



## Guarana

Updated: January 28, 2023.

## OVERVIEW

### Introduction

Guarana is an extract of roasted and pulverized seeds of the plant *Paullinia cupana* which is indigenous to the Amazon Basin and whose major active components are caffeine and other xanthine alkaloids such as theophylline and theobromine. Guarana has been used as a stimulant and tonic to treat fatigue, decrease hunger and thirst and for headaches and dysmenorrhea. In conventional doses, guarana has few side effects and has not been linked to episodes of liver injury or jaundice.

### Background

Guarana is derived from the seeds of the plant *Paullinia cupana* which is native to the Amazon Basin and is cultivated as a source of guarana and caffeine in South America. The *P. cupana* seeds contain a high concentration of caffeine (2% to 8%), far higher than in coffee beans (1% to 3%). The seeds are also rich in other xanthine alkaloids such as theophylline and theobromine as well as catechins, epicatechins and procyanidins. Guarana is produced by shelling and washing the seeds, followed by drying or roasting. The seeds are then pulverized into a powder that can be used as a food favoring, to prepare tea or as a component in energy drinks or multiingredient dietary supplements. Guarana has caffeine like effects on the heart, vasculature and central nervous system. In traditional medicine, guarana was used as a stimulant, mild diuretic and as a tonic to increase wakefulness, quell hunger and thirst, and to treat headaches, dysmenorrhea and digestive disorders. More recently, guarana has been purported to have beneficial effects on energy and endurance, as a weight loss agent, and for cognitive enhancement to increase concentration and memory. While guarana may have a mild effect on energy levels, cognition and satiety, these are generally short-lived and have minimal lasting clinical effects. In high doses, guarana can cause tremor, jitteriness, agitation, confusion, hypertension and dehydration. Most of its beneficial effects as well as its side effects can be explained by its caffeine content. Guarana is available in tablets and capsules, as liquid and in multiple commercial multiingredient supplements, particularly weight loss products and energy drinks. Daily doses range from 200 to 1000 mg daily. The use of multiple herbal products containing guarana and other sources of caffeine can result in caffeine toxicity.

### Hepatotoxicity

In small studies on guarana, there were no reports liver injury or serum enzyme elevations during treatment. Despite extensive use, guarana has not been convincingly linked to cases of clinically apparent liver injury. In large case series of drug- and HDS-related liver injury, guarana is not listed as implicated even in a single case. Use of high doses of guarana given long term in persons with preexisting liver disease or cirrhosis is discouraged.

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

## Mechanism of Injury

The mechanism by which guarana might cause liver injury is unknown. Guarana is found in many multiingredient dietary supplements and energy drinks, and it is sometimes one of many ingredients in products implicated in causing liver injury. The contribution of guarana to these cases is, however, not particularly likely.

Drug Class: [Herbal and Dietary Supplements](#)

Other names: Paullinia cupana.

## PRODUCT INFORMATION

### REPRESENTATIVE TRADE NAMES

Guarana – 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
Guarana	84929-28-2	Herbal	Not Applicable

## ANNOTATED BIBLIOGRAPHY

References updated: 28 January 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 guarana).*

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 guarana).*

Guarana. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 425-8.

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

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 no attributed to guarana).*

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 guarana).*

Stickel F, Kessebohm K, Weimann R, Seitz HK. Review of liver injury associated with dietary supplements. *Liver Int*. 2011;31:595–605. PubMed PMID: 21457433.

*(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; guarana is not discussed).*

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 horsetail).*

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 guarana).*

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 guarana).*

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 guarana).*

Martins SPDS, Ferreira CL, Del Giglio A. Placebo-controlled, double-blind, randomized study of a dry guarana extract in patients with head and neck tumors undergoing chemoradiotherapy: effects on fatigue and quality of life. *J Diet Suppl*. 2017;14:32–41. PubMed PMID: 27322597.

*(Among 60 adults with head and neck carcinoma undergoing radiotherapy and cisplatin chemotherapy treated with either guarana [25 mg] and placebo twice daily for 6 weeks, there was no difference in fatigue scores or quality of life changes between the two groups and no differences in adverse event rates or types).*

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 guarana).*

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 no case was attributed to guarana).*

Patrick M, Kim HA, Oketch-Rabah H, Marles RJ, Roe AL, Calderón AI. Safety of guarana seed as a dietary ingredient: a review. *J Agric Food Chem*. 2019;67:11281–11287. PubMed PMID: 31539257.

*(Review of the phytochemistry and safety of guarana concludes that it is not associated with any health risk when taken in doses 75 to 1200 mg of extract daily, that high doses can be associated with tachycardia, anxiety, agitation and gastrointestinal intolerance, symptoms typical of caffeine overdose; no mention of ALT elevations or hepatotoxicity).*

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]; guarana was not implicated in any cases).*

de Araujo DP, Pereira PTVT, Fontes AJC, Marques KDS, de Moraes ÉB, Guerra RNM, Garcia JBS. The use of guarana (*Paullinia cupana*) as a dietary supplement for fatigue in cancer patients: a systematic review with a meta-analysis. *Support Care Cancer*. 2021;29:7171–7182. PubMed PMID: 34146166.

*(Systematic review of the safety and efficacy of guarana in treating fatigue in patients with cancer identified 7 studies of 383 patients, among whom guarana and placebo had similar effects on fatigue, depression, sleep, anxiety and quality of life and both had similar rates of adverse events [tachycardia, insomnia, nausea and anxiety]; no mention of ALT elevations or hepatotoxicity).*

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 guarana was not implicated in any cases).*

Torres EAFS, Pinaffi-Langley ACDC, Figueira MS, Cordeiro KS, Negrão LD, Soares MJ, da Silva CP, et al. Effects of the consumption of guarana on human health: A narrative review. *Compr Rev Food Sci Food Saf*. 2022;21:272–295. PubMed PMID: 34755935.

*(Extensive review of the chemical composition of guarana, its pharmacology, biologic effects in vitro and in animal models, efficacy in human studies of mental health, depression, dyslipidemia, diabetes, obesity and cancer, and its safety and tolerability; no mention of ALT elevations during therapy or hepatotoxicity).*