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Ashwagandha

Updated: May 2, 2019.

OVERVIEW

Introduction

Ashwagandha is a popular Ayurvedic herb used as a general tonic, to increase energy and reduce stress. Ashwagandha has not been implicated in causing serum enzyme elevations during therapy, but recently has been implicated in rare cases of clinically apparent liver injury.

Background

Ashwagandha is an Ayurvedic herb that is derived from extracts of the roots of Withania somnifera, a low growing evergreen shrub that is endemic to India and Southeast Asia. Sometimes called "Indian ginseng", it is purported to have neuroprotective and antiinflammatory activities and is used to treat stress, fatigue, pain, skin diseases, diabetes, arthritis and epilepsy. It is also used as a general tonic to increase energy, reduce fatigue and counteract the effects of aging. Its efficacy in these conditions has not been consistently shown in rigorously controlled prospective studies, but it has been used in Ayurvedic medicine for centuries and is currently becoming a popular herbal product in Western countries. Withania somnifera extracts have as many as 35 different chemical constituents and the specific active ingredient responsible for its activity has not been identified. Constituents include alkaloids, steroidal lactones, saponins, withanolides, withaferins and iron. Extracts of ashwagandha are often supplied as tablets which are taken once to three times daily. Side effects are uncommon and have not been clearly defined. Large doses can cause gastrointestinal upset, diarrhea, nausea and vomiting, probably because of direct irritation to the intestinal mucosa.

Hepatotoxicity

Despite widescale use, ashwagandha is considered generally safe and without major adverse effects. In clinical trials, there have been no reports of serum enzyme elevations occurring during therapy and no mention of serious adverse events or hepatotoxicity. Recently, however, several cases of clinically apparent liver injury have been reported in patients taking commercial herbal products that are labelled as containing ashwagandha. The liver injury presented 2 to 12 weeks after starting ashwagandha with a cholestatic or mixed pattern of injury, jaundice and pruritus. Immunoallergic and autoimmune features were not prominent. Jaundice tended to be protracted but ultimately resolved without fatalities or chronic injury. Because commercial herbal preparations are often mixtures of herbs and nutritional products and can be mislabeled and contain unknown herbs and medications, it is not always clear whether the reported cases were due to ashwagandha and one of its components or to a contaminant. In several reported cases, however, the commercial product being taken was tested and found to have ashwagandha without other contaminants. Thus, clinically apparent liver injury attributable to ashwagandha appears to occur, but is rare.

Likelihood score: C (probable cause of clinically apparent liver injury).

Mechanism of Injury

The cause of hepatotoxicity from products containing ashwagandha is unclear. The possibility of mislabeling or adulteration with hepatotoxic herbal products is always an issue in commercial multiingredient dietary supplements.

Outcome and Management

The few cases of ashwagandha associated liver injury have been mild-to-moderate in severity and self-limited in course without acute liver failure or persistent liver injury. In most instances, the liver injury subsides within 1 to 3 months of discontinuing the herbal product. Rechallenge with the same product should be avoided.

Other names: Indian Ginseng, Winter Cherry, Poison Gooseberry

Drug Class: Herbal and Dietary Supplements

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Ashwagandha – Generic

DRUG CLASS

Herbal and Dietary Supplements

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Ashwagandha	90147-43-6	Unspecified	Not applicable

ANNOTATED BIBLIOGRAPHY

References updated: 02 May 2019

Zimmerman HJ. Unconventional drugs. Miscellaneous drugs and diagnostic chemicals. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999: pp. 731-4.

(Expert review of hepatotoxicity published in 1999; several herbals are discussed, including comfrey, Jin Bu huan, germander, chaparral leaf, skullcap and valerian, but not ashwagandha).

Liu LU, Schiano TD. Hepatotoxicity of herbal medicines, vitamins and natural hepatotoxins. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 2nd ed. New York: Informa Healthcare USA, 2007, pp. 735.

(Review of hepatotoxicity of herbal and dietary supplements [HDS]; ashwagandha is not discussed).

No authors listed. Ashwagandha. In, Natural Medicines: comprehensive database. Available at: http://naturaldatabase.therapeuticresearch.com

(Compilation of short monographs on herbal medications and natural products).

Sudhir S, Budhiraja RD, Miglani GP, Arora B, Gupta LC, Garg KN. Pharmacological studies on leaves of Withania somnifera. Planta Med 1986; (1): 61-3. PubMed PMID: 3703993.

(In rat models of acute and chronic inflammation and carbon tetrachloride hepatotoxicity, alcohol extracts of Withania somnifera leaves decreased edema, inflammation and hepatic injury).

Mishra LC, Singh BB, Dagenais S. Scientific basis for the therapeutic use of Withania somnifera (ashwagandha): a review. Altern Med Rev 2000; 5: 334-46. PubMed PMID: 10956379.

(Review of published literature on Withania somnifera, a commonly used herb in Ayurvedic medicine, said to have antiinflammatory, antitumor, antistress, antioxidant, immune modulatory, hemopoietic and rejuvenating properties; toxicity studies have been done largely in laboratory animals, but adverse effects have not been demonstrated).

Chopra A, Lavin P, Patwardhan B, Chitre D. A 32-week randomized, placebo-controlled clinical evaluation of RA-11, an Ayurvedic drug, on osteoarthritis of the knees. J Clin Rheumatol 2004; 10: 236-45. PubMed PMID: 17043520.

(Controlled trial of 32 week course of RA-11 versus placebo in 90 patients with osteoarthritis, found improvements in clinical symptoms but no side effects or changes in serum ALT, AST or Alk P levels).

van der Hooft CS, Hoekstra A, Winter A, de Smet PA, Stricker BH. [Thyrotoxicosis following the use of ashwagandha]. Ned Tijdschr Geneeskd 2005; 149: 2637-8. Dutch. PubMed PMID: 16355578.

(32 year old previously healthy woman developed poor appetite, weight loss, shakiness, palpitations 6 weeks after starting an herbal preparation of ashwagandha and shortly after increasing the dose [TSH <0.01 mU/L, free T4 33.9 pmol/L: normal 11-22], symptoms and abnormal thyroid tests resolving spontaneously soon after stopping).

Chopra A, Saluja M, Tillu G, Venugopalan A, Narsimulu G, Sarmukaddam S, Patwardhan B. Evaluating higher doses of Shunthi - Guduchi formulations for safety in treatment of osteoarthritis knees: A Government of India NMITLI arthritis project. J Ayurveda Integr Med 2012; 3: 38-44. PubMed PMID: 22529679.

(Among 92 patients with symptomatic osteoarthritis of the knees treated for 6 weeks with one of four herbal preparations [2 with ashwagandha], adverse events were uncommon and mild, and none of 45 patients developed serum ALT or AST elevations).

Kumar G, Srivastava A, Sharma SK, Rao TD, Gupta YK. Efficacy & safety evaluation of Ayurvedic treatment (Ashwagandha powder & Sidh Makardhwaj) in rheumatoid arthritis patients: a pilot prospective study. Indian J Med Res 2015; 141: 100-6. PubMed PMID: 25857501.

(Among 86 patients with rheumatoid arthritis treated with ashwagandha [5 gm twice daily] for 3 weeks followed by "Sidh Makardhwaj" for 4 weeks, symptom scores improved with treatment while ALT and AST levels did not change, serum mercury levels increased 4-fold).

Palliyaguru DL, Singh SV, Kensler TW. Withania somnifera: From prevention to treatment of cancer. Mol Nutr Food Res 2016; 60: 1342-53. PubMed PMID: 26718910.

(Review of the concept of chemoprevention of cancer and the evidence that ashwagandha might be effective based upon in vivo studies of apoptosis, angiogenesis, stress response, inflammation, and cancer prevention in animal models).

Choudhary D, Bhattacharyya S, Bose S. Efficacy and safety of ashwagandha (Withania somnifera (L.) Dunal) root extract in improving memory and cognitive functions. J Diet Suppl 2017; 14: 599-612. PubMed PMID: 28471731.

(Among 50 adults treated with ashwagandha [300 mg twice daily] or placebo for 8 weeks, measures of memory, attention and information processing improved more with ashwagandha, and tolerability was "excellent"; no mention of ALT elevations or hepatotoxicity).

Choudhary D, Bhattacharyya S, Joshi K. Body Weight management in adults under chronic stress through treatment with Ashwagandha root extract: a double-blind, randomized, placebo-controlled trial. J Evid Based Complementary Altern Med 2017; 22: 96-106. PubMed PMID: 27055824.

(Among 52 adults with chronic stress treated with ashwagandha or placebo for 8 weeks, scores for perceived stress decreased more with the herbal extract and adverse events were uncommon and mild).

Inagaki K, Mori N, Honda Y, Takaki S, Tsuji K, Chayama K. A case of drug-induced liver injury with prolonged severe intrahepatic cholestasis induced by Ashwagandha. Kanzo 2017; 58: 448-54. Not in PubMed

(20 year old man developed jaundice a month after increasing the dose of ashwagandha [bilirubin 20.7 mg/dL, ALT 94 U/L, Alk P 343 U/L, INR 1.02], jaundice persisting for more than 2 months, but ultimately resolving).