REVIEW ARTICLE

# Can Traditional Treatment Such as Ashwagandha Be Beneficial in Treating Depression?

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## ABSTRACT

**Background** • This study provides a path for many studies that may have been forgotten in the past to the use of modern-day knowledge supporting the use of traditional treatments, specifically *Withania somnifera* (ashwagandha).

**Primary Study Objective** • The primary objective of this study was to bring back traditional therapy that could prove to be economically beneficial and possibly helpful to many clients with depression with few or no associated adverse events.

**Intervention** • The key components of ashwagandha include 12 alkaloids and 35 withanolides, which have been proven in various studies to be beneficial in the treatment of anxiety and stress. While research supports that withanolides and alkaloides work as antidepressants and are the main reason ashwagandha is beneficial for depression, the mechanism of action in unknown. Studies also show that withanolides may bolster the immune system, increase stamina, fight inflammation and infection, combat tumors, reduce stress, revive the libido, protect the liver and soothe jangled nerves. Both of these molecules are steroidal and are similar in action and appearance. Ashwagandha stimulates the activation of immune system cells such as lymphocytes and has also been shown to inhibit inflammation and improve memory in animal experiments. (*Altern Ther Health Med.* 2023;29(1):36-39).


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## INTRODUCTION

Several pharmaceutical industries have emerged in recent years that aim to solve the world's every day, hectic, fast-paced, problems. Everyone requires solutions as quickly as possible, so, what's a better solution than using drugs? Especially in the field of mental illness, the pharmaceutical industry has developed many medicines like antipsychotics, antidepressants, anti-anxiety, mood-stabilizing and stimulant medications.[1] These are just the main types of drugs—if you include their subtypes, the total number of drugs available is tremendous.

Research has discovered multiple good treatments for people around the globe. But to date, a large number of countries has difficulty buying those drugs for economic reasons, and this is even truer for the individuals who use them. And more than one-third of individuals would not respond to these medications even if they were available to them.[2] Researchers continue to look for a perfect cure to treat major depressive disorders (MDD), and this seems to continue to be a mirage. Despite having so many options for therapies and drugs that have been established by modern medical science, the generation that has solutions at their fingertips has started looking for other options to treat MDD, which has again opened up routes that point towards the path of alternative therapies.

Alternative therapy encompasses a variety of disciplines that includes everything from diet and exercise to mental conditioning and lifestyle changes. Despite evidence of their benefit, a lack of systematic research has made it much less likely they will be used by a patient with MDD. Maybe now is the time to pause and review some of the alternative medications that already exist for the treatment of depression. The findings of this literature review will touch upon the antidepressant properties of ashwagandha, its adverse events, and will open doors for future research.

## METHODOLGY

### Search Criteria

We targeted both original research papers and review articles indexed by PubMed, EMBASE, PsycINFO,

MEDLINE, ScienceDirect and Research Gate. We usedthe search terms "depression," "ways to treat depression," "current treatments for depression," "ashwagandha," "history of ashwagandha," "different uses of ashwagandha," "active components of ashwagandha," "why ashwagandha is good for depression" and "studies on ashwagandha." These database terms reflect the multidisciplinary nature of the research, which includes the medical, psychological and social fields.

**Selection Criteria**

The literature included in this study comprised research papers and texts that addressed the effects of MDD and different methods of treating it. This study aimed to include all types of study participants including the general population, professional care givers and patients. This broad category was limited after eliminating therapies and alternative medicines that were not effective. Literature and texts in any other language but English were excluded from the review.

The texts for this study were obtained from the York Library (UK), King's College London Library (UK), Princeton University Library (USA), Manchester Central Library (UK), and Passaic Public Library (USA). The reference list of all review articles that were identified were screened to cross-check any missing articles of interest.

**Exclusion Criteria**

We retrieved 259 citations from the papers and texts and excluded 239 of them, which left 20 papers and texts for further analysis. We did not identify any international guidelines related to alternative medicine. The main reasons for exclusion were: (1) The article did not directly discuss ashwagandha but rather other medicinal herbs that were not used for mental health; (2) there was no evidence to support the claims that were made by the investigator(s); (3) the article repeated the same information as other articles; (4) the articles included current treatments such as selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors or monoamine oxidase inhibitors.

## ASHWAGANDHA

Ashwagandha (*Withania somnifera* [L.] *Dunal*) is a small shrub belonging to the *Solanaceae* family. It grows prolifically in dry regions of South Asia, Central Asia and Africa, and is regularly used in Ayurveda, the traditional Hindu system of medicine.[3] *W somnifera* (WS) in today's world is used for many diseases. including general debility and exhaustion, emaciation, memory loss, nerve diseases, cough, anemia and insomnia,[4] which are also some of the symptoms of MDD. Modern clinicians are most likely to use WS for chronic fatigue, anxiety, insomnia, and chronic heart and vascular disorders. Study after study continues to confirm the stress tolerance, performance- and endurance-enhancing benefits of this herb. The medicine was tested in rats against chronic unpredictable stress behavior, depression, glucose metabolism, suppressed male sexual behavior, suppressed immune function and cognitive dysfunction. Stomach ulcer, adrenal gland entropy, vitamin C level, and levels of stress hormones were also measured. Surprisingly, the herb showed benefit in them all.[5]

WS produces antioxidant activity in the brain, which explains its effectiveness as an anti-stressor agent.[6] The components believed to be active in ashwagandha have been extensively studied. Withanolides are thought to account for the multiple medicinal applications of ashwagandha. These molecules are steroidal and are similar in both action and appearance. The main reason to consider ashwagandha for the treatment of depression is the phytochemicals and nutrients in the root of the herb, which include alkaloids, beta-sitosterol, chlorogenic acid, scopoletin, withaferin, amino acids and choline.[7] Moreover, the major constituents of the root are steroidal alkaloids and steroidal lactones withanine, somniferine, somnince, somnifernine, withaninine, pseudo-withanine, tropine, pseudo-tropine, ashwagandhanolide, cuscohygrine, anferine, anhydryine, sitoindoside 7 and 8, and several steroidal lactones found in the leaves called withanolides.[8]

**Mechanism of Action**

Potential mechanisms of ashwagandha's anxiolytic effects may be its antioxidant and anti-inflammatory effects. Inflammation and oxidative stress are increased during times of high stress and higher levels have been demonstrated in adults with depression and anxiety. In preclinical studies, it was found that ashwagandha can also influence GABAergic and serotonin activity, which has antidepressant and anxiolytic activity. Despite these mechanisms, which are discussed separately, their effects certainly do not occur in isolation and the interaction of all these mechanisms may be responsible for the positive, mood-enhancing effects of ashwagandha.[9] It has also been shown to influence neurological, endocrine and cardiovascular activity, which adds on to its anti-stressor activity. In animal stress models, ashwagandha has been shown to possess anxiolytic, antidepressant and neuroprotective effects.[10] A study of the anti-stressor properties of ashwagandha also claimed that it reduces cortisol and DHEA-S, and participants taking ashwagandha suggest it has a moderating effect on hypothalamic-pituitary-adrenal (HPA) axis activity in stressed adults. This may be associated with stress-lowering effects.[1] In the same study, it was also observed that anxiety levels were reduced by 41% in patients taking ashwagandha, compared with the 24% reduction experienced by patients taking a placebo. Further confirmation of the mood-enhancing effects of ashwagandha was provided by positive overall improvements in the Depression, Anxiety and Stress Scale – 21 items (DASS-21) score, a measure of depression, anxiety and stress symptoms.[12]

**Animal Studies and Clinical Research**

In an animal study, laboratory animals were subjected to mild electrical shocks that produced chronic stress, resulting in learning problems, immunosuppression, high blood sugar levels, increased level of stress hormones, stomach ulcers and male sexual dysfunction.[13] But when the animals were given

ashwagandha before receiving the shocks, their stress symptoms were significantly reduced. Other studies agree and "support the use of ashwagandha as anti-stress adaptogen."[14] In addition, animal studies show the herb's antioxidant action helps protect the liver and kidneys.

In another animal study conducted by Jayanti, et al, forced swim test (FST) and tail suspension test (TST) models were used to screen for depression in mice. In FST, mice were forced to swim in a restricted area, which induced immobility behavior. In TST, mice were suspended by the tips of their tails from a metal rod, which also induced a state of immobility in the animals. This immobility causes a state of despair, similar to depression in humans.[15] Ashwagandha extract at a dose of 20 and 40 mg/kg produced significant dose-dependent antidepressant-like effects on behavior despair tests, as they reduced immobility time. The decrease produced in the combination group (WS plus imipramine 10 mg/kg each) was comparable to that produced by the standard imipramine dose (15 mg/kg). These results suggest that WS enhances the effect of imipramine on stress-induced immobility time.

In the same study, mice given reserpine (2.5 mg/kg) were observed for ptosis, catatonia and sedation at 1, 2, 3 and 4 hours and scored on a scale from 0 to 3. WS (40 mg/kg) and imipramine (15 mg/kg) significantly reduced reserpine-induced ptosis, catatonia and sedation. Moreover, combinations consisting of sub-therapeutic doses of WS and imipramine (10 mg/kg each) also produced significant reserpine antagonism in mice.[16]

In another study, WS (20 and 50 mg/kg) was administered orally once daily for 5 days. The results were compared with those elicited with benzodiazepine lorazepam (0.5 mg/kg intraperitoneally [IP]) in anxiolytic studies and the tricyclic antidepressant imipramine (10 mg/kg IP) in antidepressant investigations. Both these standard drugs were administered once, 30 minutes prior to the tests. WS glycowithanolides (WSG) induced an anxiolytic effect comparable with that produced by lorazepam in tests of the elevated plus-maze, social interaction and feeding latency in an unfamiliar environment. Further, both WSG and lorazepam reduced rat brain levels of tribulin, an endocoid marker of clinical anxiety, after the levels were increased following administration of the anxiogenic agent pentylenetetrazole. WSG also exhibited an antidepressant effect comparable with that of imipramine.[17]

In a 2006 study, treatment with a single dose of WS root extract at 25, 37.5, 50, 100 and 200 mg/kg IP and a combination of WS (37.5 mg/kg IP) and either imipramine (2.5 mg/kg IP) or fluoxetine (2.5 mg/kg IP) produced a significant decrease in MIT (mean immobility time) in FST. Also, a single dose of WS (100 mg/kg) and its combination group significantly reduced MIT in mice given reserpine, suggesting that the antidepressant effects of imipramine as well as fluoxetine were enhanced by concomitant administration of WS.[18]

A number of studies on WS, or its major active principles, have shown its antioxidant, adaptogen, anxiolytic, antidepressant, memory enhancing, anti-inflammatory, anti-ulcerogenic, anti-parkinsonian and anti-carcinogenic properties. More human studies are needed to determine the safety and efficacy of WS and its effects on humans, which serves as a great idea for future research.

### Adverse Events

Ashwagandha has nearly no adverse events when taken for short periods (weeks to a few months), but taken long term (7 to 10 years) it is associated with some mild to moderate adverse events such as headache and upset stomach.[19] In extremely rare cases, in which the patient has an allergic reaction to ashwagandha, it can also result in rapid heartbeat.[20]

When the economic aspects of ashwagandha are compared with other medications, one researcher found that approximately 1 kg of ashwagandha costs about Rs. 56 (US $0.79).[21] According to a study by Kennedy, et al, medicinal herbs are more cost-effective than the medicines we commonly use in every day medical practice.[22] Hence, more research should be done on treating illness or disorders with natural medicines, which would be both cost-effective and have fewer or no adverse events.

### Study Limitations

One major limitation of this literature review was that the investigators were not able to conduct proper testing in a lab before writing this review. Another major limitation was that not all claims have been proven by other researchers; some remain unclear due to a lack of evidence with regard to ashwagandha use in humans; the claim of ashwagandha being beneficial as an antidepressant has only been examined in lab mice using mazes. There were no robust publications and there are limited randomized clinical trials of alternative treatments, especially ashwagandha. Furthermore, some functionalities and properties of ashwagandha may be underreported due to the biased medical research in the field. However, researchers may be interested in this drug for future studies.

## CONCLUSION

The field of traditional Indian medicine has great potential to reach a wide and diverse population who have economic restraints, but its long-term effects, including adverse events, need to be studied. Ashwagandha has a huge potential to revolutionize the treatment of mental health.

The results of this literature review suggest some promising findings about ashwagandha being an extremely useful resource for depression, but this study has also found that there is still a lack of evidence to support the use and effectiveness of ashwagandha, especially in major depressive disorders (MDD). The main reason to consider using ashwagandha as an antidepressant are the phytochemicals and nutrients found in the root of the herb. Moreover, chemicals like alkaloids and lactones, collectively known as withanolides, play a major role as antidepressants. Pharmacological studies have confirmed that plant preparations of ashwagandha have anti-inflammatory, antioxidant, anticancer, anxiolytic and immunomodulatory effects.[23] Ashwagandha has also been shown to influence

neurological, endocrine and cardiovascular activity. Research also shows that withanolides may bolster the immune system, increase stamina, fight inflammation and infection, combat tumors, reduce stress, revive libido, protect the liver and soothe jangled nerves.[24]

The field of MDD treatment is rapidly evolving as increasing awareness of adverse events with current MDD medications has led this generation of physicians to look for alternatives. However, due to the lack of research, the validity of ashwagandha for the treatment of MDD has not been confirmed. The findings of this review are promising. Ashwagandha is an extremely useful resource for the treatment of depression, but this study also found that there is still a lack of evidence supporting the use and effectiveness of ashwagandha. The findings of this literature review provide a plan for some important research, and the authors are willing to conduct a randomized controlled trial of ashwagandha.

## REFERENCES


1. Grohol JM. Introduction to Depression. Psych Central. https://psychcentral.com/depression/introduction-to-depression/. Published January 9, 2017.
2. Truschel J. Depression Definition and DSM-5 Diagnostic Criteria. Psycom.net. https://www.psycom.net/depression-definition-dsm-5-diagnostic-criteria/. Last updated September 25, 2020. Accessed February 5, 2022.
3. Khalsa KPS, Tierra M. *The Way of Ayurvedic Herbs: The Most Complete Guide to Natural Healing and Health with Traditional Ayurvedic Herbalism*. Twin Lakes, WI: Lotus; 2008.
4. Bremness L. *The Essential Herbs Handbook: More than 100 Herbs for Well-Being, Healing, and Happiness*. London, UK: Duncan Baird Publishers; 2009.
5. Castleman M. *The New Healing Herbs: The Essential Guide to More than 130 of Nature's Most Potent Herbal Remedies*. New York, NY: Rodale; 2017.
6. Gaby A, Ackerson A. *The Natural Pharmacy Complete A-Z Reference to Alternative Treatments for Common Health Conditions*. New York, NY: Three Rivers Press; 2006.
7. Balch PA. *Prescription for Nutritional Healing: The A-to-Z Guide to Supplements*. New York, NY: Penguin Group; 2010.
8. Buhner SH. *Herbal Antibiotics Natural Alternatives for Treating Drug-Resistant Bacteria*. North Adams, MA: Storey Pub.; 2012.
9. Duke JA. *The Green Pharmacy Herbal Handbook: Your Comprehensive Reference to the Best Herbs for Healing*. New York, NY: St. Martins Paperbacks; 2002.
10. Devkar ST, Kandhare AD, Sloley BD, et al. Evaluation of the bioavailability of major withanolides of Withania somnifera using an in vitro absorption model system. *J Adv Pharm Technol Res*. 2015; 6(4):159-164. www.ncbi.nlm.nih.gov/pmc/articles/PMC4630722/0
11. Lopresti AL, Smith SJ, Malvi H, Kodgule R. An investigation into the stress-relieving and pharmacological actions of an ashwagandha (Withania somnifera) extract: A randomized, double-blind, placebo-controlled study. *Medicine (Baltimore)*. 2019;98(37):e17186. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6750292/.
12. Bhattacharya SK, Bhattacharya A, Sairam K, et al. Anxiolytic-antidepressant activity of Withania somnifera glycowithanolides: an experimental study. *Phytomedicine* 2000;7:463-469.
13. Faravelli C, Lo Sauro C, Lelli L, et al. The role of life events and HPA axis in anxiety disorders: a review. *Curr Pharm Des*. 2012;18(35):5663-5674. https://pubmed.ncbi.nlm.nih.gov/22632471/.
14. Watt GVD, Laugharne J, Janca A. Complementary and alternative medicine in the treatment of anxiety and depression. *Curr Opinion Psychiatr*. 2008;21(1):37-42. doi:10.1097/yco.0b013e3282f2d814.
15. Rodrigues AL, da Silva GL, Mateussi AS, et al. Involvement of monoaminergic system in the antidepressant-like effect of the hydroalcoholic extract of Siphocampylus verticillatus. *Life Sci*. 2002;70(12):1347-1358. https://pubmed.ncbi.nlm.nih.gov/11885577/.
16. Anti-depressant effects of Withania somnifera fat (Ashwagandha Ghrutha) extract in experimental mice. ResearchGate. *Inter J Pharma Biosci*. 2013;3(1):33-42. https://www.researchgate.net/publication/249656563_Anti-depressant_effects_of_Withania_somnifera_fat_Ashwagandha_Ghrutha_extract_in_experimental_mice.
17. Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. Anxiolytic-antidepressant activity of Withania somnifera glycowithanolides: an experimental study. *Phytomedicine*. 2000;7(6):463-469. doi:10.1016/S0944-7113(00)80030-6 https://pubmed.ncbi.nlm.nih.gov/11194174/.
18. Shah PC, Trivedi NA, Bhatt JD, Hemavathi KG. Effect of Withania somnifera on formed swimming immobility in mice and its interaction with various drugs. *Indian J Physiol Pharmacol*. 2006;50(4):409-415. https://pdfs.semanticscholar.org/039a/885f9ab5afc9b3713510dc2aae1df9ad762a.pdf.
19. What are the side effects of ashwagandha supplements? ConsumerLab.com. https://www.consumerlab.com/answers/side-effects-of-ashwagandha-supplements/ashwagandha-side-effects/. Last updated January 1, 2021. Accessed February 5, 2022.
20. Verma K, Thakur NS. Economic analysis of ashwagandha (*Withania somnifera L.*) based agroforestry land use systems in mid hills Western Himalayas. *Indian J Agroforestry*. 2010;12:62-70.
21. Kulkarni SK, Dhir A. Withania somnifera: an Indian ginseng. Progress in neuro-psychopharmacology & biological psychiatry. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008;32(5):1093-1105. doi:10.1016/j.pnpbp.2007.09.011
22. Kennedy DA, Hart J, Seely D. Cost effectiveness of natural health products: a systematic review of randomized clinical trials. *Evid Based Complement Alternat Med*. 2009;6(3):297-304. doi:10.1093/ecam/nem167
23. National Center for Biotechnology Information (NCBI). Ashwagandha. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. https://www.ncbi.nlm.nih.gov/books/NBK548536/. Accessed February 6, 2022.
24. Delgado JL. *The Buena Salud Guide to Overcoming Depression and Enjoying Life*. New York, NY: Newmarket Press; 2011.