

Areca Nut

Updated: March 22, 2023.

OVERVIEW

Introduction

Areca nut, commonly known as betel nut, is the fruit of the Areca palm (*Areca catechu*), which is found in tropical areas of the Pacific, south Asia and eastern Africa. The major use of areca nut is as a recreational stimulant typically chewed wrapped in betel leaves (*Piper betle*), powdered with calcium hydroxide (slaked lime), and flavored with mint, clove or tobacco. Areca nut has also been used as an extract in traditional medicine as a cathartic or as treatment of intestinal parasites. Areca nut has not been linked to cases of clinically apparent acute liver injury, but epidemiologic studies from Asia have found a strong link between habitual betel nut chewing and oral cancer, and it may also increase the risk of cirrhosis and hepatocellular carcinoma.

Background

Areca nut is not a nut but rather the seed containing fruit of the areca palm (*Areca catechu*), which is found in tropical areas of the Pacific, South Asia and Western Africa, where it is frequently cultivated. Chewing areca nut for its recreational stimulant effect is the most common use of the herb which is also called betel nut chewing for the betel leaves (*Piper betle*) in which the areca nut is wrapped. Chewing areca nut releases a central nervous system stimulant that causes a heightened awareness, increased stamina, euphoria and feeling of well-being. Betel nut chewing is the fourth most common form of substance abuse (after caffeine, alcohol, and nicotine) and is practiced by 10% of the world's population. The active components of areca nut are thought to be the arecal alkaloids, including arecoline, arecaidine, guvacine and guvacolin which have cholinergic (predominantly muscarinic) and other psychoactive properties. Other ingredients include tannins, such as arecatannin and gallic acid, oil gum, and lignin. Habitual betel nut chewing is associated with serious long term health risks including cancer, heart disease and cirrhosis.

In India and China, areca nut extracts have also been used in traditional medicine as treatment of parasitic diseases and to improve digestion, diarrhea, abdominal distension, dyspepsia and jaundice. The only widely accepted medicinal use of *Areca catechu* at present is in veterinary medicine where it is used as a cathartic and treatment for tapeworm in horses, cattle and dogs. Areca nut is considered unsafe for human consumption by the U.S. Food and Drug Administration (FDA), and it is not approved for any medical condition. Nevertheless, areca nut is available over-the-counter in the United States and in Europe, typically in Asian markets in forms that can be used in chewing. *Areca catechu* nut chewing is most common in India, Pakistan, southeast Asia, Micronesia, and western Africa. In these areas, areca catechu nut use disorders are common and are the focus of government and public health efforts to decrease its use. Adverse events associated with use of *Areca catechu* extracts have not been well defined, but chewing betel nut is associated with palpitations, arrhythmias, hypotension, chest pain, dyspnea, tachypnea, acute myocardial infarction, chronic kidney disease, and

nephrolithiasis. Importantly, areca nut has carcinogenic potential in vitro and in vivo, and long term, habitual betel nut chewing has been linked to oral and esophageal cancer. In addition, cross sectional population based and cohort studies have suggested that betel nut chewing is also a risk factor for cirrhosis and hepatocellular carcinoma.

Hepatotoxicity

There have been few studies on the clinical effects and adverse effects of betel nut chewing or of extracts of the areca nut. However, there have been no reports of acute liver injury and marked serum aminotransferase elevations attributed to betel nut chewing or of use of areca nut extracts. On the other hand, several cross sectional epidemiologic studies have linked regular betel nut chewing with a higher prevalence of hepatic cirrhosis and hepatocellular carcinoma. The excess risk of cirrhosis and liver cancer from areca nut use is independent and apparently synergistic with hepatitis B and C virus infection and nonalcoholic fatty liver disease.

Likelihood score for Areca catechu extract use: E (unlikely cause of clinically apparent acute liver injury).

Likelihood score for Areca catechu nut chewing: C (probable cause of increased risk of cirrhosis and hepatocellular carcinoma with habitual use).

Mechanism of Injury

Areca nut has multiple components that might promote carcinogenesis, but the major candidate is the psychoactive areca alkaloids, including arecoline, arecaidine, guavacoline, and guavacine.

Outcome and Management

Acute hepatotoxicity from areca nut has not been described. Habitual use of areca nut chewing should be discouraged, particularly in persons with underlying chronic liver disease, chronic alcohol abuse or fatty liver.

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

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Areca catechu – Generic

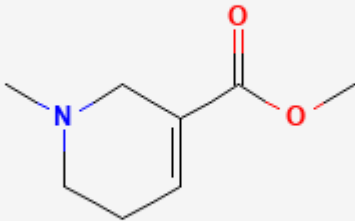
DRUG CLASS

Herbal and Dietary Supplements

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Areca catechu	89957-52-8	Herbal	Not Applicable

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DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Arecoline	63-75-2	C ₈ -H ₁₃ -N-O ₂	

While areca catechu nut has multiple components, its major alkaloid is arecoline which is believed to be the active component responsible for its central nervous system stimulation.

ANNOTATED BIBLIOGRAPHY

References updated: 22 March 2023

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 betel nut or Areca catechu).

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 betel nut chewing or Areca catechu).

Areca catechu. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 19-26.

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

Boucher BJ, Mannan N. Metabolic effects of the consumption of Areca catechu. Addict Biol. 2002;7:103–10. PubMed PMID: 11900629.

(Areca or betel nut chewing is an addictive behavior practiced by at least 10% of the world's population, the active ingredients of Areca catechu being the arecal alkaloids, arecoline, arecaidine, guvacine and guvacoline which have cholinergic and psychoactive properties).

- Tsai JF, Jeng JE, Chuang LY, Ho MS, Ko YC, Lin ZY, Hsieh MY, et al. Habitual betel quid chewing and risk for hepatocellular carcinoma complicating cirrhosis. *Medicine (Baltimore)*. 2004;83:176–187. PubMed PMID: 15118544.
- (In a cross sectional, case control study of 630 Taiwanese adults, a history of habitual betel nut chewing was more frequent among patients with hepatocellular carcinoma [25%] and patients with cirrhosis without cancer [16%], than in healthy controls [5%]).*
- 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 Areca catechu among products associated with 5 or more reports).*
- Wu GH, Boucher BJ, Chiu YH, Liao CS, Chen TH. Impact of chewing betel-nut (*Areca catechu*) on liver cirrhosis and hepatocellular carcinoma: a population-based study from an area with a high prevalence of hepatitis B and C infections. *Public Health Nutr*. 2009;12:129–35. PubMed PMID: 18410705.
- (In a population based study from Taiwan, betel nut chewing was found to be a risk for both cirrhosis and hepatocellular cancer [a 4-5 fold increase in prevalence] which was independent from and synergistic with HCV and HBV infection).*
- Peng W, Liu YJ, Wu N, Sun T, He XY, Gao YX, Wu CJ. *Areca catechu* L. (Arecaceae): a review of its traditional uses, botany, phytochemistry, pharmacology and toxicology. *J Ethnopharmacol*. 2015;164:340–56. PubMed PMID: 25681543.
- (Extracts of Areca catechu have been used in Chinese and Indian traditional medicine for treatment of parasitic disease and to improve digestion, diarrhea, abdominal distension, dyspepsia and jaundice, while also being used as a stimulant (betel nut chewing), the fourth most common agent of abuse worldwide).*
- Liu YJ, Peng W, Hu MB, Xu M, Wu CJ. The pharmacology, toxicology and potential applications of arecoline: a review. *Pharm Biol*. 2016;54:2753–2760. PubMed PMID: 27046150.
- (Review of the pharmacological activities of arecoline including effects on central nervous system, cardiac, digestive and endocrine system).*
- Chou YT, Li CH, Sun ZJ, Shen WC, Yang YC, Lu FH, Chang CJ, Wu JS. A positive relationship between betel nut chewing and significant liver fibrosis in NAFLD subjects, but not in non-NAFLD ones. *Nutrients*. 2021;13:914. PubMed PMID: 33799865.
- (Among 5967 adults undergoing a general medical evaluation and abdominal ultrasound, a history of ongoing or previous areca nut chewing was more frequent among those with fatty liver than those without [7.4% vs 4.2%] and non-invasive measures of fibrosis were higher in those with fatty liver but not among those with a history of areca nut chewing who did not have fatty liver).*
- 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 Areca catechu).*
- 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 mention Areca catechu).*

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 Areca catechu).

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 Areca catechu).

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 none were listed as containing Areca catechu).

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 Areca catechu or betel nut chewing in the compendium of implicated agents).

Osborne PG, Ko YC, Wu MT, Lee CH. Intoxication and substance use disorder to Areca catechu nut containing betel quid: a review of epidemiological evidence, pharmacological basis and social factors influencing quitting strategies. *Drug Alcohol Depend*. 2017;179:187–197. PubMed PMID: 28787696.

(Description and review of Areca catechu nut use disorder which affects an estimated 200 to 400 persons worldwide and is relatively understudied, even though habitual areca nut chewing is a major cause of oral and esophageal carcinoma).

Horenstein NA, Quadri M, Stokes C, Shoaib M, Papke RL. Cracking the betel nut: cholinergic activity of areca alkaloids and related compounds. *Nicotine Tob Res*. 2019;21:805–812. PubMed PMID: 29059390.

(Analysis of the cholinergic activity of the areca alkaloids indicates that while arecoline and guvacoline are both activators of muscarinic acetylcholine receptors, only arecoline has nicotinic acetylcholine receptor activity).

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 cases were attributed to betel nut chewing or Areca catechu).

Tungare S, Myers AL. Retail availability and characteristics of addictive Areca nut products in a US metropolis. *J Psychoactive Drugs*. 2021;53:256–271. PubMed PMID: 33491557.

(Areca nut products were found to be available in all five South-Asian markets visited in Houston, Texas, often not labelled as to contents, concentrations, uses, or potential adverse effects and usually in forms that were meant to be used for betel nut chewing).

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]; areca catechu nut 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 none were attributed to Areca catechu).