recovery following illness episodes in bipolar disorder, yet data on treatment interventions are sparse. We assessed the cognitive effects of a standardized extract of the medicinal herb Withania somnifera (WSE) in bipolar disorder.

METHOD:
Sixty euthymic subjects with DSM-IV bipolar disorder were enrolled in an 8-week, double-blind, placebo-controlled, randomized study of WSE (500 mg/d) as a procognitive agent added adjunctively to the medications being used as maintenance treatment for bipolar disorder. Study enrollment and data analyses were completed between December 2008 and September 2012. Cognitive testing at baseline and 8 weeks assessed primary efficacy outcomes. Psychopathology and adverse events were monitored at scheduled visits.

RESULTS:
Fifty-three patients completed the study (WSE, n = 24; placebo, n = 29), and the 2 groups were matched in terms of demographic, illness, and treatment characteristics. Compared to placebo, WSE provided significant benefits for 3 cognitive tasks: digit span backward ($P = .035$), Flanker neutral response time ($P = .033$), and the social cognition response rating of the Penn Emotional Acuity Test ($P = .045$). The size of the WSE treatment effect for digit span backward was in the medium range ($\text{Cohen } d = 0.51$; 95% CI, 0.25-0.77). None of the other cognitive tasks showed significant between-group differences. Mood and anxiety scale scores remained stable, and adverse events were minor.

CONCLUSIONS:
Although results are preliminary, WSE appears to improve auditory-verbal working memory (digit span backward), a measure of reaction time, and a measure of social cognition in bipolar disorder. Given the paucity of data for improving cognitive capacity in bipolar disorder, WSE offers promise, appears to have a benign side-effects profile, and merits further study.