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# **Bitter Melon**Updated: March 20, 2023.

#### **OVERVIEW**

#### Introduction

Bitter melon is a climbing vine that produces an oblong, green fruit that resembles a cucumber and can be eaten but is very bitter. Extracts of bitter melon fruit have been used in traditional medicine and most recently as a hypoglycemic agent to treat diabetes. Bitter melon extracts have not been associated with serum enzyme elevations during therapy nor have they been implicated in cases of clinically apparent liver injury.

# **Background**

Bitter melon (Momordica charantia) is a climbing vine found in tropical and subtropical areas that produces a green, deeply ridged or warty oblong fruit resembling a cucumber. The fruit, although quite bitter, can be eaten raw but more frequently is used in cooking or in preparing teas. Extracts of the fruit have also been used in traditional medicine for multiple conditions including constipation, dyspepsia, ulcer disease, cough, respiratory illnesses, gout, arthritis, skin disease and wounds. Claims have been made that bitter melon has antiviral effects which may be beneficial in human immunodeficiency virus (HIV) infection and that it has antineoplastic activities that may be effective for cancer. None of these purported effects, however, have been demonstrated in clinical trials in humans. Studies in animals as well as humans have shown that bitter melon extracts can lower blood sugar for which reason it has been marketed as a treatment of type 2 diabetes. The components of bitter melon responsible for the hypoglycemic effects are not known, but the fruit extracts contain alkaloids, glycosides, saponins, triterpenes, oils, steroids sterols, polysaccharides, resins and proteins, several of which have been shown to have effects on glucose metabolism in cell culture or animal models. The exact mechanism of the hypoglycemic effect of bitter melon is not known. In placebo controlled clinical trials in patients with diabetes or glucose intolerance, bitter melon extracts have had only a modest effect on serum glucose levels and little or no effect on fasting plasma glucose or hemoglobin A1c levels. Bitter melon has not been approved for the treatment of diabetes or any other medical condition in the United States by the FDA. Nevertheless, bitter melon extracts are available over-the-counter as a dietary supplement in multiple forms including liquid, powders and tablets. The typical recommended dose is 500 to 1000 mg taken in two to three times daily. Bitter melon extracts are usually well tolerated, but side effects can include abdominal discomfort, heartburn, constipation or diarrhea, nausea and vomiting, dizziness, headache and hypoglycemia. Rare but potentially severe adverse effects include severe hypoglycemia, coma and seizures. Bitter melon is a potential abortifacient and should not be used in pregnancy or in women of childbearing age not using effective contraception.

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# Hepatotoxicity

In multiple, largely short-term clinical studies of different preparations and concentrations of bitter melon extracts, adverse side effects were usually described as uncommon and minimal with either no change or slight improvement in serum aminotransferase levels. Despite wide-spread use, there have been no published reports of serum enzyme elevations or clinically apparent liver injury attributable to bitter melon extracts.

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

# **Mechanism of Injury**

The mechanism by which bitter melon extracts might cause liver injury is unknown.

### **Outcome and Management**

Hepatotoxicity from extracts of bitter melon fruit or leaves has not been reported.

Drug Class: Herbal and Dietary Supplements

Other names: Goya, Bitter Apple, Bitter Gourd, Bitter Squash, Balsam Pear.

#### PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Bitter Melon - 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
Bitter Melon	128529-78-2	Herbal	Not Applicable

# **ANNOTATED BIBLIOGRAPHY**

References updated: 20 March 2023

Abbreviations: 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 bitter melon extract).

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.

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(*Review of hepatotoxicity of herbal and dietary supplements [HDS] published in 2007; no mention of bitter melon).* 

- Bitter melon. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 405-410.
- (Compilation of short monographs on herbal medications and dietary supplements).
- Basch E, Gabardi S, Ulbricht C. Bitter melon (Momordica charantia): a review of efficacy and safety. Am J Health Syst Pharm. 2003;60:356–9. PubMed PMID: 12625217.
- (Review of the efficacy and safety of bitter melon as therapy for diabetes concludes that it may have hypoglycemic effects, but the data are not sufficient to recommend its use; no mention of ALT elevations or hepatotoxicity in humans treated with bitter melon).
- Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic review of herbs and dietary supplements for glycemic control in diabetes. Diabetes Care. 2003;26:1277–94. PubMed PMID: 12663610.
- (Systematic review of 36 herbs and dietary supplements used for glycemic control in patients with diabetes or glucose intolerance identified 108 trials with 4565 patients but concluded that the data for efficacy was inconclusive, but that few adverse events were reported and that several agents including bitter melon [Momordica charantia] had preliminary promising results).
- Dans AM, Villarruz MV, Jimeno CA, Javelosa MA, Chua J, Bautista R, Velez GG. The effect of Momordica charantia capsule preparation on glycemic control in type 2 diabetes mellitus needs further studies. J Clin Epidemiol. 2007;60:554–9. PubMed PMID: 17493509.
- (Among 40 adults with diabetes with elevated hemoglobin A1c [HbA1c] levels despite oral hypoglycemic therapy who were treated with either bitter melon [3 gm daily] or placebo capsules for 3 months, there were no changes in body weight, HbA1c levels or fasting blood glucose levels in either group, while adverse events included diarrhea and abdominal pain, serum ALT and AST declined slightly in both groups).
- 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 in a Swedish Registry does not list bitter melon among products associated with 5 or more reports).
- 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 bitter melon).
- Fuangchan A, Sonthisombat P, Seubnukarn T, Chanouan R, Chotchaisuwat P, Sirigulsatien V, Ingkaninan K, et al. Hypoglycemic effect of bitter melon compared with metformin in newly diagnosed type 2 diabetes patients. J Ethnopharmacol. 2011;134:422–8. PubMed PMID: 21211558.
- (Among 129 patients with newly diagnosed diabetes treated with bitter melon [500, 1000 or 2000 mg] or metformin [1000 mg] daily for 4 weeks, fasting and postprandial blood glucose decreased with metformin but not with bitter melon, and adverse events included headache, dizziness, and palpitations, and one patient with preexisting elevations had minor further increases in ALT [from 82 to 102 U/L] and AST levels [from 73 to 105 U/L] on bitter melon [500 mg daily] that resolved with stopping).
- 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.

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(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 mention or list bitter melon extract).

- 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 bitter melon).
- 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).
- 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 bitter melon extract).
- 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 bitter melon).
- 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 bitter melon).
- Peter EL, Kasali FM, Deyno S, Mtewa A, Nagendrappa PB, Tolo CU, Ogwang PE, et al. Momordica charantia L. lowers elevated glycaemia in type 2 diabetes mellitus patients: Systematic review and meta-analysis. J Ethnopharmacol. 2019;231:311–324. PubMed PMID: 30385422.
- (A metaanalysis of trials of bitter melon extracts in type 2 diabetes identified 10 studies with 1045 patients treated with 2 to 6 gm of bitter melon daily for 4 to 16 weeks, and demonstrated an overall but inconsistent modest improvement in HbA1c and blood glucose levels, while adverse events were generally mild, largely gastrointestinal with diarrhea and abdominal pain, and with no change or mild improvements in serum aminotransferase levels and no treatment related serious adverse events).
- Kim SK, Jung J, Jung JH, Yoon N, Kang SS, Roh GS, Hahm JR. Hypoglycemic efficacy and safety of Momordica charantia (bitter melon) in patients with type 2 diabetes mellitus. Complement Ther Med. 2020;52:102524. PubMed PMID: 32951763.
- (Among 96 Korean patients with diabetes who were treated with bitter melon [2380 mg capsules] or placebo daily for 12 weeks, HbA1c levels did not change with bitter melon therapy and fasting glucose levels improved minimally [-5 mg/dL] and adverse events included anorexia, nausea, abdominal discomfort, and skin rash, but rates were similar with placebo and serum liver enzyme test results did not change).

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Majeed M, Majeed A, Nagabhusahnam K, Mundkur L, Paulose S. A randomized, double-blind clinical trial of a herbal formulation (GlycaCare-II) for the management of type 2 diabetes in comparison with metformin. Diabetol Metab Syndr. 2021;13:132. PubMed PMID: 34789340.

- (Among 60 patients with newly diagnosed diabetes or glucose intolerance treated with a commercial herbal formulation with bitter melon [but also Cinnamomum cassia, Pterocarpus marsupium, Gymnema sylvestre, Salacia reticulata and Eugenia jambolana] or metformin [500 mg] twice daily for 60 days, fasting blood glucose and HbA1c levels decreased similarly in both groups and there were no adverse events and ALT and AST levels did not change).
- 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 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]; bitter melon was not listed among the 79 implicated products).
- 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 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 bitter melon is not mentioned).