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# **Horny Goat Weed**

Updated: August 8, 2022.

### **OVERVIEW**

#### Introduction

Horny goat weed is a low growing plant with leathery leaves found in wetlands in many areas of the world, extracts of which have been used in traditional medicine as a tonic, aphrodisiac and antirheumatic agent. Oral forms of horny goat weed have been not been linked to serum aminotransferase elevations or to instances of clinically apparent liver injury.

## **Background**

Horny goat weed is a member of the genus *Epimedium*, a low growing perennial plant found throughout Asia, and parts of Europe and Africa, which has been used in traditional medicine for centuries as a tonic, aphrodisiac and antirheumatic agent. Extracts of the leaves and stems of horny goat weed are purported to have activity in improving sexual dysfunction, menstrual irregularities, osteoporosis, asthma, nephritis and cardiovascular disease. Over 200 chemical constituents have been identified in the plant, among which are flavonoids, lignans, ionones, phenol glycosides and sesquiterpenes. The active ingredients that have antiinflammatory, immunomodulatory, antiviral and hepatoprotective activities are believed to be flavonoids, such as icariin, icaritin or epimedin. Clinical studies of extracts of *Epimedium* have shown promising effects in the treatment of high blood pressure, coronary artery disease and sexual satisfaction, but these effects have not been proven in rigorous prospective controlled trials. Horny goat weed is available in multiple forms in tablets and capsules of 250 or 500 mg, the usual dose being one tablet or capsule daily. Horny goat weed is often combined with other botanicals, the combinations dictated by the purported use. Horny goat weed is generally well tolerated without adverse events; minor side effects may include abdominal discomfort and nausea. Rare instances of hypersensitivity reactions, skin rash and allergic dermatitis have been described.

## Hepatotoxicity

In small clinical trials of horny goat weed, serum enzyme elevations and episodes of acute liver injury have not been reported. There have, however, been rare reports of liver injury in patients taking multi-ingredient products that contain epimedium, although the attribution of injury to horny goat weed has not always been very clear. In large registries and case series on drug and herbal product induced liver injury, horny goat weed has not been listed. Furthermore, cases of severe clinically apparent liver injury has not been reported with horny goat weed.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

2 LiverTox

## **Mechanism of Injury**

Horny goat weed has several hundred chemical constituents, none of which has been shown to be particularly toxic or to cause liver injury.

Other names: Bishop's hat, fairy wings, rowdy lamb herb, barrenwort, Yin Yang Huo

Drug Class: Herbal and Dietary Supplements

#### PRODUCT INFORMATION

#### REPRESENTATIVE TRADE NAMES

Horny goat weed – Generic

**DRUG CLASS** 

Herbal and Dietary Supplements

**SUMMARY INFORMATION** 

Fact Sheet at MedlinePlus, NLM

#### CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Horny Goat Weed	E700000000	Herbal	Not Applicable

## ANNOTATED BIBLIOGRAPHY

References updated: 08 August 2022

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 herbal medications are discussed, but not horny goat weed).

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. 733-54.

(Review of hepatotoxicity of herbal and dietary supplements [HDS] published in 2007; no mention of horny goat weed).

Stedman C. Herbal hepatotoxicity. Semin Liver Dis. 2002;22:195–206. PubMed PMID: 12016550.

(Review and description of patterns of liver injury due to herbals, including discussion of potential risk factors, and herb-drug interactions).

Estes JD, Stolpman D, Olyaei A, Corless CL, Ham JM, Schwartz JM, Orloff SL. High prevalence of potentially hepatotoxic herbal supplement use in patients with fulminant hepatic failure. Arch Surg. 2003;138:852–8. PubMed PMID: 12912743.

(Among 20 patients undergoing liver transplantation for acute liver failure during 2001-2, 10 were potentially caused by herbals, but none attributed to horny goat weed).

Horny Goat Weed 3

Jacobsson I, Jönsson AK, Gerdén B, Hägg S. Spontaneously reported adverse reactions in association with complementary and alternative medicine substances in Sweden. Pharmacoepidemiol Drug Saf. 2009;18:1039–47. PubMed PMID: 19650152.

- (Review of 778 spontaneous reports of adverse reactions to herbals to Swedish Registry found none attributable to horny goat weed).
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- (77 year old man developed a painful maculopapular rash 4 days after starting a herbal remedy containing Ginkgo biloba and horny goat weed; "liver function tests" were normal).
- Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology. 2010;52:2065–76. PubMed PMID: 20949552.
- (Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 [11%] were attributed to drug induced liver injury of which 12 [9%] were due to herbals, including several herbal mixtures, usnic acid, Ma Huang, black cohosh, and Hydroxycut, but not horny goat weed).
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- (Review of current understanding of liver injury from herbals and dietary supplements focusing upon Herbalife and Hydroxycut products, green tea, usnic acid, noni juice, Chinese herbs, vitamin A and anabolic steroids; horny goat weed is not discussed).
- Ma H, He X, Yang Y, Li M, Hao D, Jia Z. The genus Epimedium: an ethnopharmacological and phytochemical review. J Ethnopharmacol. 2011;134:519–41. PubMed PMID: 21215308.
- (Horny goat weed is a genus of 52 species [Epimedium], the stems and leaves of which are used in traditional medicine as a tonic, aphrodisiac and antirheumatic).
- Teschke R, Wolff A, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: a tabular compilation of reported cases. Liver Int. 2012;32:1543–56. PubMed PMID: 22928722.
- (A systematic compilation of all publications on the hepatotoxicity of specific herbals identified 185 publications on 60 different herbs, herbal drugs and supplements but does not list or mention horny goat weed).
- Punyawudho B, Puttilerpong C, Wirotsaengthong S, Aramwit P. A randomized, double-blind, placebo-controlled crossover study of Cappra® for the treatment of mild or mild to moderate erectile dysfunction in Thai male. Afr J Tradit Complement Altern Med. 2012;10:310–5. PubMed PMID: 24146455.
- (Controlled crossover trial of Cappra [5 ingredients including Epimedium] vs placebo for 2 weeks in 63 men with mild to moderate erectile dysfunction found slight improvements in erectile dysfunction with Cappra, and adverse events of tachycardia, dizziness and facial numbness but no changes in ALT or AST).
- Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation and outcomes in patients with drug-induced liver injury in the general population of Iceland. Gastroenterology. 2013;144:1419–25. PubMed PMID: 23419359.
- (In a population based study of drug induced liver injury from Iceland, 96 cases were identified over a 2 year period, 15 of which [16%] were attributed to HDS products, but none were listed as containing horny goat weed).
- Bunchorntavakul C, Reddy KR. Review article: herbal and dietary supplement hepatotoxicity. Aliment Pharmacol Ther. 2013;37:3–17. PubMed PMID: 23121117.
- (Systematic review of literature on HDS associated liver injury; does not mention horny goat weed).

4 LiverTox

Navarro VJ, Seeff LB. Liver injury induced by herbal complementary and alternative medicine. Clin Liver Dis. 2013;17:715–35. PubMed PMID: 24099027.

- (Review of the epidemiology, regulatory status, diagnosis, pathogenesis and causes of liver injury from herbal products with specific discussion of conjugated linoleic acid, ephedra, germander, green tea, usnic acid, flavocoxid, aloe vera, chaparral, greater celandine, black cohosh, comfrey, kava, skullcap, valerian, noni juice, pennyroyal and traditional herbal remedies).
- Nishimatsu H, Kitamura T, Yamada D, Nomiya A, Niimi A, Suzuki M, Fujimura T, et al. Improvement of symptoms of aging in males by a preparation LEOPIN ROYAL containing aged garlic extract and other five of natural medicines comparison with traditional herbal medicines (Kampo). Aging Male. 2014;17:112–6. PubMed PMID: 24844765.
- (Controlled trial of "Leopin Royal" [garlic, ginseng, bezoar, velvet antler, cuscuta seed and epimedium] vs Kampo [as a control] in 49 elderly men for 6 months found no differences in changes in sexual function scales, or on testosterone, FSH, LH or estradiol levels between the two groups; adverse events of the herbal remedy included epigastric discomfort and rash).
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- (Among 839 cases of liver injury from drugs collected in the US between 2004 and 2013, 130 were due to HDS products, including 45 from body building agents [probably anabolic steroids] and 85 from diverse HDS products but none were listed as containing horny goat weed).
- Navarro VJ, Lucena MI. Hepatotoxicity induced by herbal and dietary supplements. Semin Liver Dis. 2014;34:172–93. PubMed PMID: 24879982.
- (Review of the international regulatory framework for HDS products and the epidemiology, clinical presentation, diagnosis and cause of HDS associated liver injury with tables and discussion of the most commonly implicated agents, but does not include mention of horny goat weed).
- Cui T, Kovell RC, Brooks DC, Terlecki RP. A urologist's guide to ingredients found in top-selling nutraceuticals for men's sexual health. J Sex Med. 2015;12:2105–17. PubMed PMID: 26531010.
- (Description and assessment of over-the-counter nutraceuticals used for male sexual dysfunction includes a discussion of horny goat weed for which there is a dearth of evidence of any activity).
- Seeff LB, Bonkovsky HL, Navarro VJ, Wang G. Herbal products and the liver: a review of adverse effects and mechanisms. Gastroenterology. 2015;148:517–532.e3. PubMed PMID: 25500423.
- (Extensive review of herbal associated liver injury does not discuss horny goat weed).
- Dietz BM, Hajirahimkhan A, Dunlap TL, Bolton JL. Botanicals and their bioactive phytochemicals for women's health. Pharmacol Rev. 2016;68:1026–1073. PubMed PMID: 27677719.
- (Review of botanicals used to treat premenstrual syndrome, urinary tract infections, nausea of pregnancy, lactation, menopausal symptoms and breast cancer; horny goat weed has been used to enhance libido in men and women and alleviating symptoms of menopause and premenstrual syndrome, the active ingredient likely being icaritin which appears to have estrogenic bioactivity).
- Brown AC. Liver toxicity related to herbs and dietary supplements: online table of case reports. Part 2 of 5 series. Food Chem Toxicol. 2017;107:472–501. PubMed PMID: 27402097.
- (Description of an online compendium of cases of liver toxicity attributed to HDS products, lists none as due to horny goat weed).

Horny Goat Weed 5

Medina-Caliz I, Garcia-Cortes M, Gonzalez-Jimenez A, Cabello MR, Robles-Diaz M, Sanabria-Cabrera J, Sanjuan-Jimenez R, et al; Spanish DILI Registry. Herbal and dietary supplement-induced liver injuries in the Spanish DILI Registry. Clin Gastroenterol Hepatol. 2018;16:1495–1502. PubMed PMID: 29307848.

- (Among 856 cases of hepatotoxicity enrolled in the Spanish DILI Registry between 1994 and 2016, 32 were attributed to herbal products, the most frequent cause being green tea [n=8] and Herbalife products [n=6], while none were attributed to horny goat weed).
- Balasubramanian A, Thirumavalavan N, Srivatsav A, Yu J, Hotaling JM, Lipshultz LI, Pastuszak AW. An analysis of popular online erectile dysfunction supplements. J Sex Med. 2019;16:843–852. PubMed PMID: 31036522.
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- (Among 37 ingredients used to treat male sexual dysfunction, most frequent are Tribulus, Eurycoma longifolia, zinc, L-arginine, horny goat weed and yohimbe; horny goat weed has some evidence of efficacy but "must be viewed with caution").
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- (Among 367 cases of hepatotoxicity enrolled in the Latin American DILI Network between 2011 and 2019, 29 [8%] were attributed to herbal products, the most frequent being green tea [n=7], Herbalife products [n=5] and garcinia [n=3], while none was attributed to horny goat weed).
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- (Systematic review of the literature on herb induced liver injury identified 446 references describing 936 cases due to 79 different herbal products, the most common being He Shou Wu [91], green tea [90] Herbalife products [64], kava kava [62], and greater celandine [48]; none was attributed to horny goat weed or epimedium).