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Yohimbine

Updated: May 25, 2015.

OVERVIEW

Introduction

Yohimbine is an indole alkaloid derived from the bark of the Central African yohimbe tree (Pausinystalia yohimbe) that is widely used as therapy for erectile dysfunction. Yohimbine use has been associated with occasional severe adverse events, but has not been linked to serum enzyme elevations or clinically apparent acute liver injury.

Background

Yohimbine (yoe him' been) is a popular and widely used herbal which was traditionally used in Africa for multiple conditions including cough, fever, leprosy, heart disease and as an anesthetic, hallucinogen and aphrodisiac. In the West, yohimbe became popular as a sexual stimulant and used to treat erectile dysfunction. Yohimbe is derived from the bark of the African evergreen tree Pausinystalia yohimbe (synonym, P. johimbe). The bark extract has multiple constituents, but the focus of most interest has been yohimbine, an indole alkaloid which has been shown to be an alpha 2 adrenergic receptor antagonist. In animal models, yohimbine increases sexual activity and is likely to act by engagement and inhibition of the alpha 2 adrenergic receptors in the corpus cavernosum, causing sustained engorgement of the corporeal tissue of the penis. Yohimbine has been chemically synthesized and is the synthetic form is currently marketed in the United States. The herbal bark extract may have other active components and is purported to be more potent and have more side effects. In clinical trials, synthetic yohimbine has had a consistent, although limited effect on erective dysfunction. Its effect on sexual desire is less well defined. The usual recommended dose of purified yohimbine is 5 to 10 mg three times a day. Drug tolerance or tachyphylaxis may occur. Side effects are usually mild and transient and are typical of alpha 2 adrenergic inhibition, including insomnia, anxiety, palpitations, chest pain, sweating, blurred vision and hypertension. Overdose can cause hypotension, tachycardia, seizures, paralysis and coma; deaths from overdose have been described.

Hepatotoxicity

In small clinical trials and case series, yohimbine therapy has not been linked to serum enzyme elevations or clinical liver disease. Although yohimbine is often found in weight loss and muscle building herbal combinations, it has not been associated with cases of clinically apparent acute liver injury.

Drug Class: Herbal and Dietary Supplements

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Yohimbine – Generic

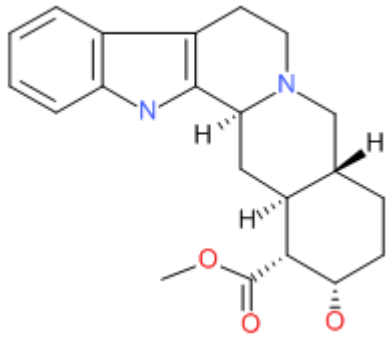
DRUG CLASS

Herbal and Dietary Supplements

SUMMARY INFORMATION

Fact Sheet at National Center for Complementary and Integrative Health, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Yohimbine	146-48-5	C21-H26-N2-O3	

ANNOTATED BIBLIOGRAPHY

References updated: 25 May 2015

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; hepatotoxicity of herbal medications is discussed, but yohimbine is not mentioned).

Seeff L, Stickel F, Navarro VJ. Hepatotoxicity of herbals and dietary supplements. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013, pp. 631-58. *(Review of hepatotoxicity of herbal and dietary supplements [HDS]*

; yohimbine is not discussed).

Yohimbe. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 926-30.

(Compilation of short monographs on herbal medications and dietary supplements).

Carlsson C. Herbs and hepatitis. Lancet 1990; 336: 1068. PubMed PMID: 1977040.

(Analysis of laboratory results from 395 patients found higher ALT levels among 53 patients taking herbals [55 U/L] than among those who did not [12 U/L]).

Eisenberg DM, Kessler RC, Foster C, Norlock FE, Calkins DR, Delbanco TL. Unconventional medicine in the United States. Prevalence, costs, and patterns of use. N Engl J Med 1993; 328: 246-52. PubMed PMID: 8418405.

(Among 1539 adults interviewed by telephone, 34% used an unconventional therapy during the previous 12 months, including 3% using herbal medicines).

Sandler B, Aronson P. Yohimbine-induced cutaneous drug eruption, progressive renal failure, and lupus-like syndrome. Urology 1993; 41: 343-5. PubMed PMID: 8470320.

(42 year old man developed skin rash one day after taking 3 tablets of yohimbine with fever, periorbital edema, erythroderma and desquamation, 19% eosinophils, progressive renal failure and polyserositis, requiring long term corticosteroids; no mention of hepatic involvement).

De Smet PA, Smeets OS. Potential risks of health food products containing yohimbe extracts. BMJ 1994; 309: 958. PubMed PMID: 7950687.

(Letter stressing the risks of yohimbine extracts and questioning the advisability of its general availability without a suitable warning labeling and lack of quality control, products often being mislabeled and the safe dosage not established, particularly in patients with autonomic dysfunction or heart disease).

Vogt HJ, Brandl P, Kockott G, Schmitz JR, Wiegand MH, Schadrack J, Gierend M. Double-blind, placebo-controlled safety and efficacy trial with yohimbine hydrochloride in the treatment of nonorganic erectile dysfunction. Int J Impot Res 1997; 9: 155-61. PubMed PMID: 9315493.

(Placebo controlled trial in 86 men with erectile dysfunction; side effects occurred in 30% of yohimbine recipients, but in only 10% of placebo recipients, but the nature and types of the side effects were not mentioned).

Ernst E, Pittler MH. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. J Urol 1998; 159: 433-6. PubMed PMID: 9649257.

(Systematic review of literature on yohimbine for erectile dysfunction identified 7 trials [419 patients], all of which showed evidence of efficacy; adverse events were uncommon; no mention of liver injury or ALT elevations).

Morales A. Yohimbine in erectile dysfunction: the facts. Int J Impot Res 2000; 12 Suppl 1: S70-74. PubMed PMID: 10845767.

(Review of history, chemistry, mechanism of action, animal studies, clinical effects and safety of yohimbine, decrying the lack of scientifically rigorous clinical trials).

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

(Review and description of patterns of herbal induced liver injury, including discussion of potential risk factors, and herb-drug interactions; yohimbine is not mentioned).

De Smet PAGM. Herbal remedies. N Engl J Med 2002; 347: 2046-56. PubMed PMID: 12490687.

(Review of status and difficulties of herbal medications including lack of standardization, federal regulation, contamination, safety, hepatotoxicity and drug-herb interactions; specific discussion of 4 herbs with therapeutic promise: ginkgo, hawthorn, saw palmetto and St. John's wort).

Ernst E. Adulteration of Chinese herbal medicines with synthetic drugs: a systematic review. J Intern Med 2002; 252:107-13. PubMed PMID: 12190885.

(Systematic review of literature on adulteration of herbals with conventional medications, in 15 case reports and 2 cases series of 21 patients; included NSAIDs, corticosteroids, benzodiazepines, diuretics and antidiabetic medications, in up to 24% of products).

Schiano TD. Hepatotoxicity and complementary and alternative medicines. Clin Liver Dis 2003; 7: 453-73. PubMed PMID: 12879994.

(Comprehensive review of herbal associated hepatotoxicity, including common patterns of presentation; yohimbine not discussed).

Pittler MH, Ernest E. Systematic review: hepatotoxic events associated with herbal medicinal products. Aliment Pharmacol Ther 2003; 18: 451-71. PubMed PMID: 12950418.

(Systematic review of published cases of hepatotoxicity due to herbal medications listing 52 case reports or case series, most common agents being celandine [3], chaparral [3], germander [8], Jin Bu Huan [3], kava [1], Ma huang [3], pennyroyal [1], skullcap [2], Chinese herbs [9], valerian [1]; yohimbine not mentioned).

Myers SP, Cheras PA. The other side of the coin: safety of complementary and alternative medicine. Med J Aust 2004; 181: 222-5. PubMed PMID: 15310261.

(Discussion of the safety of complementary and alternative medicines).

García-Cortés M, Borraz Y, Lucena MI, Peláez G, Salmerón J, Diago M, Martínez-Sierra MC, et al. Liver injury induced by "natural remedies": an analysis of cases submitted to the Spanish Liver Toxicity Registry. Rev Esp Enferm Dig 2008; 100: 688-95. PubMed PMID: 19159172.

(Among 521 cases of drug induced liver injury submitted to Spanish registry, 13 [2%] were due to herbals, none attributed to yohimbine).

Chalasani N, Fontana RJ, Bonkovsky HL, Watkins PB, Davern T, Serrano J, Yang H, Rochon J; Drug Induced Liver Injury Network (DILIN). Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. Gastroenterology 2008; 135: 1924-34. PubMed PMID: 18955056.

(Among 300 cases of drug induced liver disease in the US collected between 2004 and 2008, 9% of cases were attributed to herbal medications; yohimbine was listed as present in some combinations implicated in cases, but not as the sole or main implicated agent).

Haller C, Kearney T, Bent S, Ko R, Benowitz N, Olson K. Dietary supplement adverse events: report of a one-year poison center surveillance project. J Med Toxicol 2008; 4: 84-92. PubMed PMID: 18570167.

(Surveillance of dietary supplement related poison control calls in California in 2006; identified 275 calls, yohimbine accounting for 10 cases with symptoms of anxiety, diaphoresis, hypertension, palpitations, headache and chest pain and one death).

Giampreti A, Lonati D, Locatelli C, Rocchi L, Campailla MT. Acute neurotoxicity after yohimbine ingestion by a body builder. Clin Toxicol (Phila) 2009; 47: 827-9. PubMed PMID: 19640235.

(37 year old male bodybuilder developed fatigue, vomiting, seizures and coma, 2 hours after ingesting 5 grams of yohimbine [bilirubin normal; ALT 79 U/L, CPK 1042 U/L], resolving rapidly).

Navarro VJ. Herbal and dietary supplement hepatotoxicity. Semin Liver Dis 2009; 29: 373-82. PubMed PMID: 19826971.

(Overview of the regulatory environment, clinical patterns, and future directions in research with herbal and dietary supplements; no mention of yohimbine).

Ho CC, Tan HM. Rise of herbal and traditional medicine in erectile dysfunction management. Curr Urol Rep 2011; 12: 470-8. PubMed PMID: 21948222.

(Herbals are used increasingly as therapy of erectile dysfunction, often with little medical evidence of benefit; agents include ginseng, Epimedium, Tribulus terrestris, and yohimbine).

Rebiere H, Guinot P, Civade C, Bonnet PA, Nicolas A. Detection of hazardousweight-loss substances in adulterated slimming formulations using ultra-high-pressure liquid chromatography with diode-array

detection. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 2012; 29: 161-71. PubMed PMID: 22150438.

(Among 32 weight loss products available over-the-counter tested for contaminants, many contained caffeine and several had sibutramine, rimonabant, synephrine or yohimbine).

Stickel F, Kessebohm K, Weimann R, Seitz HK. Review of liver injury associated with dietary supplements. Liver Int 2011; 31: 595-605. PubMed PMID: 21457422.

(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; no mention of yohimbine).

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 no publications implicated yohimbine).

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, but does not discuss or mention yohimbine).

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, including 15 attributed to herbals or dietary supplements, but none to yohimbine).

Hernández N, Bessone F, Sánchez A, di Pace M, Brahm J, Zapata R, A Chirino R, et al. Profile of idiosyncratic drug induced liver injury in Latin America. An analysis of published reports. Ann Hepatol 2014; 13: 231-9. PubMed PMID: 24552865.

(Systematic review of literature of drug induced liver injury in Latin American countries published from 1996 to 2012 identified 176 cases, none of which were attributed to herbal supplements such as yohimibe).

Navarro VJ, Barnhart H, Bonkovsky HL, Davern T, Fontana RJ, Grant L, Reddy KR**,** et al. Liver injury from herbals and dietary supplements in the U.S. Drug-Induced Liver Injury Network. Hepatology 2014; 60: 1399-408. PubMed PMID: 25043597.

(Among 130 cases of liver injury attributed to an herbal or dietary supplement, none were specifically linked to yohimbine).

Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al.; United States Drug Induced Liver Injury Network. Features and Outcomes of 899 Patients With Drug-Induced Liver Injury: The DILIN Prospective Study. Gastroenterology 2015; 148: 1340-1352.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, herbal and dietary supplements accounted for 146 cases [16%], but none were specifically linked to yohimibe).