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NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Uva Ursi. [Updated 2020 Mar 28].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Uva Ursi

Updated: March 28, 2020.

OVERVIEW

Introduction

Uva ursi is an herbal extract derived from the leaves of the Arctostaphylos, a small evergreen shrub, which has been used in Native American traditional medicine for treatment of urinary tract symptoms and as a diuretic. Treatment with extracts of uva ursi has not been specifically linked to serum aminotransferase elevations or to instances of clinically apparent acute liver injury.

Background

Uva ursi is an herbal product derived from the fresh or dried leaves of the plant Arctostaphylos uva-ursi or bearberry, named for the grape-like clusters of orange berries that are commonly eaten by bears. Both Arctostaphylos and uva-ursi mean "grape of the bears", the former in Greek and the latter in Latin. Uva ursi leaves contain several phytochemicals, including ursolic acid, tannic acid, gallic acid, oils, resins, hydroquinone glycosides (mainly "arbutin"), and flavonoids. The active component of uva ursi is suspected to be hydroquinone, and particularly arbutin and methyl arbutin which may have antiinflammatory and antiseptic activities that are excreted in the urine. Uva ursi has been used to treat dysuria, cystitis, urethritis, and kidney and bladder stones. It has also been recommended for inducing diuresis and to treat constipation. In addition, the leaves of Arctostaphylos have been dried and smoked as tobacco, while leaves and berries have also been used as food. While uva ursi has been used extensively in traditional medicine, there is no convincing medical evidence that it is effective in treating urinary tract infections or urinary symptoms. More recently, uva ursi has been included in multiingredient dietary supplements meant for a variety of conditions such as to induce weight loss, promote wellness, prevent the effects of aging and to increase energy and stamina. Uva ursi is typically available in tablets and capsules of 150, 455 and 505 mg and is taken one to three times daily. It can also be prepared as tea from dried leaves or a powdered extract. Commercial products that contain uva ursi include SLIMQUICK Ultra and Animal Cuts. Side effects are not common but, in high doses, may include nausea, vomiting, tinnitus, shortness of breath and allergic reactions. Rare but potentially severe reactions to high doses of uva ursi may include convulsions, delirium and cardiovascular collapse.

Hepatotoxicity

Uva ursi has not been linked to serum enzyme elevations during therapy although there have been few prospective studies of its adverse effects on laboratory test results. There have been no convincing published instances of clinically apparent liver injury attributed to uva ursi. The frequency of hypersensitivity reactions to uva ursi is not known.

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

Other Names: Bearberry, Bear grape, Mountain cranberry, Redberry, Kinnikinnik, Arctostaphylos

Drug Class: Herbal and Dietary Supplements

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Uva Ursi – Generic

DRUG CLASS

Herbal and Dietary Supplements

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Arctostaphylos Uva-ursi Extract	84776-10-3	Unspecified	

ANNOTATED BIBLIOGRAPHY

References updated: 28 March 2020

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 linked to liver injury are discussed, but uva ursi 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 herbals does not mention uva ursi).

Uva-Ursi. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 868-71.

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

Larsson B, Jonasson A, Fianu S. Prophylactic effect of UVA-E in women with recurrent cystitis: a preliminary report. Curr Ther Res. 1993;53:441–3.

(Among 57 women with frequent episodes of cystitis treated with UVA-E [unknown dose] or placebo for one month, episodes of cystitis occurred in the next year in none of 30 treated with uva ursi but in 5 of 27 receiving placebo).

Yarnell E. Botanical medicines for the urinary tract. World J Urol. 2002;20:285–93. PubMed PMID: 12522584.

(Review of botanical agents that are purported to have effects in urologic conditions including uva ursi which is approved for treatment of lower urinary tract infection by the German Commission E; the active component is believed to be arbutoside which is hydrolyzed in the stomach releasing hydroquinone that is absorbed and metabolized to the glucuronide in the liver, which is then rapidly excreted in the urine where free hydroquinone is released [if urine is alkaline] and acts locally as an antiseptic; an issue is that hydroquinone is potentially carcinogenic so that uva ursi is recommended in short courses only and not to be taken chronically).

Schindler G, Patzak U, Brinkhaus B, von Niecieck A, Wittig J, Krähmer N, Glöckl I, et al. Urinary excretion and metabolism of arbutin after oral administration of Arctostaphylos uvae ursi extract as film-coated tablets and aqueous solution in healthy humans. J Clin Pharmacol. 2002;42:920–7. PubMed PMID: 12162475.

(In 16 healthy volunteers given arbutin either as tea made from uva ursi leaves or as an extract prepared as tablets, hydroquinone glucuronide and sulfate were rapidly detected in urine with lesser amounts of free hydroquinone in all subjects regardless of ingested form of uva ursi).

Wang L, Del Priore LV. Bull's-eye maculopathy secondary to herbal toxicity from uva ursi. Am J Ophthalmol. 2004;137:1135–7. PubMed PMID: 15183807.

(57 year old woman who ingested uva ursi tea preparations several times daily for 3 years developed "bull's eye" maculopathy which is typical of hydroxychloroquine macular injury, suggesting that hydroquinone from uva ursi which inhibits tyrosine kinase and melanin synthesis can cause macular injury as well).

Russo MW, Galanko JA, Shrestha R, Fried MW, Watkins P. Liver transplantation for acute liver failure from drug-induced liver injury in the United States. Liver Transpl. 2004;10:1018–23. PubMed PMID: 15390328.

(Among ~50,000 liver transplants reported to UNOS between 1990 and 2002, 270 [0.5%] were done for drug induced acute liver failure, including 7 [5%] for herbal medications, none were specifically attributed to uva ursi).

Quintus J, Kovar KA, Link P, Hamacher H. Urinary excretion of arbutin metabolites after oral administration of bearberry leaf extracts. Planta Med. 2005;71:147–52. PubMed PMID: 15729623.

(Hydroquinone glucuronide and sulfate were detected in urine within 2-6 hours of ingestion of a single 150 mL preparation of tea using bearberry leaves).

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

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

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

(Review of the problems of causality assessment in herbal and dietary supplement [HDS] associated liver disease, including the variable clinical presentations, the complexity and lack of information on their components, absence of controlled trials demonstrating safety and efficacy, the possibility of contamination or incorrect labeling and frequent underreporting of herbal use by patients. Regulation of HDS is under DSHEA, which requires manufacturers to determine safety and prohibits claims of efficacy in treating specific diseases. The US Pharmacopeia sets standards for food and drugs and includes HDS; HDS induced liver injury is a growing problem and currently accounts for at least 10% of cases of acute liver injury due to medications).

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; no mention of uva ursi).

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, but none were attributed to uva ursi).

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 uva ursi was not listed or mentioned).

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 85 cases of HDS associated liver injury [not due to anabolic steroids] enrolled in a US prospective study between 2004 and 2013, none were attributed to uva ursi).

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;148:1340–52.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a prospective database between 2004 and 2012, HDS were implicated in 145 [16%], the single major herbal cause being green tea and none were attributed to uva ursi, although it was a component of several implicated multiingredient products [Navarro et al Hepatology 2014]).

García-Cortés M, Robles-Díaz M, Ortega-Alonso A, Medina-Caliz I, Andrade RJ. Hepatotoxicity by dietary supplements: A tabular listing and clinical characteristics. Int J Mol Sci. 2016;17:537. PubMed PMID: 27070596.

(Listing of published cases of liver injury from HDS products, but does not mention or list uva ursi).

Brown AC. An overview of herb and dietary supplement efficacy, safety and government regulations in the United States with suggested improvements. Part 1 of 5 series. Food Chem Toxicol 2017; 107 (Pt A): 449-71.

(Summary of the US regulations on safety and efficacy of herbal and dietary supplements).

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 (Pt A): 472-501.

(Description of an online compendium of cases of liver toxicity attributed to HDS products, does not mention or list uva ursi).

Vega M, Verma M, Beswick D, Bey S, Hossack J, Merriman N, Shah A, et al; Drug Induced Liver Injury Network (DILIN). The incidence of drug- and herbal and dietary supplement-induced liver injury: preliminary findings from gastroenterologist-based surveillance in the population of the State of Delaware. Drug Saf. 2017;40:783–7. PubMed PMID: 28555362.

(A prospective, population based registry of cases of drug induced liver injury occurring in Delaware during 2014, identified 20 cases [2.7 per 100,000] overall, including 6 due to HDS products, all of which were proprietary multiingredient products, none specifically listing uva ursi as a component).

Navarro VJ, Khan I, Björnsson E, Seeff LB, Serrano J, Hoofnagle JH. Liver injury from herbal and dietary supplements. Hepatology. 2017;65:363–73. PubMed PMID: 27677775.

(Review of the problems of liver injury and HDS products, mentions that multiingredient dietary supplements account for the major of cases but does not mention uva ursi as a component).

Moore M, Trill J, Simpson C, Webley F, Radford M, Stanton L, Maishman T, et al. Uva-ursi extract and ibuprofen as alternative treatments for uncomplicated urinary tract infection in women (ATAFUTI): a factorial randomized trial. Clin Microbiol Infect. 2019;25:973–80. PubMed PMID: 30685500.

(Among 382 women with urinary tract symptoms suggestive of infection treated with ibuprofen vs uva ursi vs both vs placebo for 3-5 days before recommending antibiotics, urinary symptoms were not different after 2-4 days in the four groups and subsequent use of antibiotics was unaffected by uva ursi, although recommendations to delay treatment resulted in a decrease in antibiotic use).

Datta R, Juthani-Mehta M. Antibiotic-sparing agents for uncomplicated cystitis: uva-ursi and ibuprofen not ready for primetime. Clin Microbiol Infect. 2019;25:922–4. PubMed PMID: 31035018.

(Editorial in response to Moore et al [2019] mentioning that uva ursi had no effect on urinary symptoms, but that delaying start of antibiotics for a few days by recommending ibuprofen to see if symptoms improve on their own decreases antibiotic use without increasing rates of serious complications).