



FAMILY Solanaceae

**CAUTION**: Ashwagandha should not be confused with another plant commonly known as <u>Winter</u> <u>Cherry</u>. Also, avoid confusion with other herbs used as adaptogens, such as <u>American Ginseng</u>, <u>Panax Ginseng</u>, and <u>Eleuthero</u>.

#### **Other Common Names**

Ajagandha, Amangura, Amukkirag, Asan, Asana, Asgand, Asgandh, Asgandha, Ashagandha, Ashvagandha, Ashwaganda, Ashwanga, Asoda, Asundha, Asvagandha, Aswagandha, Avarada, Ay urvedic Ginseng, Cerise d'Hiver, Clustered Wintercherry, Ghoda Asoda, Ginseng Ayurvédique, Ginseng Indien, Hayahvaya, Indian Ginseng, Indian Winter Cherry, Kanaje Hindi, Kuthmithi, Orovale, Peyette, Samm Al Ferakh, Samm Al Rerakh, Sogade-Beru, Strychnos, Turangi-Ghanda, Vajigandha, Winter Cherry, Withania.

#### Overview

Ashwagandha is a small evergreen shrub found in dry areas of India and the Middle East, as well as parts of Africa (14863,32533). Ashwagandha is used in traditional medicine, usually as an adaptogenic herb (14863,32525,90650,90651). Adaptogens are theorized to help the body resist physiological and psychological stress.

#### **WARNINGS**

Ashwagandha is sometimes substituted or adulterated with a similar plant, Withania coagulans (3710).

Coronavirus disease 2019 (COVID-19): Despite claims to the contrary, there is no good evidence to support using ashwagandha for COVID-19. Recommend healthy lifestyle choices and proven prevention methods instead. For more information about natural medicines and COVID-19, see our latest articles and resources.

## Safety

POSSIBLY SAFE ...when used orally and appropriately, short-term. Ashwagandha has been used with apparent safety in doses of up to 1250 mg daily for up to 6 months

(3710,11301,19271,90649,90652,90653,97292,101816,102682,102683)

(102684,102685,102687,103476,105824,109586,109588,109589,109590). ...when used topically. Ashwagandha lotion has been used with apparent safety in concentrations up to 8% for up to 2 months (111538).

PREGNANCY: LIKELY UNSAFE ...when used orally. Ashwagandha has abortifacient effects (12).

**LACTATION**: Insufficient reliable information available; avoid using.

## **Adverse Effects**

**General:** Orally, ashwagandha seems to be well-tolerated. Topically, no adverse effects have been reported. However, a thorough evaluation of safety outcomes has not been conducted.

#### **Most Common Adverse Effects:**

*Orally*: Diarrhea, gastrointestinal upset, nausea, and vomiting. However, these adverse effects do not commonly occur with typical doses.

### Serious Adverse Effects (Rare):

Orally: Some case reports raise concerns about acute liver failure, hepatic encephalopathy, and the need for liver transplantation with ashwagandha treatment.

#### Dermatologic

Orally, dermatitis has been reported in three of 42 patients in a clinical trial (19276).

#### Endocrine

A case report describes a 73-year-old female who had taken an ashwagandha root extract (unspecified dose) for 2 years to treat hypothyroidism which had been previously managed with levothyroxine. The patient was diagnosed with hyperthyroidism after presenting with supraventricular tachycardia, chest pain, tremor, dizziness, fatigue, irritability, hair thinning, and low thyroid stimulating hormone (TSH) levels. Hyperthyroidism resolved after discontinuing ashwagandha (108745).

#### Gastrointestinal

Orally, large doses may cause GI upset, diarrhea, and vomiting secondary to irritation of the mucous and serous membranes (3710). When taken orally, nausea and abdominal pain (19276,110490) and gastritis and flatulence (90651) have been reported.

#### Genitourinary

In one case report, a 28-year-old male with a decrease in libido who was taking ashwagandha 5 grams daily over 10 days subsequently experienced burning, itching, and skin and mucous membrane discoloration of the penis, as well as an oval, dusky, eroded plaque (3 cm) with erythema on the glans penis and prepuce (32537).

#### Hepatic

Orally, ashwagandha in doses of 154-1350 mg daily has played a role in several case reports of liver injury. In most of these cases, other causes of liver injury were excluded, and liver failure did not occur. Symptoms included jaundice, pruritus, malaise, fatigue, lethargy, weight loss, nausea, diarrhea, abdominal pain, stool discoloration, and dark urine. Symptom onset was typically 2-12 weeks from first intake, although in some cases onset occurred after more than 12 months of use (102686,107372,110490,110491,111533,111535). In most cases, liver enzymes normalized within 1-5 months after discontinuation of ashwagandha (102686,107372,110491,111535). However, treatment with corticosteroids, lactulose, ornithine, ursodeoxycholic acid, and plasmapheresis, among other interventions, was required in one case (111533). Rarely, use of oral ashwagandha has been reported to cause hepatic encephalopathy and liver failure requiring liver transplantation (110490).

### Neurologic/CNS

Orally, ashwagandha has been reported to cause drowsiness (110492).

## **Effectiveness**

#### **POSSIBLY EFFECTIVE**

Generalized anxiety disorder (GAD). Oral ashwagandha may modestly improve symptoms of anxiety in patients with GAD.

<u>Details:</u> Clinical practice guidelines from the World Federation of Societies of Biological Psychiatry (WFSBP) and the Canadian Network for Mood and Anxiety Treatments (CANMAT) provisionally recommend ashwagandha root extract at doses of 300-600 mg, standardized to 5% withanolides, daily as monotherapy or adjunctive therapy in patients with GAD. This recommendation is based on a review of three preliminary clinical trials with consistent results (<u>110318</u>). Two of these studies are described below.

A small clinical trial in patients with GAD who are taking selective serotonin reuptake inhibitors (SSRIs) shows that taking ashwagandha 1 gram daily for 6 weeks reduces symptoms of anxiety by 48%, compared with a 27% reduction in patients taking placebo. Furthermore, by the end of treatment, 72% of patients taking ashwagandha were determined to have mild symptoms of GAD,

compared with only 32% of those taking placebo (102687). Another preliminary clinical trial in patients aged 16 years and older with GAD shows that taking ashwagandha root powder granules 4 grams three times daily for 60 days moderately improves anxious mood in 58% of patients, compared with no moderate improvement in the placebo group. Mild improvement occurred in 82% of patients in the placebo group and 40% of patients in the ashwagandha group (90654).

Insomnia. Oral ashwagandha may modestly improve sleep in patients with insomnia or non-restorative sleep.

Details: A small meta-analysis in patients with insomnia and healthy patients shows that taking a specific ashwagandha root extract (KSM-66, Ixoreal Biomed) 250-600 mg daily or a specific root and leaf extract (Shoden, Arjuna Natural) 120 mg daily for 6-12 weeks modestly improves overall sleep, as well as sleep quality, sleep latency, total sleep time, wake time after sleep onset, and sleep efficiency, when compared with placebo. Effects were more pronounced in those with insomnia, with doses of at least 600 mg daily, and with treatment durations of at least 8 weeks (106784). These findings may be limited by heterogeneity of the included studies. In patients with non-restorative sleep, clinical research shows that taking a specific ashwagandha extract (Shoden, Arjuna Natural Private Ltd) 125 mg daily for 6 weeks increases sleep quality by 72%, compared with an improvement of 29% in patients taking placebo. Small to moderate improvements also occurred in total sleep time, sleep latency, and number of times awake (103476).

Stress. Oral ashwagandha seems to help reduce stress and may also reduce stress-related weight gain.

Details: A meta-analysis of seven small clinical studies in healthy adults, patients with chronic stress, or patients with psychiatric conditions shows that taking ashwagandha 240-1000 mg daily for 8-12 weeks improves stress when compared with placebo (109587). Clinical studies included in this meta-analysis that evaluated adults with chronic stress show that taking specific ashwagandha root extracts 240 mg daily (Shoden, Arjuna Natural Ltd.) or 300 mg twice daily (KSM-66, Ixoreal Biomed) for 60 days reduces perceived stress levels by 30% to 44% and decreases cortisol levels by 22% to 28% when compared with baseline. These improvements remain significant when compared with the changes seen for patients treated with placebo (90652,95617,101816,102682). In adults reporting moderate to high stress levels, clinical research shows that treatment with specific slow-release capsules containing another ashwagandha root extract (Prolanza), 300 mg daily for 90 days, lowers perceived stress scores and cortisol levels when compared with placebo (107371). In healthy college students, clinical research also shows that taking ashwagandha root extract 350 mg twice daily for 30 days improves qualitative perceptions of stress management, but not stress scores, when compared with placebo (109589,109590). Other clinical research shows that taking ashwagandha root extract 500 mg twice daily may prevent stress-related weight gain when compared with placebo (95617).

#### **INSUFFICIENT RELIABLE EVIDENCE to RATE**

Aging. A small clinical study suggests that oral ashwagandha may modestly improve well-being, sleep, and alertness in elderly patients.

<u>Details:</u> A small clinical trial in individuals aged 65-80 years shows that taking ashwagandha root extract (KSM-66, Ixoreal Biomed) 600 mg daily for 12 weeks improves overall well-being, sleep quality, and mental alertness by small to moderate amounts when compared with placebo (102684).

Antipsychotic-induced metabolic side effects. It is unclear if ashwagandha is beneficial for attenuating the metabolic side effects of antipsychotic agents.

<u>Details:</u> One preliminary clinical trial shows that taking a specific ashwagandha extract (Cap Strelaxin, M/s Pharmanza Herbal Pvt. Ltd.) 400 mg three times daily for one month reduces serum triglycerides by 12% and fasting blood glucose by 15% when compared with baseline levels. Patients were taking atypical antipsychotics and had modestly elevated triglycerides and fasting blood glucose levels at baseline (90649). The validity of these findings is limited by the lack of a comparator group.

Anxiety. It is unclear if oral ashwagandha is beneficial for reducing anxiety.

<u>Details:</u> One small clinical study shows that taking ashwagandha root (Swiss Herbals) 300 mg twice daily for 12 weeks, in combination with standard psychotherapy interventions, including dietary counseling, deep breathing exercise instruction, and a multivitamin, reduces anxiety scores when compared with standard psychotherapy interventions and placebo (19271). However, other clinical research in young adults shows that a specific ashwagandha root and leaf extract (NooGandha, Specnova LLC) 225 mg or 400 mg daily for 30 days produces similar improvements in self-reported anxiety, stress, and depression scores when compared with placebo (107370).

Asthma. Although there has been interest in using oral ashwagandha for asthma, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

Athletic performance. It is unclear if ashwagandha is beneficial for improving athletic performance.

<u>Details:</u> A meta-analysis of four small clinical trials shows that taking ashwagandha increases aerobic capacity in athletes and non-athletes based on the measurement of maximum oxygen consumption. Effective doses ranged from 500-1000 mg daily for up to 12 weeks (102683). Another meta-analysis shows that taking ashwagandha in doses of 120-1250 mg daily, as a single dose or divided twice daily, for up to 6 months seems to improve muscle strength, speed, time to exhaustion, recovery time, and cardiorespiratory fitness in athletes and non-athletes (105824). However, the validity of this analysis is reduced by the lack of a control group, the varied training levels of the subjects, and the wide range of outcomes assessed. More research is needed to determine whether taking ashwagandha can improve athletic performance.

Attention deficit-hyperactivity disorder (ADHD). Oral ashwagandha has only been evaluated in combination with other ingredients; its effect when used alone is unclear.

<u>Details:</u> In a preliminary clinical trial, children with ADHD were given a combination herbal extract formula (Nurture & Clarity), containing ashwagandha, white peony root, gotu kola, blue-green algae, bacopa, and sage, 3 mL three times daily for 4 months. Measures of attention, cognition, and impulse control improved significantly in children receiving ashwagandha when compared with

placebo (19272). The dose of ashwagandha in the combination product was not reported, and the effect of ashwagandha alone in ADHD is unclear.

Back pain. Although there has been interest in using oral or topical ashwagandha for back pain, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

Bipolar disorder. It is unclear if oral ashwagandha is beneficial for improving cognitive function in adults with bipolar disorder.

<u>Details:</u> Clinical research shows that taking ashwagandha extract (Sensoril, Natreon, Inc.) 250 mg daily for 1 week and then 250 mg twice daily for 7 weeks, improves some, but not all, measures of cognition by a small-to-moderate amount when compared with placebo (90653).

Bronchitis. Although there has been interest in using oral ashwagandha for bronchitis, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

Cerebellar ataxia. It is unclear if oral ashwagandha is beneficial for improving balance in patients with cerebellar ataxia.

<u>Details:</u> A small, open-label study evaluating ashwagandha 500 mg three times daily in combination with Ayurvedic therapy for one month showed improvement in balance indices in subjects with cerebellar ataxia when compared with baseline (<u>19273</u>). The validity of this finding is limited by the lack of a comparator group. Additionally, it is unclear if this effect is due to ashwagandha, other ingredients, or the combination.

Chemotherapy-related fatigue. Evidence is limited to one small clinical study in patients with breast cancer.

<u>Details:</u> In preliminary clinical research in patients with breast cancer, taking ashwagandha powdered root extract 2 grams (Himalaya Drug Co) three times daily through six cycles of chemotherapy decreases chemotherapy-related fatigue when compared with no treatment. Fatigue scores were 16% to 52% higher in the control group when compared to the ashwagandha group (90651).

Chronic obstructive pulmonary disease (COPD). It is unclear if oral ashwagandha is beneficial in patients with COPD.

<u>Details:</u> A small clinical study in patients with stable COPD shows that taking ashwagandha root extract 250 mg twice daily for 12 weeks, along with conventional therapy, improves measures of lung function and exercise tolerance, but not quality of life, when compared with conventional therapy alone (109588).

Cognitive function. Although there has been interest in using oral ashwagandha for cognitive function, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

Coronavirus disease 2019 (COVID-19). It is unclear if ashwagandha is beneficial for COVID-19.

<u>Details:</u> Preliminary clinical research in adults hospitalized with COVID-19 shows that taking a specific combination product, (Artovid-20, Bioved Pharmaceuticals) containing ashwagandha, ginger, turmeric, and Boswellia, 1,776 mg orally twice daily for 14 days shortens the duration of symptoms by 0.9 days when compared with placebo. Taking the combination product also modestly reduced the severity ratings of some symptoms, such as sore throat and cough, however, these improvements are unlikely to be clinically relevant (109899).

Diabetes. It is unclear if oral ashwagandha is beneficial for type 2 diabetes.

<u>Details:</u> In patients with type 2 diabetes, preliminary clinical research shows that ashwagandha 3 grams daily for 30 days decreases blood glucose to a degree similar to oral hypoglycemic drugs (19274). However, this study did not compare ashwagandha directly to a group taking oral hypoglycemic drugs.

**Fibromyalgia**. Although there has been interest in using oral ashwagandha for fibromyalgia, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

Hiccups. Although there has been interest in using oral ashwagandha for hiccups, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

Hypercholesterolemia. It is unclear if ashwagandha is beneficial for hypercholesterolemia.

<u>Details:</u> A very small clinical study in subjects with hypercholesterolemia shows that ashwagandha 3 grams daily for 30 days decreases serum cholesterol, triglyceride, low-density lipoprotein (LDL) cholesterol, and very low-density lipoprotein (VLDL) cholesterol levels when compared with baseline (19274). The validity of these findings is limited by the lack of a comparator group.

Hypothyroidism. It is unclear if ashwagandha is beneficial for hypothyroidism.

<u>Details:</u> Preliminary clinical research in adults with subclinical hypothyroidism shows that taking a specific ashwagandha root extract (KSM-66, Ixoreal Biomed) 300 mg twice daily for 8 weeks increases triiodothyronine (T3) and thyroxine (T4) levels by 42% and 20%, respectively, and reduces serum TSH levels by 17% from baseline. These changes are significant when compared with placebo (97292). However, the effects of ashwagandha on thyroid hormone levels in patients with overt hypothyroidism, or in patients taking prescription thyroid hormones, is unknown.

**Infertility**. Although there has been interest in using oral ashwagandha for infertility in females, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

Male infertility. It is unclear if oral ashwagandha is beneficial for male infertility.

<u>Details:</u> Preliminary clinical research in males with infertility shows that taking ashwagandha root powder for approximately 3 months modestly improves hormone levels, as well as sperm count and motility, when compared with baseline (<u>19275,90650</u>). The validity of these findings is limited by the lack of a comparator group. One study used a specific ashwagandha root extract (KSM-66

Ashwagandha, Ixoreal Biomed) 225 mg three times daily; another study provided doses of 5 grams daily (19275,90650).

Menopausal symptoms. Oral ashwagandha may be beneficial for menopausal symptoms.

<u>Details:</u> A small clinical study in healthy adults in perimenopause shows that taking a specific ashwagandha root extract (KSM-66, Ixoreal Biomed) 300 mg twice daily for 8 weeks improves menopausal symptom severity by 24%, compared with 11% in those receiving placebo. Quality of life and hot flashes also were improved in those taking ashwagandha (106785).

Obsessive-compulsive disorder (OCD). It is unclear if ashwagandha is beneficial for OCD.

<u>Details:</u> Preliminary clinical research shows that taking ashwagandha root extract 120 mg after meals for 6 weeks, in conjunction with prescribed selective-serotonin reuptake inhibitors (SSRIs), might reduce OCD symptom severity when compared with prescribed SSRIs alone. The dose was initiated at 30 mg daily and increased by 30 mg every 4 days. Although OCD scores were significantly reduced when compared with placebo, it should be noted that scores were already significantly lower in the placebo group at baseline (95618).

Osteoarthritis. Oral ashwagandha has only been evaluated in combination with other ingredients; its effect when used alone is unclear.

<u>Details:</u> In patients with osteoarthritis, taking a specific combination supplement, containing ashwagandha 450 mg, Ayurvedic zinc complex 50 mg, guggul 100 mg, and turmeric 50 mg (Articulin-F) two capsules three times daily for 3 months reduces symptoms of pain and swelling when compared with placebo. However, there were no radiological improvements (19276). It is unclear if this effect is due to ashwagandha, other ingredients, or the combination.

Parkinson disease. Oral ashwagandha has only been evaluated in combination with other ingredients; its effect when used alone is unclear.

<u>Details:</u> In patients with Parkinson disease, a small clinical study shows that taking a product containing ashwagandha 14.5 grams, cowhage 4.5 grams, Hyoscyamus reticulantus 0.75 grams, and Sida cordifolia 14.5 grams in lukewarm milk twice daily for 56 days improves symptoms like tremor, stiffness, and cramps when compared with baseline. The therapy followed 28 days of cleansing or eliminative therapy using Ayurvedic remedies (6899). The validity of these findings is limited by the lack of a comparator group. Also, it is unclear if these effects are due to ashwagandha, other ingredients, or the combination. Cowhage contains levodopa, which may contribute to any benefit seen with this combination product.

Psychological well-being. It is unclear if oral ashwagandha is beneficial for improving psychological well-being in college students.

<u>Details:</u> A small clinical study in healthy college students shows that taking ashwagandha root extract 350 mg twice daily for 30 days improves perceptions of well-being, including improvements in energy, mental clarity, food cravings, and sleep quality, when compared with placebo. Qualitative

analysis also suggests these students had improvements in stress management, but stress scores were not reduced when compared with placebo (109589,109590).

Rheumatoid arthritis (RA). It is unclear if ashwagandha is beneficial for improving symptoms of RA.

<u>Details:</u> Preliminary clinical research shows that taking ashwagandha powder 5 grams twice daily for 3 weeks, followed by 4 weeks of sidh makardhwaj (a mixture of gold, mercury, and sulfur) 100 mg with honey daily, modestly improves symptoms in about 50% of males and 60% of females with RA when compared with baseline (95620). The lack of a control group limits the validity of this finding. Additionally, the effect of ashwagandha powder alone is unclear.

Sexual dysfunction. Small clinical studies suggest that oral ashwagandha root extract may help improve sexual arousal and sexual desire in some females and males with sexual dysfunction.

<u>Details:</u> Two, small clinical studies in adult females with sexual dysfunction show that taking ashwagandha root extract (KSM-66, Ixoreal Biomed) 300 mg twice daily with food for 8 weeks in conjunction with or without counseling increases the number of successful sexual encounters and improves orgasms, satisfaction, lubrication, and arousal when compared with placebo or counseling alone (95619,110492). Also, a small clinical study in adult males with low sexual desire shows that taking the same ashwagandha root extract 300 mg twice daily after meals for 8 weeks improves subjective sexual functioning scores, including measures of sexual arousal, sexual desire, sexual behavior, and orgasm, when compared with placebo (109586).

Tuberculosis. Although there has been interest in using oral ashwagandha for tuberculosis, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

Vitiligo. Although there has been interest in using oral ashwagandha for vitiligo, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

Wrinkled skin. It is unclear if topical ashwagandha is beneficial in individuals with wrinkled skin.

<u>Details:</u> A small clinical study in healthy adults with photoaged skin shows that applying ashwagandha root extract 8% lotion daily for 60 days improves physician-rated scores for skin wrinkles, hydration, brightness, tone, and pigmentation and improves other measures of skin elasticity and hydration when compared with placebo. However, changes in melanin content did not differ between treatment groups (111538).

Wound healing. Although there has been interest in using topical ashwagandha for healing of skin ulcers and skin sores, there is insufficient reliable information about the clinical effects of ashwagandha for this condition.

More evidence is needed to rate ashwagandha for these uses.

## **Dosing & Administration**

#### Adult

Oral:

Ashwagandha has most often been used in doses of up to 1000 mg daily for up to 12 weeks. See <u>Effectiveness</u> section for condition-specific information.

Ashwagandha extract is often standardized to withanolide content, with concentrations ranging from 1.5% to 35% (19271,90650,90652,90653,106786).

#### Children

Oral:

Research is limited; typical dosing is unavailable.

#### Standardization & Formulation

Ashwagandha root by Swiss Herbals, used in some clinical trials, has been standardized to 1.5% withanolides (19271). Another standardized product is Sensoril (Natreon, Inc.), containing a minimum of 8% withanolides and 32% oligosaccharides, and a maximum of 2% withferin A (90653). KSM-66 (Ixoreal Biomed) is standardized to withanolide ≥ 5% and contains alkaloids, the amino acids threonine, valine, methionine, isoleucine, lysine, aspartic acid, and arginine, complex sugars such as oligosaccharides and fructooligosaccharides, and vitamin A, calcium, and iron (90650,90652,109586). Shoden (Arjuna Natural Inc) is standardized to 35% withanolide glycosides (101816,103476,106786).

## **Interactions with Drugs**

#### **ANTIDIABETES DRUGS**

Interaction Rating = Moderate Be cautious with this combination.

<u>Severity</u> = High • <u>Occurrence</u> = Possible • <u>Level of Evidence</u> = **B** 

Theoretically, taking ashwagandha with antidiabetes drugs might increase the risk of hypoglycemia.

### **Details**

There is preliminary clinical evidence suggesting that ashwagandha might lower blood glucose levels. Theoretically, ashwagandha might have additive effects when used with antidiabetes drugs and increase the risk of hypoglycemia (19274,90649,102685).

#### **ANTIHYPERTENSIVE DRUGS**

Interaction Rating = Moderate Be cautious with this combination.

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Severity = Moderate • Occurrence = Possible • Level of Evidence = D
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Theoretically, taking ashwagandha with antihypertensive drugs might increase the risk of hypotension.

#### Details

Animal research suggests that ashwagandha might lower systolic and diastolic blood pressure (19279). Theoretically, ashwagandha might have additive effects when used with antihypertensive drugs and increase the risk of hypotension.

#### BENZODIAZEPINES

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Interaction Rating = Moderate Be cautious with this combination.
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<u>Severity</u> = High • <u>Occurrence</u> = Possible • <u>Level of Evidence</u> = D
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Theoretically, taking ashwagandha might increase the sedative effects of benzodiazepines.

#### Details

There is preliminary evidence that ashwagandha might have an additive effect with diazepam (Valium) and clonazepam (Klonopin) (3710). This may also occur with other benzodiazepines.

#### **CNS DEPRESSANTS**

<u>Interaction Rating</u> = <u>Moderate</u> Be cautious with this combination.

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Severity = High • Occurrence = Possible • Level of Evidence = D
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Theoretically, taking ashwagandha might increase the sedative effects of CNS depressants.

#### **Details**

Ashwagandha seems to have sedative effects. Theoretically, this may potentiate the effects of barbiturates, other sedatives, and anxiolytics (3710).

### **IMMUNOSUPPRESSANTS**

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Interaction Rating = Moderate Be cautious with this combination.
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Severity = High • Occurrence = Possible • Level of Evidence = D
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Theoretically, taking ashwagandha might decrease the effects of immunosuppressants.

### **Details**

Ashwagandha has demonstrated immunostimulant effects in humans (3710,3711,4114,11301,106786). Animal research has shown that ashwagandha can attenuate the immunosuppression caused by cyclophosphamide (3711,4114).

#### THYROID HORMONE

Interaction Rating = Moderate Be cautious with this combination.

<u>Severity</u> = Moderate • <u>Occurrence</u> = Probable • <u>Level of Evidence</u> = **B** 

Ashwagandha might increase the effects and adverse effects of thyroid hormone.

#### Details

Concomitant use of ashwagandha with thyroid hormones may cause additive therapeutic and adverse effects. Preliminary clinical research and animal studies suggest that ashwagandha boosts thyroid hormone synthesis and secretion (19281,19282,97292). In one clinical study, ashwagandha increased triiodothyronine (T3) and thyroxine (T4) levels by 41.5% and 19.6%, respectively, and reduced serum TSH levels by 17.4% from baseline in adults with subclinical hypothyroidism (97292).

# **Interactions with Supplements**

**HERBS AND SUPPLEMENTS WITH HYPOTENSIVE EFFECTS**: Theoretically, ashwagandha might have hypotensive effects.

#### **Details**

Animal research suggests that ashwagandha might lower blood pressure (19279). Theoretically, combining ashwagandha with other herbs and supplements with hypotensive effects might increase the risk of hypotension.

**HERBS AND SUPPLEMENTS WITH SEDATIVE PROPERTIES**: Theoretically, ashwagandha might have sedative effects.

#### <u>Details</u>

Theoretically, concomitant use with herbs that have sedative properties might enhance therapeutic and adverse effects (11301). See other products with sedative-hypnotic activity here.

## **Interactions with Conditions**

### **AUTOIMMUNE DISEASES**

Ashwagandha has demonstrated immunostimulant effects in humans (3710,3711,4114,11301,106786). Theoretically, ashwagandha might exacerbate autoimmune diseases by stimulating immune activity.

Until more is known, avoid or use with caution in patients with autoimmune diseases such as multiple sclerosis, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), or others.

#### **PERIOPERATIVE**

Ashwagandha has sedative effects. Theoretically, ashwagandha might cause additive CNS depression when combined with anesthesia and other medications during and after surgical procedures. Tell patients to discontinue ashwagandha at least 2 weeks before elective surgical procedures.

#### **THYROID DISORDERS**

Theoretically, ashwagandha might exacerbate hyperthyroidism by increasing thyroid hormone levels; use with caution in patients with hyperthyroidism or those being treated with thyroid hormones. Ashwagandha has been shown to stimulate thyroid hormone synthesis or secretion in human and animal research (3710,19281,19282,97292).

## **Interactions with Lab Tests**

## **DIGOXIN SERUM ASSAY**

Taking ashwagandha might result in falsely elevated digoxin levels in some serum assays. Ashwagandha contains withaferin A, which has a similar structure to digoxin (14863,16417). Ashwagandha can falsely elevate digoxin levels when using fluorescence polarization immunoassays (FPIA), microparticle enzyme immunoassays (MEIA) or the Abbott Digoxin III assay (14863,16417). The Beckman assay for digoxin seems to be only minimally affected (14863). The Roche Tina-Quant turbidimetric inhibition immunoassay is only affected by very high ashwagandha levels, equivalent to plasma levels after an overdose (16417).

### **Overdose**

There is insufficient reliable information available about the presentation or treatment of overdose with ashwagandha.

## **Pharmacokinetics**

There is insufficient reliable information available about the pharmacokinetics of ashwagandha.

## **Mechanism of Action**

General: The applicable parts of ashwagandha are the root and berry. Ashwagandha contains several active constituents including alkaloids (isopelletierine, anaferine), steroidal lactones (withanolides, withaferins), and saponins (4116,11301). It also contains salvigenin, withaperuvin 1, eucommiol, vicosalactone B, anamides D and E, and asomidienone (108744). Ashwagandha does not contain nicotine as some researchers have reported (3710). Some of the withanolides are structurally similar to ginsenosides from ginseng (14863). Withaferin A has a similar structure to digoxin, and can be bound and neutralized by digoxin immune fab (Digibind) (14863).

Ashwagandha does not seem to have any effect on the laboratory monitoring of acetaminophen, salicylates, phenytoin, phenobarbital, carbamazepine, valproic acid, procainamide (including N-acetyl procainamide), theophylline, gentamicin, or tobramycin (14863).

**Analgesic effects**: Animal model research suggests that ashwagandha has a variety of pharmacological effects including analgesic effects (3710).

Anticancer effects: Ashwagandha is of interest for the treatment of cancer. In laboratory research, the withanolides and ashwagandha extract had cytotoxic effects in cancer cells and other laboratory models (32509,32517,32518,32538,32548,32551,32552).

Anticonvulsant effects: Ashwagandha might have anticonvulsant activity, by binding to the gamma-aminobutyric acid (GABA) receptor (3710).

Antidiabetic effects: Ashwagandha is of interest for diabetes. In humans and in animal diabetic models, ashwagandha extract reduces blood glucose and glycated hemoglobin (HbA1c). In vitro, ashwagandha extract increases the uptake of glucose into adipocytes and muscle cells. Possible active constituents include withaferin A and withanolide A. In addition, three withanolides inhibited alpha-glucosidase in vitro (102685).

**Anti-inflammatory effects**: In animal research, ashwagandha had anti-inflammatory effects in the bladder (3711).

**Antioxidant effects**: Animal model research suggests that ashwagandha has a variety of pharmacological effects including antioxidant effects (4116,11301,32558,102685).

**Antipyretic effects**: Animal model research suggests that ashwagandha has a variety of pharmacological effects including analgesic and antipyretic effects (3710).

Anti-stress effects: Some researchers think ashwagandha has a so-called "anti-stressor" effect (4113). Preliminary research suggests ashwagandha suppresses stress-induced increases of dopamine receptors in the corpus striatum of the brain (3710). It also appears to reduce stress-induced increases of plasma corticosterone, blood urea nitrogen, and blood lactic acid (11301).

Anxiolytic effects: Ashwagandha seems to have anxiolytic effects in laboratory research (32506), possibly by acting as a gamma-aminobutyric acid (GABA) mimetic agent (3710). Animal studies have demonstrated that ashwagandha can enhance serotonergic transmission through modulation of the postsynaptic serotonin (5-HT) receptors (95618).

Blood pressure effects: In animal experiments, ashwagandha decreased blood pressure (32560).

Immunologic effects: Ashwagandha and its constituents seem to have immunomodulatory effects. The withanolides and sitoindosides seem to cause a mobilization of macrophages, phagocytosis, and lysosomal enzymes (11301). In healthy adults, an ethanolic extract of ashwagandha root and leaf has been shown to increase production of immunoglobulins, interferon-gamma, interleukin-4, and T cells, B cells, and natural killer cells when compared with baseline (106786). Animal research also suggests ashwagandha might reduce cyclophosphamide-induced immunosuppression and leukopenia (3711,4114,32550). Ashwagandha also seems to increase bone marrow cell and white blood cell count in radiation-treated animals (3711). It remains unclear, however, what net effect whole ashwagandha preparations have on the immune system (3710,3711).

**Liver enzyme effects**: In vitro studies using human liver microsomes show that the water, ethanol, methanol, and ethyl acetate extracts of ashwagandha root may induce cytochrome P450 (CYP) 3A4 enzymes, although any clinical significance is unclear. The ethanol and methanol extracts may also inhibit CYP2B6 (108744).

Memory effects: In animal and human research, ashwagandha or its constituents improved memory function (32563,90653). Mechanisms of action may involve the restoration of pre- and post-synapses in cortical neuron axons and dendrites, increased axonal density, or increased peripheral nervous system myelin (32526). Also, the withanolides have shown cholinesterase inhibitory potential in laboratory research (32521,32522).

**Reproductive effects**: In clinical research, ashwagandha seems to improve sperm count and motility in adult males. These effects seem to be related to improved levels of testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin (19275).

Respiratory effects: Ashwagandha seems to stimulate respiratory function (3710).

**Sedative effects**: Central nervous system depressant properties have been reported in animal studies (11301).

Smooth muscle effects: Ashwagandha seems to cause smooth muscle relaxation (3710).

**Thyroid effects**: Ashwagandha seems to stimulate thyroid synthesis and/or secretion (3710). In clinical and animal research, ashwagandha has been reported to stimulate thyroid function, increasing serum triiodothyronine (T3) and thyroxine (T4) concentrations and reducing serum thyroid stimulating hormone (TSH) levels (19281,19282,97292).

## Classifications

<u>Hypoglycemic Agents, Immunomodulators, Immunostimulants, Sedative-Hypnotic Agents, Adaptogens, Testosterone Enhancers</u>

# References

See Monograph References