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Dihydromyricetin

Updated: August 16, 2023.

OVERVIEW

Introduction

Dihydromyricetin is a naturally occurring flavonoid found in the many plant species and is thought to be the active ingredient of several traditional Japanese, Chinese, and Korean medicines that are used to treat fever, parasite infections, liver diseases, and hangovers. Dihydromyricetin preparations have not been linked to instances of serum enzyme elevations or clinically apparent liver injury with jaundice.

Background

Dihydromyricetin (DHM) is a flavonoid found in many plants including Ampelopsis grossedentata (Chinese vine tea), Hovenia dulcis (Japanese raisin tree) and some pinus and Cedrus species. These herbal products are purported to be beneficial for cough, fever, colds, sore throat, vomiting, jaundice, nephritis, and hangovers. The suspected active ingredient is the flavonoid dihydromyricetin, purified preparations of which have been studied extensively in vitro and in vivo. Studies in cell cultures and in animal models have suggested that DHM has antioxidant, antiinflammatory, antibacterial and antineoplastic activities. DHM has been reported to improve glycemic control in diabetic animals, to lower serum cholesterol levels in animals with dyslipidemia, to improve cognitive function in models of brain injury, and to reduce liver injury in animal models of hepatotoxicity and alcoholic liver disease. Despite the many studies of DHM in animal models of disease, there have been few clinical trials of DHM in patients with diabetes, hyperlipidemia, neurologic diseases, or liver injury. In one small placebo-controlled trial of DHM in patients with nonalcoholic fatty liver, DHM resulted in greater improvements in serum aminotransferase levels, in fasting serum glucose and in LDL cholesterol levels without a change in body weight or in hepatic fat concentration as assessed by ultrasound. DHM is not approved for any use or disease in humans in the United States but is available in nutrition centers and on the internet. The typical dose in 300 to 1000 mg daily. The few studies of short term DHM therapy in humans reported no adverse events or evidence to toxicity to date. DHM is also a prominent component of several herbal medications including Japanese raisin tree and Chinese vine tea and is found in low concentrations in many plants, fruits and seeds.

Hepatotoxicity

DHM has not been subjected to many prospective trials of safety but is widely described as being well tolerated and without side effects. There have been no clinical case reports of clinically apparent liver injury with jaundice attributed to DHM, and it is not mentioned or listed in large case series or systematic reviews of the literature on herbal and dietary supplement induced liver injury. Thus, at this time, there is little evidence that DHM in typical oral doses or as a component of herbal products or teas causes clinically apparent liver injury in humans.

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

Mechanism of Injury

DHM has not been linked to serum enzyme elevations during therapy or clinically apparent liver injury. The mechanism by which DHM might cause liver injury is not known. DHM is poorly absorbed, is fairly rapidly metabolized, and its metabolic byproducts have not been fully defined.

Drug Class: Herbal and Dietary Supplements

Other names: Ampeloptin, Ampelopsin

PRODUCT INFORMATION

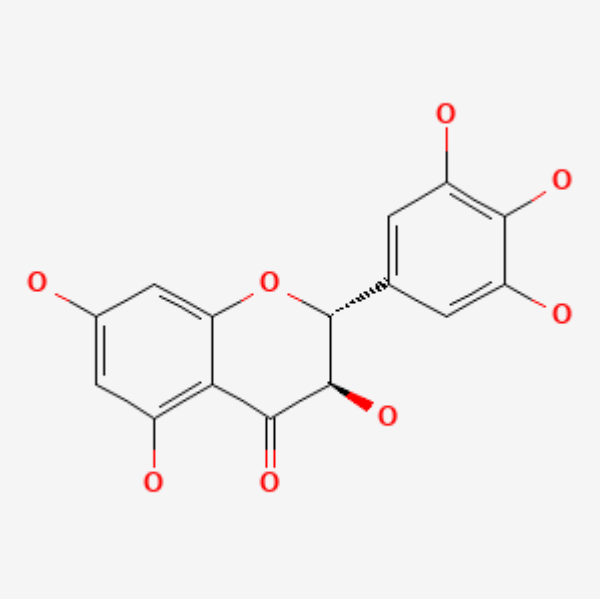
REPRESENTATIVE TRADE NAMES

Dihydromyricetin – Generic

DRUG CLASS

Herbal and Dietary Supplements

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Dihydromyricetin	27200-12-0	C15-H12-O8	

A polyphenolic hydroxy dihydroflavonol.

ANNOTATED BIBLIOGRAPHY

References updated: 16 August 2023

Abbreviations: DHM, dihydromyricetin; HDS, herbal and dietary supplements.

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 dihydromyricetin [DHM]).

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.

(Among 778 spontaneous reports of adverse reactions to herbal and alterative medicines to a national Swedish Registry, no cases were attributed to DHM).

Shen Y, Lindemeyer AK, Gonzalez C, Shao XM, Spigelman I, Olsen RW, Liang J. Dihydromyricetin as a novel anti-alcohol intoxication medication. J Neurosci. 2012;32:390-401. PubMed PMID: 22219299.

(Rats given intraperitoneal injections of DHM had decreased voluntary intake of alcohol, less evidence of alcohol central nervous system effects, and fewer signs of subsequent alcohol withdrawal, the effects were attributed to DHM's effects on GABA signaling).

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 herbal products identified 185 publications on 60 different herbs, herbal drugs and supplements but does not list or mention DHM).

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 DHM).

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; no mention of DHM).

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 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 no case was attributed specifically to DHM).

Chen S, Zhao X, Wan J, Ran L, Qin Y, Wang X, Gao Y, et al. Dihydromyricetin improves glucose and lipid metabolism and exerts anti-inflammatory effects in nonalcoholic fatty liver disease: A randomized controlled trial. Pharmacol Res. 2015;99:74-81. PubMed PMID: 26032587.

(Among 60 Chinese adults with nonalcoholic fatty liver disease treated with DHM [150 mg] or placebo twice daily for 3 months, weight did not change and hepatic steatosis as assessed by ultrasound improved similarly in the two groups, while serum ALT, AST and GGT levels decreased more in the DHM- than placebo treated subjects as did fasting glucose, LDL cholesterol, tumor necrosis factor alpha, CK-18 and FGF21 levels, and there were no adverse events in either group).

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, does not list or discuss DHM).

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], no mention of DHM).

Ran L, Wang X, Lang H, Xu J, Wang J, Liu H, Mi M, Qin Y. Ampelopsis grossedentata supplementation effectively ameliorates the glycemic control in patients with type 2 diabetes mellitus. Eur J Clin Nutr. 2019;73:776-782. PubMed PMID: 30089792.

(Among 80 patients with type 2 diabetes on various antidiabetic medications treated with DHM [760 mg] or placebo once daily for 1 month, fasting glucose levels decreased in DHM treated subjects compared to placebo but there were no changes in lipid or insulin levels, and there were "no adverse reactions" in either group).

Skotnicová A, Boubínová G, Boštíková Z, Dušková Š, Šulc M, Kutinová-Canová N, Mráz J, et al. Does dihydromyricetin impact on alcohol metabolism. Physiol Res. 2020;69(Suppl 4):S573-S581. PubMed PMID: 33656905.

(Studies in vivo and in vitro in rats found no evidence that DHM affects alcohol metabolism or has hepatoprotective effects against alcohol induced liver injury).

Silva J, Yu X, Moradian R, Folk C, Spatz MH, Kim P, Bhatti AA, et al. Dihydromyricetin protects the liver via changes in lipid metabolism and enhanced ethanol metabolism. Alcohol Clin Exp Res. 2020;44:1046-1060. PubMed PMID: 32267550.

(In a mouse model of alcohol induced liver injury, oral administration of DHM was associated with less liver steatosis and triglyceride levels which was attributed to changes in lipid metabolism and enhancement of ethanol metabolism as well as suppression of immune responses).

Chen J, Wang X, Xia T, Bi Y, Liu B, Fu J, Zhu R. Molecular mechanisms and therapeutic implications of dihydromyricetin in liver disease. Biomed Pharmacother. 2021;142:111927. PubMed PMID: 34339914.

(Review of the potential mechanisms of action of DHM in treating liver disease as shown in multiple animal models and in vitro systems of cell injury).

Verster JC, van Rossum CJI, Scholey A. Unknown safety and efficacy of alcohol hangover treatments puts consumers at risk. Addict Behav. 2021;122:107029. PubMed PMID: 34225031.

(Analysis of over-the-counter or internet available dietary supplements advertised to treat or prevent hangovers [n=82], found that most contained vitamins and minerals, and 49% contained milk thistle, 48% DHM, 45% N-acetyl cysteine [NAC], 27% alpha lipoic acid, and at least two dozen other herbs, but without providing information of concentration and without any clinical studies of efficacy or safety in support of the use of any of the components).

Ballotin VR, Bigarella LG, Brandão ABM, Balbinot RA, Balbinot SS, Soldera J. Herb-induced liver injury: Systematic review and meta-analysis. World J Clin Cases. 2021;9:5490-5513. PubMed PMID: 34307603.

(Systematic review of the literature on HDS 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]; DHM is not listed or discussed).

Bessone F, García-Cortés M, Medina-Caliz I, Hernandez N, Parana R, Mendizabal M, Schinoni MI, et al. Herbal and dietary supplements-induced liver injury in Latin America: experience from the LATINDILI Network. Clin Gastroenterol Hepatol. 2022;20:e548-e563. PubMed PMID: 33434654.

(Among 367 cases of hepatotoxicity enrolled in the Latin American Drug-Induced Liver Injury 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]; DHM is not mentioned).

Wang Y, Wang J, Xiang H, Ding P, Wu T, Ji G. Recent update on application of dihydromyricetin in metabolic related diseases. Biomed Pharmacother. 2022;148:112771. PubMed PMID: 35247719.

(Review of the in vitro and in vivo studies of dihydromyricetin demonstrating antiinflammatory, antitumor, antioxidant and antibacterial activity with applications in nonalcoholic fatty liver, alcoholic liver disease, chemical injury to the liver, acute liver failure and liver cancer, "with almost no toxicity").

Gong H, Xu H, Li M, Zhang D. Molecular mechanism and therapeutic significance of dihydromyricetin in nonalcoholic fatty liver disease. Eur J Pharmacol. 2022;935:175325. PubMed PMID: 36265611.

(Review of the possible mechanism of action of DHM in treating nonalcoholic fatty liver from many in vitro and in vivo studies suggests that it has antiinflammatory and antioxidant activities and may act via sirtuin-dependent pathways).

Al Omran AJ, Watanabe S, Hong EC, Skinner SG, Zhang M, Zhang J, Shao XM, et al. Dihydromyricetin ameliorates social isolation-induced anxiety by modulating mitochondrial function, antioxidant enzymes, and BDNF. Neurobiol Stress. 2022;21:100499. PubMed PMID: 36532369.

(In mice housed alone suffering from "social isolation-induced anxiety", administration of DHM decreased evidence of the mouse anxiety as well as changing mitochondrial function, levels of antioxidant enzymes and brain derived neurotrophic factor).

Miao X, Luo P, Liu J, Wang J, Chen Y. Dihydromyricetin ameliorated nonalcoholic steatohepatitis in mice by regulating the composition of serous lipids, bile acids and ileal microflora. Lipids Health Dis. 2023;22:112. PubMed PMID: 37533083.

(In mice given a methionine and choline deficient diet, treatment with DHM was associated with similar degrees of weight loss, but less hepatic fat and triglycerides and lower serum ALT [but not AST] levels, which was attributed to less increase in toxic bile acids and lipids and more benign ileal microflora).