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Nux Vomica Updated: March 3, 2023.

OVERVIEW

Introduction

Nux vomica is an extract of the seeds of the Strychos nux-vomica or strychnine tree used in traditional and homeopathic medicine with purported benefits for a wide range of conditions including heart disease and cancer. Nux vomica contains strychnine and brucine, two toxic alkaloids banned or severely restricted in most countries. The toxicity of Nux vomica is manifested by neuromuscular hyperexcitability with agitation and muscular spasms followed by convulsions, rhabdomyolysis, metabolic acidosis and respiratory and cardiac arrest. Ingestion of Nux vomica has not been shown to cause serum aminotransferase elevations or liver injury.

Background

Nux vomica is prepared from the seeds of the Strynos nux-vomica tree, which is native to India and Southeast Asia. The dried, processed seeds have been used in Ayurvedic and traditional Asian medicine for a wide variety of conditions including gastritis, constipation, influenza, arthritis, musculoskeletal disorders, heart disease and cancer. However, the Nux vomica seeds also contain appreciable concentrations of the alkaloid poisons strychnine and brucine. Strychnine is a well known toxin which is associated with both intentional and accidental poisoning for which reason it is banned or restricted in most countries of the world, being used only in baits to kill feral animals such as rats and moles. While strychnine and brucine have antineoplastic, antiinflammatory and antioxidant activity in cell culture, the therapeutic window of their effects is narrow, and they have not been shown to have beneficial medicinal effects in prospective studies in humans. Nevertheless, Nux vomica products can been purchased on the internet and in nutrition stores and are generally recommended for indigestion, nausea, vomiting and as a hangover cure. The Nux vomica seeds are typically dried and processed resulting in a decrease in the concentration of the toxic alkaloids. Indeed, testing currently available commercial products by sensitive analytic methods often fails to detect either strychnine or brucine. The toxicity of strychnine is due to its inhibition of postsynaptic, neuroinhibitory glycine receptors found in the spinal cord and central nervous system. Toxicity arises within a few hours of ingestion of Nux vomica seeds with anxiety, agitation, heightened sensation, twitching, and muscular spasms, which can progress to convulsions while conscious, chest and back pain, hyperthermia, rhabdomyolysis, renal dysfunction, and respiratory or cardiac failure. In severe cases death occurs within 24 hours of the ingestion. Mild cases may have transient agitation and muscle spasms lasting only a few hours.

Hepatotoxicity

Small prospective studies of extracts of *Nux vomica* do not mention serum aminotransferase elevations or acute liver injury, but also did not generally include monitoring of liver tests. There have been no reports of acute liver

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injury attributed to use of *Nux vomica* products. Descriptions of the toxicity of strychnine and *Nux vomica* have not mentioned acute liver injury and in several case reports serum enzyme levels have been reported to be normal at the time of initial presentation. Some fatal cases have been attributed to multiorgan failure, probably the result of shock and hyperthermia.

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

Mechanism of Injury

The mechanism of toxicity of *Nux vomica* appears to be due to the toxic alkaloids, strychnine and brucine, which act by blocking neuroinhibitory, postsynaptic glycine receptors which results in muscle hyperexcitability, spasms, tonic-clonic muscular activity, and with higher doses, paralysis of pulmonary musculature and respiratory failure.

Outcome and Management

Hepatotoxicity from extracts of *Nux vomica* has not been reported.

Drug Class: Herbal and Dietary Supplements

Other names: Strychnine, Poison Fruit, Slang Nuts.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Nux vomica – Generic

DRUG CLASS

Herbal and Dietary Supplements

CHEMICAL FORMULA AND STRUCTURE

| DRUG | CAS REGISTRY NUMBER | MOLECULAR FORMULA | STRUCTURE |
|---------|---------------------|-------------------|---|
| Brucine | 357-57-3 | C23-H26-N2-O4 | Hama Hama Hama Hama Hama Hama Hama Hama |

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Table continued from previous page.

| DRUG | CAS REGISTRY NUMBER | MOLECULAR FORMULA | STRUCTURE |
|------------|---------------------|-------------------|-----------|
| Strychnine | 57-24-9 | C21-H22-N2-O2 | N H H H O |

ANNOTATED BIBLIOGRAPHY

References updated: 03 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 Nux vomica).

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 Nux vomica).

Nux vomica. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 607-9.

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

O'Callaghan WG, Joyce N, Counihan HE, Ward M, Lavelle P, O'Brien E. Unusual strychnine poisoning and its treatment: report of eight cases. Br Med J (Clin Res Ed). 1982;285(6340):478.

(Eight persons developed acute strychnine poisoning within 30 minutes of inhaling a white powder thought to be cocaine; one patient dying of cardiac arrest, the others with varying degrees of muscle spasms and convulsions all having raised CPK levels; no mention of liver injury or serum aminotransferase levels).

Boyd RE, Brennan PT, Deng JF, Rochester DF, Spyker DA. Strychnine poisoning. Recovery from profound lactic acidosis, hyperthermia, and rhabdomyolysis. Am J Med. 1983;74:507–12. PubMed PMID: 6829597.

(42 year old man ingested strychnine and developed progressive muscle spasms, respiratory arrest, metabolic acidosis, renal failure, hyperthermia and muscle injury [CPK 8218 U/L] and was treated with paralysis,

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artificial ventilation, fluid replacement, treatment of acidosis and he eventually recovered; no mention of liver injury or serum aminotransferase levels).

- Katz J, Prescott K, Woolf AD. Strychnine poisoning from a Cambodian traditional remedy. Am J Emerg Med. 1996;14:475–7. PubMed PMID: 8765115.
- (58 year old Cambodian woman developed dizziness, abdominal pain, muscle spasms, and "awake" seizures shortly after ingestion of "slang nut" and was admitted with lactic acidosis, recovering with supportive therapy, testing of the product revealed it to be seeds from the Strychnos nux-vomica tree).
- Chan TY. Herbal medicine causing likely strychnine poisoning. Hum Exp Toxicol. 2002;21:467–8. PubMed PMID: 12412642.
- (A 42 year old woman treated with "magianzi" prepared from dried and processed Nux Vomica seeds developed tonic contractures of the limb muscles, perioral numbness, chest tightness and difficulty breathing within hours of drinking a second bowl of a herbalist prescribed herbal decoction, ultimately recovering with supportive therapy; liver function tests were said to be normal).
- Barquero Romero J, Redondo López JM, Galeano Díaz F, Pérez Miranda M. Med Clin (Barc). 2004;122:318–9. [Fatal acute pancreatitis in a patient who received an homeopathic treatment]. PubMed PMID: 15030747.
- (67 year old man with type 2 diabetes developed severe epigastric pain and nausea 2 weeks after starting a homeopathic medication that included Nux vomica and Rhys Toxicodendron [Atlantic poison oak], evaluation revealed an acute hemorrhagic and ultimately fatal pancreatitis despite absence of history of clinical evidence of alcohol use, gallstones or liver injury [ALT 38 U/L, AST 27 U/L]).
- 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 cases attributed to Nux vomica).
- 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 Nux vomica).
- Parker AJ, Lee JB, Redman J, Jolliffe L. Strychnine poisoning: gone but not forgotten. Emerg Med J. 2011;28:84. PubMed PMID: 20810461.
- (49 year old woman developed acute agitation followed by muscle spasms within hours of suicidal ingestion of strychnine with progressive respiratory failure, lactic acidosis and CK levels rising from normal to 6262 U/L by day 2, but ultimate recover; no mention of liver injury or serum aminotransferase elevations).
- Achappa B, Madi D, Babu YP, Mahalingam S. Rituals can kill A fatal case of brucine poisoning. Australas Med J. 2012;5:421–3. PubMed PMID: 23024715.
- (29 year old man developed intractable and ultimately fatal convulsions within hours of drinking a decoction that he made from the bark of a strychnine tree that he had mistaken for a Alsonia scholar tree, which had been used by his family in a yearly celebration; no mention of liver test abnormalities).
- 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 Nux vomica).

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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 Nux vomica).
- 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 Arnica montana).
- 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 Nux vomica).
- Prat S, Hoizey G, Lefrancq T, Saint-Martin P. An unusual case of strychnine poisoning. J Forensic Sci. 2015;60:816–7. PubMed PMID: 25702781.
- (A 69 year old Canadian man was found dead at home, apparently after suicidal ingestion of rat poison with high levels of strychnine).
- Ponraj L, Mishra AK, Koshy M, Carey RAB. A rare case report of Strychnos nux-vomica poisoning with bradycardia. J Family Med Prim Care. 2017;6:663–665. PubMed PMID: 29417029.
- (39 year old Indian man made a concoction with 6 leaves of the Strychnos nux-vomica tree, and rapidly developed vomiting, agitation, muscle twitches and muscle tenderness followed by bradycardia and electrocardiographic changes, but with normal blood tests and full recovery within a few days).
- Singhapricha T, Pomerleau AC. A case of strychnine poisoning from a Southeast Asian herbal remedy. J Emerg Med. 2017;52:493–495. PubMed PMID: 27856027.
- (40 year old Cambodian woman presented with jaw pain and muscle spasms and strychnine detected in plasma and urine a few hours after drinking from a bottle that she thought was vodka but was actually "slang nuts", a local preparation of Nux vomica seeds; recovering with supportive care; no mention of hepatic injury).
- 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 Nux vomica).
- 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.

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(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 Nux vomica).

- Lu L, Huang R, Wu Y, Jin JM, Chen HZ, Zhang LJ, Luan X. Brucine: A review of phytochemistry, pharmacology, and toxicology. Front Pharmacol. 2020;11:377. PubMed PMID: 32308621.
- (Review of the chemistry, pharmacology and toxicity of brucine, a major component found in Nux vomica seeds which has antineoplastic and antiinflammatory activities in vitro but a narrow therapeutic window; "although brucine has an impressive preclinical profile in pharmacology research, serious toxicity limits its clinical applications").
- Downs J, Wolf CE, Williams G, Cumpston KL, Kershner E, Wills BK. Negligible Nux vomica: homeopathic Nux vomica remedies don't contain strychnine? Toxicon. 2021;200:1–2. PubMed PMID: 34181973.
- (None of a number of Nux vomica products purchased from homeopathic medicine and nutrition stores tested positive for strychnine or brucine using sensitive high-pressure liquid chromatography assays).
- Abhilash KP, Murugan S, Rabbi AS, Pradeeptha S, Pradeep R, Gunasekaran K. Deliberate self-poisoning due to plant toxins: verdant footprints of the past into the present. Indian J Crit Care Med. 2021;25:392–397. PubMed PMID: 34045805.
- (Among 150 patients seen over a 2 year period in an emergency room in South India with deliberate self-poisoning with plant products, the mortality rate was 9%, most were due to oleander [59%] or aduvanthalai [31%], but 4 were due to Nux vomica, all of which survived).
- 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]; Nux vomica is not 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 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 Nux vomica is not mentioned).