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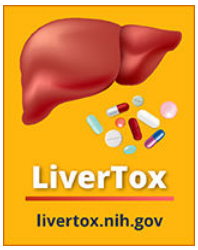


Turmeric

Updated: May 11, 2021.

OVERVIEW

Introduction

Turmeric is a popular herb derived from the roots of the plant Curcuma longa found mostly in India and Southern Asia. Turmeric has an intense yellow color and distinct taste and is used as a dye as well as a spice in the preparation of curry. Turmeric and its purified extract curcumin are also used medically for their purported antiinflammatory and antioxidant effects to treat digestive complaints including ingestion, diarrhea and liver diseases. Turmeric and curcumin have been associated with a low rate of transient serum enzyme elevations during therapy and while having a long history of safety, turmeric products have recently been implicated in over a dozen instances of clinically apparent acute liver injury.

Background

Turmeric (tur mer' ik) is a widely used herbal product derived from the roots of Curcuma longa, a perennial plant belonging to the ginger family (Zingiberaceae) that is native to India but grown throughout Southern Asia and in central America. Extracts of the rhizomes of turmeric contain volatile oils and curcuminoids (such as curcumin, demethoxycurcumin and others) which are believed to be the active antiinflammatory components of the herb and are often collectively referred to as curcumin. The antiinflammatory effects of turmeric and curcumin are thought to be mediated by inhibition of leukotriene synthesis. Curcumin has also been reported to have antineoplastic effects, mediated perhaps by inhibition of intracellular kinases. Turmeric has been used in traditional Indian (Ayurvedic) medicine to treat many conditions including indigestion, upper respiratory infections and liver diseases. Turmeric and curcumin are under active evaluation as antiinflammatory and antineoplastic agents, for treatment of diabetes and hyperlipidemia and as therapy of liver diseases including nonalcoholic steatohepatitis (NASH). The scientific bases for the purported effects of turmeric are not well established and rigorous proof of its efficacy in any medical condition is lacking. Commercial preparations of turmeric and curcumin vary widely in curcuminoid content. The recommended daily dose varies widely (100 to >1,000 mg daily), depending on the preparation used (curcuminoids vs turmeric extract), formulation (tablets, liquid, root extract, tea) and indications. Side effects are uncommon and mild but may include dermatitis and gastrointestinal upset.

Hepatotoxicity

Both turmeric and curcumin were considered to be generally safe and for many years had not been linked to instances of liver injury in any consistent way. Studies of its use in various diseases showed low rates of transient and asymptomatic serum enzyme elevations during therapy, but without instances of clinically apparent acute liver injury. Indeed, turmeric was evaluated as a potential therapy of acute and chronic liver injury and although

its efficacy and safety were not clearly shown, therapy with turmeric and curcumin did not seem to worsen the preexisting liver conditions. Recently, isolated case reports of liver injury arising during use of turmeric dietary supplements have been published. Initially, these episodes were attributed to other exposures that might have accounted for the injury or possible contaminants in the commercial turmeric products. One reason given for the safety and lack of hepatotoxicity of curcumin was that it is poorly absorbed by the oral route, and it was unclear whether there was adequate systemic exposure to achieve any of the purported beneficial or adverse effects of turmeric or curcumin.

Importantly, means of increasing the bioavailability of curcumin were developed using piperine (black pepper) or nanoparticle delivery methods to increase absorption. These high bioavailability forms of turmeric were subsequently linked to several cases of liver injury and mentioned as a possible cause of outbreaks of acute hepatitis with jaundice in Italy. The clinical features of the liver injury attributed to high bioavailable forms of turmeric have recently become better defined. The latency to onset of liver injury has varied from a few weeks to as long as eight months but is typically 1 to 3 months. The onset is insidious with fatigue, nausea and poor appetite followed by dark urine and jaundice. Rash and fever are absent or mild. Laboratory tests at onset typically show marked elevations in serum aminotransferase levels (often above 1000 U/L) with only mild increases in alkaline phosphatase. Jaundice occurs if the agent is continued. While signs of hypersensitivity are not prominent, many patients develop autoantibodies and the clinical syndrome and histological features can resemble autoimmune hepatitis. Prednisone has been used to treat severe cases of turmeric hepatotoxicity, but is probably not needed as recovery is rapid once the herbal product is discontinued. Neither acute liver failure nor chronic hepatitis or vanishing bile duct syndrome have been described in cases of turmeric associated liver injury, but the hepatocellular pattern of injury and frequency of jaundice suggest that fatal instances might occur, particularly if the product is not discontinued promptly.

Likelihood score: B (likely rare cause of clinically apparent liver injury).

Drug Class: Herbal and Dietary Supplements

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Turmeric – Generic

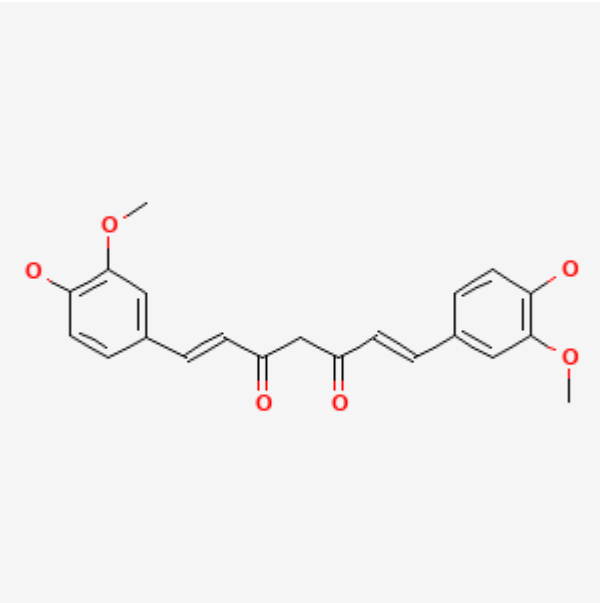
DRUG CLASS

Herbal and Dietary Supplements

COMPLETE LABELING

Fact Sheet at National Center for Complementary and Integrative Health

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Turmeric	458-37-7	C21-H20-O6	

ANNOTATED BIBLIOGRAPHY

References updated: 11 May 2021

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; turmeric and curcumin are not discussed).

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]; turmeric and curcumin are not discussed).

Turmeric. In, PDR for herbal medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 864-7.

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

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

(Review and description of patterns of liver injury, including discussion of potential risk factors, and herb-drug interactions; no mention of curcumin).

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, but not curcumin).

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

(Comprehensive review of herbal associated hepatotoxicity; curcumin is not listed as causing hepatotoxicity).

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 attributed to curcumin or turmeric use).

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 a Spanish registry, 13 [2%] were due to herbals, but none were attributed to turmeric or curcumin).

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, but none were linked to turmeric or curcumin use).

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, none of which were attributed to turmeric or curcumin).

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 HDS; curcumin is not listed as a potentially hepatotoxic botanical).

Wongcharoen W, Jai-Aue S, Phrommintikul A, Nawarawong W, Woragidpoonpol S, Tepsuwan T, Sukonthasarn A, et al. Effects of curcuminoids on frequency of acute myocardial infarction after coronary artery bypass grafting. Am J Cardiol. 2012;110:40–4. PubMed PMID: 22481014.

(Among 121 Thai patients who were undergoing coronary artery bypass surgery treated with "curminoids" or placebo for 8 days perioperatively, rates of postoperative myocardial infarction were less with curcuminoids [13% vs 30%] as were ALT elevations above 3 times ULN [0% vs 3%]).

Dulbecco P, Savarino V. Therapeutic potential of curcumin in digestive diseases. World J Gastroenterol. 2013;19:9256–70. PubMed PMID: 24409053.

(Review of pharmacokinetics, physical and molecular properties and potential uses of curcumin in digestive diseases; mentions that "as curcumin is particularly concentrated in the human liver, the risk of hepatotoxicity has been closely evaluated, but liver function tests have been shown to be unaffected with doses as high as 2 to 4 g/d").

Meng B, Li J, Cao H. Antioxidant and antiinflammatory activities of curcumin on diabetes mellitus and its complications. Curr Pharm Des. 2013;19:2101–13. PubMed PMID: 23116316.

(Review of the in vivo and in vitro evidence of antioxidant and antiinflammatory activity of curcumin and the rationale for its use in diabetes; "and it has no known side effects").

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 discuss curcumin or turmeric).

Sanmukhani J, Satodia V, Trivedi J, Patel T, Tiwari D, Panchal B, Goel A, et al. Efficacy and safety of curcumin in major depressive disorder: a randomized controlled trial. Phytother Res. 2014;28:579–85. PubMed PMID: 23832433.

(Among 60 patients with major depression treated with fluoxetine or curcumin or both for 6 weeks, improvements in depression rating scales were similar in all 3 groups and "there was no significant difference in … laboratory tests … from baseline").

Kuptniratsaikul V, Dajpratham P, Taechaarpornkul W, Buntragulpoontawee M, Lukkanapichonchut P, Chootip C, Saengsuwan J, et al. Efficacy and safety of Curcuma domestica extracts compared with ibuprofen in patients with knee osteoarthritis: a multicenter study. Clin Interv Aging. 2014;9:451–8. PubMed PMID: 24672232.

(Among 367 adults with knee osteoarthritis treated with ibuprofen [1.2 g daily] or curcumin extracts [1.5 g daily] for 4 weeks, pain, stiffness and function scores improved equally in both groups and adverse event rates were similar [36% vs 30%]; no mention of ALT elevations or hepatotoxicity).

Rahmani S, Asgary S, Askari G, Keshvari M, Hatamipour M, Feizi A, Sahebkar A. Treatment of non-alcoholic fatty liver disease with curcumin: a randomized placebo-controlled trial. Phytother Res. 2016;30:1540–8. PubMed PMID: 27270872.

(Among 80 Iranian patients with nonalcoholic fatty liver disease treated with curcumin [500 mg once daily] or placebo for 8 weeks, improvements, as assessed by ultrasonography, were more frequent with curcumin [79% vs 28%], and it was well tolerated with no serious adverse events and mean ALT levels decreased more with curcumin [from 39 to 36 U/L] than placebo [30 to 29 U/L]).

Panahi Y, Kianpour P, Mohtashami R, Jafari R, Simental-Mendía LE, Sahebkar A. Efficacy and safety of phytosomal curcumin in non-alcoholic fatty liver disease: a randomized controlled trial. Drug Res (Stuttg). 2017;67(4):244–51. PubMed PMID: 28158893.

(Among 102 patients with nonalcoholic fatty liver disease treated with curcumin [500 mg twice daily] or placebo for 8 weeks, improvements as assessed by hepatic ultrasound were more frequent with curcumin [75% vs 5%] and mean ALT levels fell from 35 to 25 U/L; there were no serious adverse events).

Mirzaei H, Shakeri A, Rashidi B, Jalili A, Banikazemi Z, Sahebkar A. Phytosomal curcumin: A review of pharmacokinetic, experimental and clinical studies. Biomed Pharmacother. 2017;85:102–12. PubMed PMID: 27930973.

(Review of the chemical characteristics, in vitro antioxidant activity and clinical effects of phytosomal curcumin; mentions that "curcumin is safe and could be tolerated even at very high doses").

Nelson KM, Dahlin JL, Bisson J, Graham J, Pauli GF, Walters MA. The essential medicinal chemistry of curcumin. J Med Chem. 2017;60:1620–37. PubMed PMID: 28074653.

(Review of the pharmacology and clinical evidence for efficacy of curcumin concludes that the multiple in vitro effects represent assay interference, that it is poorly absorbed and that there is no evidence that it has any effect in humans despite claims for benefit in many conditions including erectile dysfunction, hirsutism, baldness, cancer and Alzheimer disease).

Farzaei MH, Zobeiri M, Parvizi F, El-Senduny FF, Marmouzi I, Coy-Barrera E, Naseri R, et al. Curcumin in liver diseases: a systematic review of the cellular mechanisms of oxidative stress and clinical perspective. Nutrients. 2018;10:855. PubMed PMID: 29966389.

(Review of the in vitro and in vivo results showing activity of curcumin in decreasing oxidative stress and summary of clinical studies demonstrating efficacy in liver disease).

Saadati S, Hatami B, Yari Z, Shahrbaf MA, Eghtesad S, Mansour A, Poustchi H, et al. The effects of curcumin supplementation on liver enzymes, lipid profile, glucose homeostasis, and hepatic steatosis and fibrosis in patients with non-alcoholic fatty liver disease. Eur J Clin Nutr. 2019;73:441–9. PubMed PMID: 30610213.

(Among 50 patients with nonalcoholic liver disease given lifestyle advice and either curcumin [1500 mg] or placebo daily for 12 weeks, there were no differences between the two groups in weight loss [-2.4 vs -3.9 kg], changes in ALT [-6 vs -7 U/L] or in controlled attenuation parameter score for hepatic steatosis [-16 vs -32 dB/m]).

Lukefahr AL, McEvoy S, Alfafara C, Funk JL. Drug-induced autoimmune hepatitis associated with turmeric dietary supplement use. BMJ Case Rep. 2018;2018:bcr2018224611. PubMed PMID: 30206065.

(71 year old woman developed serum ALT elevations without jaundice 8-10 months after starting turmeric [ALT ~325 U/L, Alk P and bilirubin normal; ANA 1:320], which gradually fell into the normal range after stopping).

Luber RP, Rentsch C, Lontos S, Pope JD, Aung AK, Schneider HG, Kemp W, et al. Turmeric induced liver injury: a report of two cases. Case Reports Hepatol. 2019;2019:6741213. PubMed PMID: 31214366.

(A 52 year old woman and 55 year old man developed evidence of liver injury 1 and 5 months after starting a turmeric supplement [bilirubin 9.5 and 1.3 mg/dL, ALT 2591 and 1149 U/L, Alk P 263 and 145 U/L], which resolved on stopping and recurred in the first patient on restarting the supplement [bilirubin 3.5 mg/dL, ALT 2093 U/L], which was tested and found free of adulterants).

Suhail FK, Masood U, Sharma A, John S, Dhamoon A. Turmeric supplement induced hepatotoxicity: a rare complication of a poorly regulated substance. Clin Toxicol (Phila). 2020;58:216–7. PubMed PMID: 31271321.

(61 year old woman with polycystic liver disease developed fatigue and dark urine 6 weeks after starting turmeric supplements [bilirubin total 1.6, direct 1.0, ALT 2607 U/L, Alk P 246 U/L, ANA 1:250 normal IgG levels], responding rapidly to a course of prednisone and tests remaining normal after stopping).

Donelli D, Antonelli M, Firenzuoli F. Considerations about turmeric-associated hepatotoxicity following a series of cases occurred in Italy: is turmeric really a new hepatotoxic substance? Intern Emerg Med. 2020;15:725–6. PubMed PMID: 31278559.

(Letter mentioning an outbreak of acute cholestatic hepatitis in Italy related to use of a turmeric based dietary supplement with high bioavailability, perhaps due to its combination with piperine [black pepper] which increases curcumin absorption).

Chand S, Hair C, Beswick L. A rare case of turmeric-induced hepatotoxicity. Intern Med J. 2020;50:258–9. PubMed PMID: 32037709.

(62 year old white woman developed fatigue, rash and jaundice 10 months after starting turmeric [bilirubin >17 mg/dL, ALT 2308 U/L, Alk P not provided, ANA negative, IgG 1670 mg/dL], improving rapidly upon stopping the herbal supplement).

Nouri-Vaskeh M, Malek Mahdavi A, Afshan H, Alizadeh L, Zarei M. Effect of curcumin supplementation on disease severity in patients with liver cirrhosis: a randomized controlled trial. Phytother Res. 2020;34:1446–54. PubMed PMID: 32017253.

(Among 70 patients with cirrhosis treated with curcumin [1000 mg daily] or placebo for 3 months, those on curcumin had improvements in MELD scores [INR decreasing from 1.57 to 1.49 and bilirubin from 2.5 to 2.1], while those on placebo worsened).

Lee BS, Bhatia T, Chaya CT, Wen R, Taira MT, Lim BS. Autoimmune hepatitis associated with turmeric consumption. ACG Case Rep J. 2020;7:e00320. PubMed PMID: 32337301.

(55 year old woman developed jaundice 3 months after starting Quinol Liquid Turmeric [15 mL daily] [bilirubin 11.8 mg/dL, ALT 2743 U/L, Alk P 204 U/L, INR 1.0, ANA 1:80 rising to 1:320], biopsy showing interface hepatitis and plasma cells, and she rapidly improved once turmeric was stopped).

Lombardi N, Crescioli G, Maggini V, Ippoliti I, Menniti-Ippolito F, Gallo E, Brilli V, et al. Acute liver injury following turmeric use in Tuscany: An analysis of the Italian Phytovigilance database and systematic review of case reports. Br J Clin Pharmacol. 2021;87:741–53. PubMed PMID: 32656820.

(Analysis of the Italian Phytovigilance system identified 37 cases of liver injury attributed to high bioavailability curcumin; 7 cases reported from Tuscany included 6 women and 1 man, ages 45 to 68 years, taking turmeric for 2 weeks to 8 months [bilirubin 6 to 25 mg/dL, ALT 257 to 3303 U/L, GGT 124 to 504 U/L]; follow up after discontinuation was not always available).

Abdallah MA, Abdalla A, Ellithi M, Abdalla AO, Cunningham AG, Yeddi A, Rajendiran G. Turmeric-associated liver injury. Am J Ther. 2020;27(6):e642–e645. PubMed PMID: 31283536.

(51 year old white woman developed jaundice 2 months after starting a turmeric supplement [500 mg daily] [bilirubin total 2.4, direct 0.9 mg/dL, ALT 2484 U/L, Alk P 226 U/L], biopsy showing portal infiltrates including eosinophils, with rapid improvement upon stopping and normal liver tests 8 weeks later).

Koenig G, Callipari C, Smereck JA. Acute liver injury after long-term herbal "liver cleansing" and "sleep aid" supplement use. J Emerg Med 2021: S0736-4679(21)00004-4.

(53 year old woman developed jaundice 3-4 weeks after starting 2 herbal supplements, "Liver Detoxifier" which has 16 ingredients including turmeric and "Restful Sleep" with 5 components including valerian and melatonin [bilirubin 25.4 mg/dL, ALT 89 U/L, Alk P 174 U/L, albumin 2.0, INR 1.4], with rapid improvement on stopping).