AACT Herbal Dietary Supplements SIG Abstracts Sept 2018

1. Yellow Oleander Seed, or "Codo de Fraile" (Thevetia spp.): A Review of Its Potential Toxicity as a Purported Weight-Loss Supplement. González-Stuart A, Rivera JO.

J Diet Suppl. 2018 May 4;15(3):352-364. doi: 10.1080/19390211.2017.1353565. Epub 2017 Sep 28.

The Dietary Supplements and Health Education Act (DSHEA), passed by the United States Congress in October of 1994, defines herbal products as nutritional supplements, not medications. This opened the market for diverse products made from plants, including teas, extracts, essential oils, and syrups. Mexico and the United States share an extensive border, where diverse herbal products are available to the public without a medical prescription. Research undertaken in the neighboring cities of Ciudad Juarez, Mexico, and El Paso, Texas, USA, shows the use of herbs is higher in this border area compared to the rest of the United States. A portion of the population is still under the erroneous impression that "natural" products are completely safe to use and therefore lack side effects. We review the dangers of ingesting the toxic seed of Thevetia spp. (family Apocynaceae), commonly known as "yellow oleander" or "codo de fraile," misleadingly advertised on the Internet as an effective and safe dietary supplement for weight loss. Lack of proper quality control regarding herbs generates a great variability in the quantity and quality of the products' content. Herb-drug interactions occur between some herbal products and certain prescription pharmaceuticals. Certain herbs recently introduced into the U.S. market may not have been previously tested adequately for purity, safety, and efficacy. Due to the lack of reliable clinical data regarding the safe use of various herbal products currently available, the public should be made aware regarding the possible health hazards of using certain herbs for therapeutic purposes. The potentially fatal toxicity of yellow oleander seed is confirmed by cases reported from various countries, while the purported benefits of using it for weight loss have not been evaluated by any known clinical trials. For this reason, the use of yellow oleander seed as a dietary supplement should be avoided.

DOI: 10.1080/19390211.2017.1353565
PMID: 28956681 [Indexed for MEDLINE]

2. Acute toxic leukoencephalopathy associated with a non-prescription weight loss supplement: a report of two cases. Escamilla-Ocañas CE, Cámara-Lemarroy CR, Cantú-Martinez L, Martínez HR.

Neurol Sci. 2017 Dec;38(12):2199-2201. doi: 10.1007/s10072-017-3028-0. Epub 2017 Jun 27.

Weight loss dietary supplements are used with some frequency by an increasingly overweight population. Some products are not adequately regulated and may pose potential health risks. We report two new cases of acute toxic leukoencephalopathy (ATL) due to the use of a supplement marketed as a thermogenic weight loss aid. ATL is a heterogeneous clinic-radiological entity that has been associated with various compounds, such as chemotherapeutic drugs and immunomodulators. It is characterized by an often reversible periventricular and infratentorial demyelination. The commercialization of non-regulated weight loss products continues to be a health risk in our population.

DOI: 10.1007/s10072-017-3028-0
PMID: 28656377 [Indexed for MEDLINE]

3. Potential Influence of Centrally Acting Herbal Drugs on Transporters at the Blood-Cerebrospinal Fluid Barrier and Blood-Brain Barrier. Kibathi LW, Bae S, Penzak SR, Kumar P.

Eur J Drug Metab Pharmacokinet. 2018 Jun 1. doi: 10.1007/s13318-018-0486-6. [Epub ahead of print]

Complementary and alternative medications (CAM) with known or suspected pharmacologic activity in the central nervous system (CNS) are common. These herbal preparations may cause clinically significant drug-drug interactions (DDIs) when coadministered with medications that act in the CNS. This can result in negative outcomes such as toxicity or loss of efficacy. Most drug interaction reports with CAM focus on cytochrome P450 (CYP) modulation. However, drug interactions between CAM and conventional medications may occur via mechanisms other than CYP inhibition or induction; in particular, modulation of

drug transport proteins represents an important mechanism by which such interactions may occur. This article provides an updated review of transporter-mediated mechanisms by which herbal products may theoretically interact with centrally acting medications at the blood-brain barrier and blood-cerebrospinal fluid (CSF) barrier. Further research is required before the true clinical impact of interactions involving modulation of centrally located membrane transporters can be fully understood.

DOI: 10.1007/s13318-018-0486-6
PMID: 29858835

4. Suspected Driving Under the Influence Case Involving Mitragynine. Wright TH.

J Anal Toxicol. 2018 Sep 1;42(7):e65-e68. doi: 10.1093/jat/bky028.

Mitragynine is a novel psychoactive substance (NPS) that has emerged as a designer opioid being distributed on the street. Mitragynine, also known as kratom, has dose-dependent pharmacological effects and possesses both stimulant-like and sedative effects due to dual-binding of α-adrenergic and μ-opioid receptors. This herbal remedy readily available online has caused adverse effects including tachycardia, agitation, tremors, hallucination and death; however, this is the first reported suspected driving under the influence case involving mitragynine. Additional testing outside of the normal routine protocol for suspected impaired driving cases was performed based on the admission of kratom use from the suspect to the drug recognition expert (DRE) officer. Based on the evaluation, the DRE officer concluded that the driver was under the influence of a central nervous system stimulant and cannabis. An alkaline drug screen identified mitragynine in a 37-year-old female driver who was suspected of driving under the influence after nearly striking an oncoming vehicle. A blood amphetamine concentration was quantified at 0.052 mg/L and mitragynine and citalopram were reported qualitatively. The goal of this case study is to provide demographic history, adverse effects and a DRE evaluation in a driver known to have abused mitragynine.

DOI: 10.1093/jat/bky028
PMID: 29718282

5. Natural drugs, not so natural effects: Neonatal abstinence syndrome secondary to 'kratom'. Davidson L, Rawat M, Stojanovski S, Chandrasekharan P.

J Neonatal Perinatal Med. 2018 Aug 22. doi: 10.3233/NPM-1863. [Epub ahead of print]

BACKGROUND: Mitragyna speciosa, also known as kratom, is obtained from the coffee plant family 'Rubiaceae.' Kratom is available in the form of capsules, whole, processed and powdered leaves and as liquids. Secondary to its 'natural herb' status and opioid effects, it is misconceived to be a safe alternative for the treatment of chronic pain. The use of kratom has increased by tenfold in the United States since 2010. METHODS AND RESULTS: We report a term neonate who was born to a chronic kratom user and required treatment with opiates for neonatal drug withdrawal. CONCLUSION: Physicians should be aware of these herbal supplements and its potential withdrawal effects in newborn which cannot be picked up by the standard toxicology screen.

DOI: 10.3233/NPM-1863
PMID: 30149482

6. Kratom: a dangerous player in the opioid crisis. Tayabali K, Bolzon C, Foster P, Patel J, Kalim MO.

J Community Hosp Intern Med Perspect. 2018 Jun 12;8(3):107-110. doi 10.1080/20009666.2018.1468693. eCollection 2018.

Kratom use as a herbal supplement is on the rise in the United States, with reported medical outcomes and lethal effects suggesting a public health threat. Even though the Drug Enforcement Administration has included kratom on its drugs of concern list and the FDA has published a press release to identify it as an opioid with a potential for abuse, its therapeutic and side effects are still not well defined in the literature. Here, we present a case of a 32-year-old man witha history of kratom use who became acutely ill with a brief prodromal illness, followed by jaundice and elevated liver enzymes showing a cholestatic picture, and his successful treatment. In this case, we emphasize the need for awareness of kratom exposure as a key

contributor in the expansion of the opioid crisis, with therapeutic benefits earned at the expense of potentially lethal side effects.

DOI: 10.1080/20009666.2018.1468693
PMCID: PMC5998276
PMID: 29915645

7. Histologic Characterization of Kratom Use-Associated Liver Injury. Riverso M, Chang M, Soldevila-Pico C, Lai J, Liu X.

Gastroenterology Res. 2018 Feb;11(1):79-82. doi: 10.14740/gr990e. Epub 2018 Feb 23.

Kratom is an herbal product derived from the leaves of Southeast Asian Mitragyna speciosa trees. It has traditionally been used by indigenous people to relieve fatigue and manage pain, diarrhea, or opioid withdrawal. The use of kratom has become more commonplace in the United States for similar purposes. Only rare reports of kratom liver toxicity exist in the literature but without histologic characterization. Herein, we report one case of kratom use-associated liver toxicity in a 38-year-old patient. The patient complained of dark colored urine and light colored stools after using kratom. He had unremarkable physical examination. Laboratory testing at presentation revealed elevated alanine aminotransferase (389 U/L), aspartate aminotransferase (220 U/L), total bilirubin (5.1 mg/dL), and alkaline phosphatase (304 U/L). There was no serology evidence of viral hepatitis A, B, and C. The acetaminophen level at presentation was below detectable limits. Ultrasound examination of the right upper quadrant revealed normal echogenicity and contour of the liver without bile ductal dilatation or disease of the gallbladder. The patient underwent liver biopsy 4 days after the initial presentation which revealed a pattern of acute cholestatic liver injury including zone 3 hepatocellular and canalicular cholestasis, focal hepatocyte dropout, mild portal inflammation, and bile duct injury. Kratom was stopped, the patient improved clinically and biochemically and was discharged 8 days after the initial presentation. To our best knowledge, this is the first case report detailing the histology of kratom use-associated liver injury.

DOI: 10.14740/gr990e
PMCID: PMC5827910
PMID: 29511414

8. Herbal assault: liver toxicity of herbal and dietary supplements.

Lancet Gastroenterol Hepatol. 2018 Mar;3(3):141. doi:10.1016/S2468-1253(18)30011-6.

DOI: 10.1016/S2468-1253(18)30011-6
PMID: 29870727

9. Hepatotoxicity of Herbal Supplements Mediated by Modulation of Cytochrome P450. Brewer CT, Chen T.

Int J Mol Sci. 2017 Nov 8;18(11). pii: E2353. doi: 10.3390/ijms18112353.

Herbal supplements are a significant source of drug-drug interactions (DDIs), herb-drug interactions, and hepatotoxicity. Cytochrome P450 (CYP450) enzymes metabolize a large number of FDA-approved pharmaceuticals and herbal supplements. This metabolism of pharmaceuticals and supplements can be augmented by concomitant use of either pharmaceuticals or supplements. The xenobiotic receptors constitutive androstane receptor (CAR) and the pregnane X receptor (PXR) can respond to xenobiotics by increasing the expression of a large number of genes that are involved in the metabolism of xenobiotics, including CYP450s. Conversely, but not exclusively, many xenobiotics can inhibit the activity of CYP450s. Induction of the expression or inhibition of the activity of CYP450s can result in DDIs and toxicity. Currently, the United States (US) Food and Drug Administration does not require the investigation of the interactions of herbal supplements and CYP450s. This review provides a summary of herbal supplements that inhibit CYP450s, induce the expression of CYP450s, and/or whose toxicity is mediated by CYP450s.

DOI: 10.3390/ijms18112353
PMCID: PMC5713322
PMID: 29117101 [Indexed for MEDLINE]

10. The diagnosis and management of idiosyncratic drug-induced liver injury. Hassan A, Fontana RJ.

Liver Int. 2018 Jul 13. doi: 10.1111/liv.13931. [Epub ahead of print]

Drug-induced liver injury (DILI) is an uncommon but important cause of liver disease that can arise after exposure to a multitude of drugs and herbal and dietary supplements. The severity of idiosyncratic DILI varies from mild serum aminotransferase elevations to the development of severe liver injury that can progress to acute liver failure resulting in death or liver transplantation within days of DILI onset. Chronic liver injury that persists for more than 6 months after DILI onset is also becoming increasingly recognized in up to 20% of DILI patients. Host demographic (age, gender, race), clinical and laboratory features at DILI onset have been associated with the severity and outcome of liver injury in DILI patients. In addition to cessation of the suspect drug, other medical interventions including the use of N-acetylcysteine and corticosteroids in selected patients have shown some clinical benefit, but additional prospective studies are needed. A number of promising diagnostic, prognostic and mechanistic serum and genetic biomarkers may help improve our understanding of the pathogenesis and treatment of idiosyncratic DILI.

DOI: 10.1111/liv.13931
PMID: 30003672

11. Botanicals and Hepatotoxicity. Roytman MM, Poerzgen P, Navarro V.

Clin Pharmacol Ther. 2018 Sep;104(3):458-469. doi: 10.1002/cpt.1097. Epub 2018 Jun 19.

The use of botanicals, often in the form of multi-ingredient herbal dietary supplements (HDS), has grown tremendously in the past three decades despite their unproven efficacy. This is paralleled by an increase in dietary supplement-related health complications, notably hepatotoxicity. This article reviews the demographics and motivations of dietary supplement (DS) consumers and
the regulatory framework for DS in the US and other developed countries. It examines in detail three groups of multi-ingredient HDS associated with hepatotoxicity: OxyElite Pro (two formulations), green tea extract-based DS, and "designer anabolic steroids." These examples illustrate the difficulties in identifying and adjudicating causality of suspect compound(s) of multi-ingredient HDS-associated liver injury in the clinical setting. The article outlines future directions for further study of HDS-associated hepatotoxicity as well as measures to safeguard the consumer against it.

DOI: 10.1002/cpt.1097
PMID: 29920648

12. Herbal and Dietary Supplement-Induced Liver Injuries in the Spanish DILI Registry. Medina-Caliz I, Garcia-Cortes M, Gonzalez-Jimenez A, Cabello MR, Robles-Diaz M, Sanabria-Cabrera J, Sanjuan-Jimenez R, Ortega-Alonso A, García-Muñoz B, Moreno I, Jimenez-Perez M, Fernandez MC, Ginés P, Prieto M, Conde I, Hallal H, Soriano G, Roman E, Castiella A, Blanco-Reina E, Montes MR, Quiros-Cano M, Martin-Reyes F, Lucena MI, Andrade RJ; Spanish DILI Registry.

Clin Gastroenterol Hepatol. 2018 Sep;16(9):1495-1502. doi: 10.1016/j.cgh.2017.12.051. Epub 2018 Jan 4.

BACKGROUND & AIMS: There have been increasing reports of liver injury associated with use of herbal and dietary supplements, likely due to easy access to these products and beliefs among consumers that they are safer or more effective than conventional medications. We aimed to evaluate clinical features and outcomes of patients with herbal and dietary supplement-induced liver injuries included in the Spanish DILI Registry. METHODS: We collected and analyzed data on demographic and clinical features, along with biochemical parameters, of 32 patients with herbal and dietary supplement-associated liver injury reported to the Spanish DILI registry from 1994 through 2016. We used analysis of variance to compare these data with those from cases of liver injury induced by conventional drugs or anabolic androgenic steroid-containing products. RESULTS: Herbal and dietary supplements were responsible for 4% (32 cases) of the 856 DILI cases in the registry; 20 cases of DILI (2%) were caused by anabolic androgenic steroids. Patients with herbal and dietary supplement-induced liver injury were a mean age of 48 years and 63% were female; they presented a mean level of alanine aminotransferase 37-fold the upper limit of normal, 28% had hypersensitivity features, and 78% had jaundice. Herbal and dietary supplement-induced liver injury progressed to acute liver failure in 6% of patients, compared with none of the cases of anabolic androgenic

steroid-induced injury and 4% of cases of conventional drugs. Liver injury after repeat exposure to the same product that caused the first DILI episode occurred in 9% of patients with herbal and dietary supplement-induced liver injury vs none of the patients with anabolic androgenic steroid-induced injury and 6% of patients with liver injury from conventional drugs. CONCLUSION: In an analysis of cases of herbal and dietary supplement-induced liver injury in Spain, we found cases to be more frequent among young women than older patients or men, and to associate with hepatocellular injury and high levels of transaminases. Herbal and dietary supplement-induced liver injury is more severe than other types of DILI and re-exposure is more likely. Increasing awareness of the hepatoxic effects of herbal and dietary supplements could help physicians make earlier diagnoses and reduce the risk of serious liver damage.

DOI: 10.1016/j.cgh.2017.12.051
PMID: 29307848

13. Acute liver injury following Garcinia cambogia weight-loss supplementation: case series and literature review. Crescioli G, Lombardi N, Bettiol A, Marconi E, Risaliti F, Bertoni M, Menniti Ippolito F, Maggini V, Gallo E, Firenzuoli F, Vannacci A.

Intern Emerg Med. 2018 Sep;13(6):857-872. doi: 10.1007/s11739-018-1880-4. Epub 2018 May 25.

Herbal weight-loss supplements are sold as self-medication products, and are often used under the misconception that their natural origin guarantees their safety. Food supplements are not required to provide any benefit/risk profile evaluation before marketing; however, possible risks associated with use of herbal extracts in food supplements are becoming more and more documented in the literature. Some herbs are listed as the leading cause of herb-induced liver injury, with a severe or potentially lethal clinical course, and unpredictable herb-drug interactions. Garcinia cambogia (GC) extract and GC-containing products are some of the most popular dietary supplements currently marketed for weight loss. Here, we present four cases of acute liver failure in women taking GC extract for weight loss, and a literature review of clinical evidences about hepatic toxicity in patients taking dietary supplements containing GC extract.

DOI: 10.1007/s11739-018-1880-4
PMID: 29802521

14. Hepatotoxicity Associated with Use of the Weight Loss Supplement Garcinia cambogia: A Case Report and Review of the Literature. Kothadia JP, Kaminski M, Samant H, Olivera-Martinez M.

Case Reports Hepatol. 2018 Mar 12;2018:6483605. doi: 10.1155/2018/6483605. eCollection 2018.

The use of herbal and dietary supplements for weight loss is becoming increasingly common as obesity is becoming major health problem in the United States. Despite the popularity of these natural supplements, there are no guidelines for their therapeutic doses and their safety is always a concern. Garcinia cambogia extract with its active ingredient "hydroxycitric acid" is a component of many weight loss regimens. It suppresses fatty acid biosynthesis and decreases appetite. However, its prolonged use in weight maintenance is unknown. Here we describe a case of acute hepatitis after the use of Garcinia cambogia for weight loss.

DOI: 10.1155/2018/6483605
PMCID: PMC5867608
PMID: 29721342

15. Acute Hepatitis due to Garcinia Cambogia Extract, an Herbal Weight Loss Supplement. Sharma A, Akagi E, Njie A, Goyal S, Arsene C, Krishnamoorthy G, Ehrinpreis M.

Case Rep Gastrointest Med. 2018 Jul 26;2018:9606171. doi: 10.1155/2018/9606171. eCollection 2018.

The Drug Induced Liver Injury Network reports dietary supplements as one of the most important causes of drug induced hepatotoxicity, yet millions of people use these supplements without being aware of their potential life-threatening side effects. Garcinia cambogia (GC) extract is an herbal weight loss supplement, reported to cause fulminant hepatic failure. We present a case of a 57-year-old female with no previous history of liver disease, who presented with acute hepatitis due to GC extract taken for weight loss, which resolved after stopping it and got reaggravated on retaking it. Obtaining a history of herbal supplement use is critical in the evaluation of acute hepatitis.

DOI: 10.1155/2018/9606171
PMCID: PMC6083529
PMID: 30147968

16. A Case of Acute Severe Hepatotoxicity and Mild Constriction of Common Bile Duct Associated With Ingestion of Green Tea Extract: A Clinical Challenge. Surapaneni BK, Le M, Jakobovits J, Vinayek R, Dutta S.

Clin Med Insights Gastroenterol. 2018 Jun 5;11:1179552218779970. doi: 10.1177/1179552218779970. eCollection 2018.

Consumption of herbal and dietary supplements (HDS) has increased worldwide as potential treatment for weight reduction and metabolic enhancement. However, it has been reported that HDS can cause liver injury which accounts for 20% of hepatotoxicity in the United States. Prevention of HDS induced liver injury remains a challenge due to difficulties in identifying the hepatotoxins in these preparations and lack of federal regulations for dietary supplements. We report a case of acute severe hepatic necrosis presumably due to consumption of nutritional supplement advertised to boost vitality and stem cells in human body.

DOI: 10.1177/1179552218779970
PMCID: PMC6058416
PMID: 30057447

17. Clinicopathological features of He Shou Wu-induced liver injury: This ancient anti-aging therapy is not liver-friendly. Wang Y, Wang L, Saxena R, Wee A, Yang R, Tian Q, Zhang J, Zhao X, Jia J.

Liver Int. 2018 Aug 1. doi: 10.1111/liv.13939. [Epub ahead of print]

BACKGROUND & AIMS: Polygonum Multiflorum Thumb (PMT), an ancient anti-aging Chinese herb known traditionally as He Shou Wu, has side effects of liver toxicity. To determine the main clinical and pathological characteristics of liver toxicity induced by PMT and the clinical course after its cessation. METHODS: Data of patients, diagnosed as drug-induced liver injury and hospitalised in Beijing Friendship Hospital from August 2005 to August 2017, were retrospectively reviewed. Clinical, pathological data and outcome after cessation of He Shou Wu were obtained and analysed. Kruskal-Wallis and Chi-square ($\chi 2$) tests were performed. RESULTS: Twenty-nine patients with He Shou Wu-induced liver injury were enrolled. The median age was 53 years (range 15-74) and 75.9% (22/29) were women. The most common symptom was jaundice (79.3%, 23/29). Of nine patients with liver biopsies, six showed acute cholestatic hepatitis, two acute, and one chronic hepatocellular injury pattern. The latency, liver chemistries and outcomes were comparable between pure He Shou Wu (5 patients) and its compounds (24 patients). Twenty-five of 29 patients (86.2%) had normal serum alanine aminotransferase levels after 45 days (range: 10-138 days) and total bilirubin of 46 days (range: 0-551 days). One patient was rechallenged with He Shou Wu and two developed autoimmune features. One patient died of liver failure and three had chronic persistent liver injury. CONCLUSIONS: The main clinicopathological injury pattern of He Shou Wu-induced liver injury is moderate to severe hepatitis with or without cholestasis. Most patients recover completely; however, chronic disease and death do occur.

DOI: 10.1111/liv.13939
PMID: 30066422

18. Acute Liver Failure Induced by Carthamus tinctorius Oil: Case Reports and Literature Review. de Ataide EC, Reges Perales S, de Oliveira Peres MA, Bastos Eloy da Costa L, Quarella F, Valerini FG, Chueiri Neto F, Silveira Bello Stucchi R, de Fátima Santana Ferreira Boin I.

Transplant Proc. 2018 Mar;50(2):476-477. doi: 10.1016/j.transproceed.2018.01.010.

BACKGROUND: Acute liver failure (ALF) is a clinical syndrome that results from the abrupt loss of liver function in a patient without previous liver disease. The most frequent causes are viral hepatitis, drug induced, and autoimmune disease, but in 20% of cases no cause is identified. Carthamus tinctorius (safflower) oil is used as a dietary supplement for weight loss and antioxidant. There are 4 cases described in the literature of ALF induced by the use of this substance. The objective of this study was to report 3 cases of

ALF treated at the Clinical Hospital of the State University of Campinas that suggest the use of C tinctorius oil as a probable etiologic factor. CASE REPORTS: The 3 patients had a diagnosis of ALF according to the King's College criteria. All had a history of ingestion of this oil for weight loss. During etiologic evaluation, viral hepatitis, autoimmune diseases, or any other drug cause were excluded, thus pointing to C tinctorius oil as the triggering factor. All 3 patients underwent liver transplantation: 2 had good postoperative evolution, and 1 died 12 days after the procedure. CONCLUSIONS: Two cases are described in which the hepatic insufficiency induced by C tinctorius oil was successfully treated through liver transplantation. This highlights the risk of misuse of this substance for weight loss.

DOI: 10.1016/j.transproceed.2018.01.010
PMID: 29579831 [Indexed for MEDLINE]

19. Yogi Detox Tea: A Potential Cause of Acute Liver Failure. Kesavarapu K, Kang M, Shin JJ, Rothstein K.

Case Rep Gastrointest Med. 2017;2017:3540756. doi: 10.1155/2017/3540756. Epub 2017 Oct 24.

We present a case of acute fulminant liver failure from a liver detoxification tea. We present a 60-year-old female with weakness, lethargy, scleral icterus, jaundice, and worsening mental status. She drank herbal tea three times a day for 14 days prior to symptom development. Liver tests were elevated. Remaining laboratory tests and imaging were negative for other etiologies. An ultrasound-guided liver biopsy showed submassive necrosis. A literature search on the ingredients shows six ingredients as having hepatotoxic effects and remaining ingredients as having very sparse hepatoprotective data. Healthcare professionals should discuss herbal medication and tea use and report adverse effects.

DOI: 10.1155/2017/3540756
PMCID: PMC5674495
PMID: 29204300

20. Hepatic veno-occlusive disease related to Gynura segetum: A case report. Sun Z, Kang J, Zhang Y. Medicine (Baltimore). 2018 Apr;97(17):e0552. doi: 10.1097/MD.0000000000010552.

INTRODUCTION: Hepatic veno-occlusive disease (HVOD), as known as hepatic sinusoidal obstruction syndrome (HSOS), is an obliterative venulitis of the terminal hepatic venules, which is responsible for considerable mortality. The potential mechanism is destruction of hepatic sinusoidal endothelial cells (SEC), with sloughing and downstream occlusion of terminal hepatic venules. Here, we report a case of HVOD who have a history of ingestion of Gynura segetum for 1 month. The patient presents for abdominal pain and distension. He was diagnosed for HVOD using computerized tomography (CT) and ultrasonography of liver. And then best supportive care was added. However, without liver transplantation for financial reason, he died in 1 month after discharged from hospital. CONCLUSIONS: We think portal flow reversal was a characteristic imaging findings of HVOD, which can be listed as a specific diagnostic criterion of HVOD. Once the condition was worsening, liver transplantation should be considered as the first choice of treatment planning.

DOI: 10.1097/MD.0000000000010552
PMCID: PMC5944499
PMID: 29703039 [Indexed for MEDLINE]

21. The stimulant higenamine in weight loss and sports supplements. Cohen PA, Travis JC, Keizers PHJ, Boyer FE, Venhuis BJ.

Clin Toxicol (Phila). 2018 Sep 6:1-6. doi: 10.1080/15563650.2018.1497171. [Epub ahead of print]

BACKGROUND: Higenamine is a stimulant with cardiovascular properties recently prohibited in sport by the World Anti-Doping Agency (WADA). Higenamine is also a natural constituent of several traditional botanical remedies and is listed as an ingredient in weight loss and sports supplements sold over-the-counter in the United States. OBJECTIVES: We analyzed dietary supplements available for sale in the United States prior to WADA's prohibition of higenamine in sport for the presence and quantity of higenamine. METHODS: All supplements labeled as containing higenamine or a synonym (i.e., norcoclaurine or

demethylcoclaurine) available for sale in the United States were identified. For each brand, one sample was analyzed by NSF International (Ann Arbor, MI) and one sample by the Netherland's National Institute for Public Health and the Environment (RIVM). NSF International carried out qualitative and quantitative analyses using ultra high performance liquid chromatography (UHPLC) with tandem mass spectrometry. RIVM carried out qualitative analysis using UHPLC quadrupole time of flight mass spectrometry for an independent confirmation of identity. RESULTS: Twenty-four products were analyzed. The majority of supplements were marketed as either weight loss (11/24; 46%) or sports/energy supplements (11/24; 46%); two brands did not list a labeled indication. The quantity of higenamine (±95% CI) ranged from trace amounts to 62 ± 6.0 mg per serving. Consumers could be exposed to up to 110 ± 11 mg of higenamine per day when following recommended serving sizes provided on the label. Five products (5/24; 21%) listed an amount of higenamine, but none were accurately labeled; the quantity in these supplements ranged from <0.01% to 200% of the quantity listed on the label. CONCLUSION: Dosages of up to 62 ± 6.0 mg per serving of the stimulant higenamine were found in dietary supplements sold in the United States.

DOI: 10.1080/15563650.2018.1497171
PMID: 30188222

22. Fatal poisoning by ingestion of Taxus Baccata leaves. Pilija V, Djurendic-Brenesel M, Miletic S.

Forensic Sci Int. 2018 Sep;290:e1-e4. doi: 10.1016/j.forsciint.2018.07.017. Epub 2018 Jul 24.

In this report we describe a first suicide case in Serbia related to ingestion of Taxus baccata leaves. A 30-year old woman was found dead, and the green plant material in a plastic bag was found near her bed. Autopsy revealed dark green needle-like leaves in the stomach, similar to that contained in the plastic bag, and both were botanically identified as Taxus baccata, also known as yew. Using gas chromatography-mass spectrometry (GC-MS), 3,5-dimethoxyphenol (3,5-DMP) as toxicological evidence for the ingestion of yew leaves, was detected in biological samples. As the autopsy showed unspecific findings, and also the routine toxicological examination, based upon 3,5-DMP identification, the cause of death was determined to be suicide, caused by yew poisoning.

DOI: 10.1016/j.forsciint.2018.07.017
PMID: 30064830

23. Identification and Quantification of Thujone in a Case of Poisoning Due to Repeated Ingestion of an Infusion of Artemisia Vulgaris L. Di Lorenzo C, Ferretti F, Moro E, Ceschi A, Colombo F, Frigerio G, Lüde S, Restani P.

J Food Sci. 2018 Aug;83(8):2257-2264. doi: 10.1111/1750-3841.14273. Epub 2018 Jul 25.

Plants of the Artemisia genus are used worldwide as ingredients of botanical preparations. This paper describes the case of a 49-year-old man admitted to the emergency room at a Zurich hospital in a manic state after the ingestion of 1 L of an infusion of Artemisia vulgaris. Two monoterpenic ketones, α- and β-thujone, are present in various concentrations in Artemisia spp., but adverse effects have previously been associated only with essential oil from Artemisia absinthium and attributed to the inhibition of gamma-aminobutyric acid receptors, with consequent excitation and convulsions. The aim of this work was to examine and quantify the possible presence of thujone in the patient's serum and urine. A High Performance Liquid Chromatography (HPLC) method with isocratic separation and fluorescence detection (FLD) was set up and validated. Serum thujone concentrations were found to be 27.7 ± 3.48 μg/mL at day 0 and 24.1 ± 0.15 μg/mL on day 1. Results were confirmed by a gas chromatography with flame ionization detection (FID). Poisoning due to thujone was thus confirmed, suggesting four possible scenarios: (1) an unusually high concentration of thujone in the A. vulgaris ingested; (2) chronic exposure as the cause of the poisoning; (3) low metabolic efficiency of the patient; (4) contamination or adulteration of the plant material with other Artemisia spp., for example, A. absinthium.PRACTICAL APPLICATION: These results could aid research in the field of adverse effects of botanicals, lead to better understanding and management of similar cases of poisoning, and promote more informed use of natural products.

DOI: 10.1111/1750-3841.14273
PMID: 30044501

24. Acute-on-chronic subdural hematoma in a patient taking Red Clover herbal supplement: A case report. Hall S, Walshe E, Ajayi C, Boyle K, Griffith C.

Surg Neurol Int. 2018 Feb 21;9:43. doi: 10.4103/sni.sni_174_17. eCollection 2018.

Background: Herbal supplements are commonly used, however, their side-effect profiles are poorly understood and not subject to the same scrutiny as prescribed medications. Some herbal supplements such as St Johns' Wort are accepted to interfere with clotting pathways, however others, including Red Clover have theoretical bleeding risks based on coumarin content with very little underlying evidence. Case Description: This case reports a 65-year-old woman who suffered a spontaneous acute-on-chronic subdural hemorrhage with a significant postoperative re-hemorrhage. She had no other risk factors for coagulopathy other than a history of taking Red Clover supplements for postmenopausal symptoms. Her normal INR combined with an intraoperative thromboelastogram confirmed a coagulopathy which was more consistent with anti-platelet effects than coumarin toxicity. After tranexamic acid and platelet transfusions she had no further bleeding and made an uneventful recovery. Conclusion: This case highlights another risk factor for intracranial hemorrhage and the importance of a thorough drug history. The mechanism of Red Clover induced coagulopathy appears to be mediated through anti-platelet actions, which is consistent with in-vitro evidence reporting its role in preventing platelet adhesion.

DOI: 10.4103/sni.sni_174_17
PMCID: PMC5843970
PMID: 29541484

25. Rare cause of isolated severe coagulation failure in cirrhosis: traditional healing with fenugreek. Philips CA, Augustine P.

BMJ Case Rep. 2018 Jan 12;2018. pii: bcr-2017-223479. doi:10.1136/bcr-2017-223479.

Patients with cirrhosis develop decompensation events during the natural history of the disease that encompass ascites, variceal bleeding, hepatic encephalopathy and jaundice. Coagulation failure, defined using the international normalised ratio, even though not a decompensation event, is important in patients with stratifying cirrhosis into those who require liver transplantation for long-term survival. Isolated coagulation failure in cirrhosis is rare and usually occurs with use of anticoagulants in the setting of vascular diseases. We reported the case of a patient with compensated cirrhosis in whom, isolated severe coagulation failure was found to be due to excessive use of fenugreek milk porridge as part of traditional healing. The coagulation failure was promptly reversed with avoidance of fenugreek and supplementation with vitamin K.

DOI: 10.1136/bcr-2017-223479
PMID: 29330279 [Indexed for MEDLINE]

26. Nephrotoxicity and Chinese Herbal Medicine. Yang B, Xie Y, Guo M, Rosner MH, Yang H, Ronco C. Clin J Am Soc Nephrol. 2018 Apr 3. pii: CJN.11571017. doi: 10.2215/CJN.11571017. [Epub ahead of print]

Chinese herbal medicine has been practiced for the prevention, treatment, and cure of diseases for thousands of years. Herbal medicine involves the use of natural compounds, which have relatively complex active ingredients with varying degrees of side effects. Some of these herbal medicines are known to cause nephrotoxicity, which can be overlooked by physicians and patients due to the belief that herbal medications are innocuous. Some of the nephrotoxic components from herbs are aristolochic acids and other plant alkaloids. In addition, anthraquinones, flavonoids, and glycosides from herbs also are known to cause kidney toxicity. The kidney manifestations of nephrotoxicity associated with herbal medicine include acute kidney injury, CKD, nephrolithiasis, rhabdomyolysis, Fanconi syndrome, and urothelial carcinoma. Several factors contribute to the nephrotoxicity of herbal medicines, including the intrinsic toxicity of herbs, incorrect processing or storage, adulteration, contamination by heavy metals, incorrect dosing, and interactions between herbal medicines and medications. The exact incidence of kidney injury due to nephrotoxic herbal medicine is not known. However, clinicians should consider herbal medicine use in patients with unexplained AKI or progressive CKD. In addition, exposure to herbal medicine containing aristolochic acid may increase risk for future uroepithelial cancers, and patients require appropriate postexposure screening.

DOI: 10.2215/CJN.11571017
PMID: 29615394

27. Update of aristolochic acid nephropathy in Korea. Ban TH, Min JW, Seo C, Kim DR, Lee YH, Chung BH, Jeong KH, Lee JW, Kim BS, Lee SH, Choi BS, Han JS, Yang CW.

Korean J Intern Med. 2018 Sep;33(5):961-969. doi: 10.3904/kjim.2016.288. Epub 2018 Mar 20.

BACKGROUND/AIMS: The true incidence of aristolochic acid nephropathy (AAN) is thought to be underestimated because numerous ingredients known or suspected to contain aristolochic acid (AA) are used in traditional medicine in Korea. METHODS: We collected data on cases of AAN since 1996 via a database in Korea. We evaluated the year of AAN development, route to obtaining AA-containing herbal medicine, gender, reason for taking AA-containing herbal medicine, clinical manifestations, histological findings, phytochemical analysis, and prognosis of patients with AAN. RESULTS: Data on 16 cases of AAN were collected. Thirteen cases developed AAN before and three cases after the prohibition of AA-containing herbal medicine by the Korea Food and Drug Administration. Patients were prescribed AA-containing herbal medicine from oriental clinics or had purchased it from traditional markets. AAN was distributed in all age groups. Young females were most commonly exposed to AA-containing herbal medicine for slimming purposes and postpartum health promotion, while older adults took AA-containing compounds for the treatment of chronic diseases. The most common symptoms presented at hospitalization were nausea and vomiting, and acute kidney injury was accompanied by Fanconi syndrome in almost half of the patients. Phytochemical analysis of AA in herbal medicine was available in six cases. Progression to end stage renal disease (ESRD) was observed in seven patients (43.8%), and five patients (31.3%) had progressed to ESRD within 6 months of diagnosis.CONCLUSION: Our report shows that patients were still exposed to AA-containing herbal medicine and that there is a possibility of underdiagnosis of AAN in Korea. A stronger national supervision system of herbal ingredients and remedies in oriental medicine is needed to prevent AAN.

DOI: 10.3904/kjim.2016.288
PMID: 29551056

28. Acute Interstitial Nephritis Induced by Citrullus Colocynthis. Savaj S, Ghaffari M, Abbasi MA, Azar J.

Iran J Kidney Dis. 2017 Oct;11(5):385-387.

Acute interstitial nephritis (AIN) is known as a common cause of acute kidney injury, found in 15% to 27% of kidney biopsies. Drug-induced AIN is currently the most common cause of AIN. The most common medications causing AIN are antibiotics and nonsteroidal anti-inflammatory drugs. We describe a case of Citrullus colocynthis (herbal remedy for diabetes mellitus and weight reduction) that induced AIN. A 31-year-old woman with major thalassemia, diabetes mellitus, and hepatitis C infection was admitted because of flank pain and unexpected increase in serum creatinine level. She had been using Citrullus colocynthis for 3 months. Kidney biopsy results suggested AIN. She did not respond to steroid therapy and underwent hemodialysis. We suggest the use of Citrullus colocynthis as a herbal medicine with extreme caution.

PMID: 29038395 [Indexed for MEDLINE]

29. "Green Medicine": The Past, Present, and Future of Botanicals. Paine MF, Roe AL.

Clin Pharmacol Ther. 2018 Sep;104(3):410-415. doi: 10.1002/cpt.1168.

Botanicals are plant-derived products that have been consumed by humans for centuries. Today, the marketing and use of botanicals for health and wellness benefits continues to thrive worldwide, with consumers projected to spend more than $140 billion globally by 2024 (Global Analysis, Inc). However, research on the quality and safety of these products has lagged behind sales. Because of this divergence, opportunities abound for collaborations amongst scientists from industry, academia, and government to address these unmet public health needs. Clinical pharmacologists and toxicologists from all of these sectors play critical roles in developing harmonized approaches to achieve the common goal of ensuring botanical products with superior quality and safety.

DOI: 10.1002/cpt.1168
PMID: 30151884

30. Ayurveda metallic-mineral 'Bhasma'-associated severe liver injury. Philips CA, Paramaguru R, Augustine P.

BMJ Case Rep. 2018 Jun 29;2018. pii: bcr-2018-225590. doi: 10.1136/bcr-2018-225590.

Ayurveda Bhasma is a metallic-mineral preparation homogenised with herbal juices or decoctions and modified with heat treatment to apparently detoxify the heavy metals. It is widely recommended for the treatment of many disease conditions by practitioners of complementary and alternative medicine in the absence of good quality clinical trial evidence on its safety and efficacy. Heavy metal-induced liver injury is widely reported in the literature, and heavy metal adulteration of non-Bhasma-related Ayurveda and herbal products has been well described. We report a patient who developed severe liver injury requiring listing for liver transplantation for improved survival, after consumption of Bhasma for dyspepsia. This case describes the first documented case and toxicology analysis of Ayurveda Bhasma associated with severe drug-induced liver injury. Physicians must be alert regarding patient's use of supposedly safe Ayurveda Bhasma that may promote acute severe liver injury in the absence of other known aetiologies.

DOI: 10.1136/bcr-2018-225590
PMID: 29960971

31. Speciation and bioaccessibility of arsenic in traditional Chinese medicines and assessment of its potential health risk. Liu L, Zhang Y, Yun Z, He B, Zhang Q, Hu L, Jiang G.

Sci Total Environ. 2018 Apr 1;619-620:1088-1097. doi: 10.1016/j.scitotenv.2017.11.113. Epub 2017 Nov 29.

Arsenic in traditional Chinese medicines (TCMs) has caused public concerns about its health risk in recent years due to the high toxicity of arsenic and widespread use of those medicines throughout the world. However, in previous studies the arsenic toxicity was usually overestimated by considering the total arsenic concentration only. This work investigated the total concentration, speciation and bioaccessibility of arsenic in 84 commonly used traditional Chinese patent medicines (CPMs) and Chinese herbal medicines (CHMs) to evaluate arsenic's potential health risks to human. Arsenic was found in all the CPMs and 88% of CHMs at concentrations ranging from 0.033 to 91,000mgkg-1 and 0.012 to 6.6mgkg-1, respectively. The bioaccessibility of arsenic varied significantly and was in the range of 0.21%-90% in the CPMs and 15%-96% in the CHMs, with inorganic arsenic as the predominant species. The average daily intake dose (ADD) and hazard quotient (HQ) of arsenic in most of medicines were within the safe limits, while in certain medicines, they exceeded the safe threshold level. These excesses remind us that the potential health risk by consumption of several medicines may not be negligible and more control and monitoring of arsenic in medicines should be carried out.

DOI: 10.1016/j.scitotenv.2017.11.113
PMID: 29734587 [Indexed for MEDLINE]