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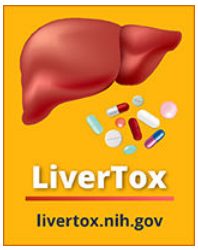
NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Noni. [Updated 2020 Mar 28].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/



Noni

Updated: March 28, 2020.

OVERVIEW

Introduction

Noni is a tropic fruit tree, the juice, roots, stems, bark, leaves and flowers of which have been used as medicinal remedies in Polynesia for centuries and recently in the Western world for a wide range of medical problems from cancer and diabetes to AIDs. A small number of isolated case reports of clinically apparent liver injury have been attributed to noni.

Background

Morinda citrifolia is a small, tropic fruit tree commonly known as Indian Mulberry, Ba Ji Tian or Noni which has been used as a food and an herbal remedy for centuries in Polynesia and Southeast Asia. Recently, noni has been introduced into Western herbal medicine as a "tropic fruit with 101 medical uses", and widely advertised and sold on the internet for a wide range of disorders including cancer, diabetes, depression, chronic fatigue, AIDS and senility. Active components in noni are many and include flavonoids, glycosides, vitamins, anthraquinones and polyunsaturated fatty acids. Studies in vitro and in animal models suggest that the active components are polysaccharide rich substances which have antitumor effects in vitro. In clinical trials, however, noni has yet to be proven to have anticancer activity. Noni juice has been marketed in the United States since 1996 and was approved as a "novel food" by the European Commission in 2003. While considered safe, several case reports of adverse events attributed to use of noni have appeared, although often criticized because of lack of chemical analysis of the actual product to exclude misidentification and contamination.

Hepatotoxicity

Several case reports have suggested that noni may account for some cases of idiosyncratic acute liver injury, although the association was weak in many cases. The latency to onset ranged from 2 to 8 weeks and the clinical features resembled acute hepatitis with a hepatocellular pattern of serum enzyme elevations. Immunoallergic features (rash, fever, eosinophilia) were not present, but some patients had high levels of autoantibodies. Nevertheless, the liver injury resolved rapidly once noni was discontinued and other features of autoimmunity were not present.

Likelihood score: C (probable rare cause of clinically apparent liver injury).

Mechanism of Injury

The mechanism of hepatotoxicity of noni is unknown. Extracts of the noni fruit have multiple components, including low levels of anthraquinones which are often cited as being hepatotoxic. However, the cases of noni

associated liver injury have had all of the characteristics of idiosyncratic liver injury rather than direct toxicity, and in vitro and in vivo studies of noni have not demonstrated evidence of intrinsic hepatotoxicity.

Outcome and Management

Hepatotoxicity attributed to noni juice has occasionally been severe and led to acute liver failure, which in at least one case necessitated emergency liver transplantation. Rechallenge studies have not been reported.

Other Names: Morinda citrifolia, Indian mulberry, Ba Ji Tian, Cheese fruit, Tahitian Noni Juice®, Xeronine

Drug Class: Herbal and Dietary Supplements

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Noni – Generic

DRUG CLASS

Herbal and Dietary Supplements

SUMMARY INFORMATION

Fact Sheet at National Center for Complementary and Integrative Health, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Noni	84929-68-0	Herbal mixture	Not applicable

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; noni is 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] mentions that noni juice has been implicated in cases of hepatitis and acute liver failure).

Noni. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007, pp 604-5.

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

Wang MY, West BJ, Jensen CJ, Nowichi D, Su C, Palu AK, Anderson G. Morinda citrifolia(noni): a literature review and recent advances in Noni research. Acta Pharmacologica Sinica. 2002;23:1127–41. PubMed PMID: 12466051.

(Extensive review of the literature on in vitro and in vivo effects of noni as well as studies in animals and humans which demonstrated lack of toxicity).

Pittler MH, Ernest E. Systematic review: hepatotoxic events associated with herbal medicinal products. Aliment Pharmacol Ther. 2003;18:451–71. PubMed PMID: 12950418.

(Systematic review of published cases of hepatotoxicity due to herbal medications listing 52 case reports or case series; noni is not listed or mentioned).

Millonig G, Stadlmann S, Vogel W. Herbal hepatotoxicity: acute hepatitis caused by a Noni preparation(Morinda citrifolia). Eur J Gastroenterol Hepatol. 2005;17:445–7. PubMed PMID: 15756098.

(45 year old man developed malaise and chest discomfort a few weeks after starting noni juice [bilirubin 0.8 mg/dL, ALT 1995 U/L, GGT 539 U/L], with resolution within 1 month of stopping).

Stadlbauer V, Fickert P, Lackner C, Schmerlaib J, Krisper P, Trauner M, Stauber RE. Hepatotoxicity of NONI juice: report of two cases. World J Gastroenterol. 2005;11:4758–60. PubMed PMID: 16094725.

(2 cases from Austria: 29 year old man developed acute liver failure after taking 1.5 L of noni juice over 3 weeks and various Chinese herbs for 7 days [bilirubin 45.3 mg/dL, ALT 1626 U/L, INR 1.4], undergoing liver transplantation 6 days later; 62 year old woman developed vomiting and diarrhea 2 months after ingesting noni juice daily for 3 months [bilirubin 2.9 mg/dL, ALT 2381 U/L, Alk P 292 U/L], resolving over next 9 months).

West BJ, Jensen CJ, Westendorf J. Noni juice is not hepatotoxic. World J Gastroenterol. 2006;12:3616–9. PubMed PMID: 16773722.

(Letter in response to Millonig [2005] and Stadlbauer [2005] questioning the link of the liver injury to noni juice intake, and reviewing studies of safety of noni in animals and man which showed no evidence of direct hepatotoxicity).

Yuce B, Gulberg V, Diebold J, Gerbes AL. Hepatitis induced by Noni juice from Morinda citrifolia: a rare cause of hepatotoxicity or the tip of the iceberg? Digestion. 2006;73:167–70. PubMed PMID: 16837801.

(24 year old woman with multiple sclerosis on beta interferon developed jaundice 4 weeks after starting noni juice [bilirubin 5.3 rising to 43.5 mg/dL, ALT 1538 to 3648 U/L, GGT 110 U/L], resolving in 4 weeks after stopping noni and 5 weeks after stopping beta interferon).

West BJ. Hepatotoxicity from interferon-beta, not noni juice. Digestion. 2006;74:47–8author reply 48. PubMed PMID: 17068398.

(Letter in response to Yuce [2006] suggesting that the liver injury was more likely due to beta interferon than noni).

López-Cepero Andrada JM, Lerma Castilla S, Fernández Olvera MD, Amaya Vidal A. Rev Esp Enferm Dig. 2007;99:179–81. [Hepatotoxicity caused by a Noni(Morinda citrifolia) preparation]. Spanish. PubMed PMID: 17516838.

(33 year old woman developed jaundice a few weeks after starting daily use of noni juice during travel to Ecuador [bilirubin 8.1 mg/dL, ALT 2740 U/L, Alk P 205 U/L, prothrombin 58%], resolving rapidly upon stopping the herbal).

West BJ, Berrio LF. Rev Esp Enferm Dig. 2007;99:737–8author reply 738. [Tahitian Noni juice is not hepatotoxic]. Spanish. PubMed PMID: 18290705.

(Letter in response to Lopez-Cepero Andrada [2007] questioning the role of noni juice in the liver injury, because of the lack of anti-HEV testing and lack of verification of the purity and identity of noni in the product).

Potterat O, Hamburger M. Morinda citrifolia(Noni) fruit—phytochemistry, pharmacology, safety. Planta Med. 2007;73:191–9. PubMed PMID: 17286240.

(Review of the history, phytochemistry, pharmacology, animal and clinical studies and safety of noni; 4 case reports of hepatotoxicity have been reported, but review by the European Food Safety Authority "concluded that there was no convincing evidence for a causal relationship").

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

Stadlbauer V, Weiss S, Payer F, Stauber RE. Herbal does not at all mean innocuous: the sixth case of hepatotoxicity associated with morinda citrifolia(noni). Am J Gastroenterol. 2008;103:2406–7. PubMed PMID: 18844633.

(43 year old man with glioblastoma developed elevated liver tests two weeks after starting noni juice [ALT rising from 34 to 516 U/L with normal bilirubin], resolving when noni juice was stopped).

West BJ, Su CX, Jensen CJ. Hepatotoxicity and subchronic toxicity tests of Morinda citrifolia(noni) fruit. J Toxicol Sci. 2009;34:581–5. PubMed PMID: 19797868.

(Noni extract was prepared from Tahitian noni fruits and tested for hepatotoxicity in vitro and in vivo; no toxicity found towards HepG2 cells or laboratory rats given a range of doses orally for up to 90 days).

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; noni juice not mentioned).

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 noni juice).

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).

Yu EL, Sivagnanam M, Ellis L, Huang JS. Acute hepatotoxicity after ingestion of Morinda citrifolia (Noni Berry) juice in a 14-year-old boy. J Pediatr Gastroenterol Nutr. 2011;52:222–4. PubMed PMID: 21119544.

(14 year old boy developed jaundice after having ingested 10 bottles of an antioxidant drink [containing green tea, aloe vera and noni] over the previous 2 months [bilirubin 4.4 rising to 12.3 mg/dL, ALT 2860 U/L, GGT 141 U/L, INR 1.7], resolving in 2 months).

Jiménez-Encarnación E, Ríos G, Muñoz-Mirabal A, Vilá LM. Euforia-induced acute hepatitis in a patient with scleroderma. BMJ Case Rep 2012; 2012.

(45 year old woman with systemic sclerosis developed jaundice 1 month after starting Euphoria, a combination herbal product whose ingredients included aloe vera, resveratrol, green tea, noni and several berries [bilirubin 17.7 mg/dL, ALT 837 U/L, Alk P 134 U/L], with slow recovery over the 18 months after 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.

(A systematic compilation of all publications on the hepatotoxicity of specific herbals identified 185 publications on 60 different herbs, herbal drugs and supplements including 6 publications on noni).

Teschke R, Schulze J, Schwarzenboeck A, Eickhoff A, Frenzel C. Herbal hepatotoxicity: suspected cases assessed for alternative causes. Eur J Gastroenterol Hepatol. 2013;25:1093–8. PubMed PMID: 23510966.

(Review of 23 publications of case series of liver injury attributed to herbals or dietary supplements found alternative causes to be "evident" in 49% of 573 cases).

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 mentions that noni has been associated with clinically apparent hepatotoxicity).

Mrzljak A, Kosuta I, Skrtic A, Kanizaj TF, Vrhovac R. Drug-Induced Liver Injury Associated with Noni (Morinda citrifolia) Juice and Phenobarbital. Case Rep Gastroenterol. 2013;7:19–24. PubMed PMID: 23467452.

(38 year old woman on phenobarbital for 9 months developed jaundice one week after starting noni juice [60 mL daily] [bilirubin 9.7 mg/dL, ALT 813 U/L, Alk P 532 U/L, INR 2.6], resolving within 6 months of stopping both noni and phenobarbital and with corticosteroid therapy).

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, including 15 [16%] due to herbal and dietary supplements, none of which were attributed to noni juice).

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 HDS induced liver injury including regulatory problems, difficulties in diagnosis and causality assessment; mentions that noni has been linked to cases of hepatitis but none were fatal).

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, noni juice was not implicated in any of the cases).

Seeff LB, Bonkovsky HL, Navarro VJ, Wang G. Herbal products and the liver: a review of adverse effects and mechanisms. Gastroenterology. 2015;148:517–32.e3. PubMed PMID: 25500423.

(Extensive review of possible beneficial as well as harmful effects of herbal products on the liver in a supplemental table lists noni as having been implicated in cases of severe acute hepatitis).

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%], none of which were attributed to noni [Navarro et al Hepatology 2014]).

Garrido-Gallego F, Muñoz-Gómez R, Muñoz-Codoceo C, Delgado-Álvarez P, Fernández-Vázquez I, Castellano G. Acute liver failure in a patient consuming Herbalife products and Noni juice. Rev Esp Enferm Dig. 2015;107:247–8. PubMed PMID: 25824932.

(56 year old woman developed jaundice while taking several Herbalife products and noni juice [bilirubin 21.5 mg/dL, ALT 940 U/L, Alk P 187 U/L, INR 2.03], with progressive liver failure and successful liver transplantation 4 weeks after presentation).

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 list those attributed to noni).

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, lists at least 8 reports of liver injury for which there was exposure to noni; however, many had other possible causes).

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 noni as a component).

Waldman W, Piotrowicz G, Sein Anand J. Przegl Lek. 2013;70:690–2. [Hepatoxic effect of a noni juice consumption--a case report]. PubMed PMID: 24466723.

(Ordered).