AACT Herbal Dietary Supplement Section Abstracts May 2024

1. **Paramo root oil: a novel culprit in salicylate poisoning.** Chakar B, Banir S, Dane C, Proschogo N, Dawson A.

   Clinical Toxicology, 62:3, 202-203, DOI: 10.1080/15563650.2024.2329347

   (Letter)

2. **Clostridium butyricum Bacteremia Associated with Probiotic Use, Japan.** Sada RM, Matsuo H, Motooka D, Kutsuna S, Hamaguchi S, Yamamoto G, Ueda A.

   Emerg Infect Dis. 2024 Apr;30(4):665-671. doi: 10.3201/eid3004.231633. Epub 2024 Feb 27.

   Clostridium butyricum, a probiotic commonly prescribed in Asia, most notably as MIYA-BM (Miyarisan Pharmaceutical Co., Ltd.; https://www.miyarisan.com), occasionally leads to bacteremia. The prevalence and characteristics of C. butyricum bacteremia and its bacteriologic and genetic underpinnings remain unknown. We retrospectively investigated patients admitted to Osaka University Hospital during September 2011-February 2023. Whole-genome sequencing revealed 5 (0.08%) cases of C. butyricum bacteremia among 6,576 case-patients who had blood cultures positive for any bacteria. Four patients consumed MIYA-BM, and 1 patient consumed a different C. butyricum-containing probiotic. Most patients had compromised immune systems, and common symptoms included fever and abdominal distress. One patient died of nonocclusive mesenteric ischemia. Sequencing results confirmed that all identified C. butyricum bacteremia strains were probiotic derivatives. Our findings underscore the risk for bacteremia resulting from probiotic use, especially in hospitalized patients, necessitating judicious prescription practices.

   DOI: 10.3201/eid3004.231633
   PMCID: PMC10977840
   PMID: 38413242

3. **A Yellow Flower With Jaundice Power: Liver Injury Attributed to Greater Celandine.** Power S, Barritt AS

   ACG Case Rep J. 2024 Apr 26;11(5):e01347. doi: 10.14309/crj.0000000000001347. eCollection 2024 May.

   Greater celandine (Chelidonium majus) leaf extracts have been used for centuries as a natural remedy for various gastrointestinal symptoms. Greater celandine is associated with several case reports of hepatotoxicity, mainly from Europe. No cases from the United States have been identified. We present a case of acute hepatitis from greater celandine in the United States in a 72-year-old man taking this herbal supplement for nausea. In patients presenting with acute liver injury, gastroenterologists should be aware of this herb and reminded to

assess for herbal and dietary supplement hepatotoxicity, especially in those remedies used to treat common gastrointestinal symptoms.

DOI: 10.14309/crj.0000000000001347
PMCID: PMC11049761
PMID: 3868207

4. **Catharanthus roseus intoxication mimicking acute cholangitis.** Chuah YY, Lee YY, Chou CK, Chang LJ.

BMC Complement Med Ther. 2024 Apr 4;24(1):139. doi: 10.1186/s12906-024-04441-1.

BACKGROUND: Catharanthus roseus, a Madagascar native flowering plant, is known for its glossy leaves and vibrant flowers, and its medicinal significance due to its alkaloid compounds. As a source of vinblastine and vincristine used in chemotherapy, Catharanthus roseus is also employed in traditional medicine with its flower and stalks in dried form. Its toxicity can lead to various adverse effects. We report a case of Catharanthus roseus juice toxicity presenting as acute cholangitis, emphasizing the importance of healthcare providers obtaining detailed herbal supplement histories.
CASE PRESENTATION: A 65-year-old woman presented with abdominal pain, fever, anorexia, and lower limb numbness. Initial diagnosis of acute cholangitis was considered, but imaging excluded common bile duct stones. Further investigation revealed a history of ingesting Catharanthus roseus juice for neck pain. Laboratory findings showed leukocytosis, elevated liver enzymes, and hyperbilirubinemia. The patient developed gastric ulcers, possibly due to alkaloids in Catharanthus roseus. No bacterial growth was noted in blood cultures. The patient recovered after discontinuing the herbal extract.
CONCLUSIONS: Catharanthus roseus toxicity can manifest as fever, hepatotoxicity with cholestatic jaundice, and gastric ulcers, mimicking acute cholangitis. Awareness of herbal supplement use and potential toxicities is crucial for healthcare providers to ensure prompt diagnosis and appropriate management. This case emphasizes the need for public awareness regarding the possible toxicity of therapeutic herbs and the importance of comprehensive patient histories in healthcare settings.

DOI: 10.1186/s12906-024-04441-1
PMCID: PMC10993546
PMID: 38575897 [Indexed for MEDLINE]

5. **Striking Cholestatic Giant Cell Hepatitis Resulting in Fulminant Liver Failure After Garcinia Cambogia Use.** Flerova E, Ambilil M, Civan JM, Sass DA, Maley WR, Pulinthanathu R, Huang J.

   Int J Surg Pathol. 2024 May;32(3):619-624. doi: 10.1177/10668969231186926.

   Garcinia cambogia, a weight control herbal, can cause mild liver toxicity with nonspecific histologic changes. Herein, we reported a case of herbal-induced fulminant cholestatic giant cell hepatitis due to garcinia cambogia use. A 65-year-old woman with breast cancer treated 18 years earlier was admitted for obstructive jaundice for 2 weeks. She started using garcinia cambogia 3 months ago for weight loss. Physical exam showed scleral icterus. Serum studies excluded Wilson's disease, systemic infection including COVID-19 (coronavirus disease 2019), autoimmune hepatitis, and metabolic or toxicologic causes. An urgent liver biopsy showed severe giant cell hepatitis in absence of HSV-1/2, cytomegalovirus, HBsAg and HBcAg (immunostain), and EBV (in situ hybridization).Despite supportive therapy, the patient developed grade 2-3 hepatic encephalopathy and necessitated liver transplant. The explanted liver was markedly atrophy, in which the most striking histologic finding was diffuse distribution of multinucleated giant hepatocytes with syncytial pattern in a background of extensive zone-1 accentuated, geographic, hemorrhagic, confluent hepatocytic necrosis, along with remarkable hepatocytic and canalicular cholestasis. Marked hepatocellular and sinusoidal iron orverload present. The patient recovered uneventfully.

   DOI: 10.1177/10668969231186926
   PMID: 37461217 [Indexed for MEDLINE]

6. **Cassia angustifolia and tacrolimus interaction in a liver transplant patient, a case report.** Beltrá-Picó I, Díaz-González M, Nalda-Molina R, Ramon-Lopez A, Pascual-Bartolomé S, Miralles-Macià CF, Rodríguez-Soler M, Más-Serrano P.

   Br J Clin Pharmacol. 2024 Apr 24. doi: 10.1111/bcp.16079. Online ahead of print.

   Cassia angustifolia is a species of plant from the Senna family that has traditionally been used as a laxative in different herbal products and commercial medicines. Even though there are few documented drug-plant interactions, the use of C. angustifolia with different drugs may have additive effects, such as with other laxatives or potassium-depleting diuretics. Its use also increases peristalsis which, may reduce drug absorption. The combination with digoxin has been associated with an increased risk of digoxin toxicity, probably due to an increase in plasma digoxin concentrations and hypokalaemia. We present a case with supratherapeutic trough concentration of tacrolimus, an immunosuppressive agent, and a herbal product in a liver transplant patient after concomitant intake of tacrolimus and a herbal product based on C. angustifolia, suggesting a possible drug-lant interaction through by P-glycoprotein. We observed an increase in the patient's blood concentration 2.8-fold and the area under the curve at steady state 2.1-fold. This interaction could be of clinical relevance, given the dose-dependent side effects of tacrolimus, such as nephrotoxicity, neurotoxicity, hypertension, hyperglycaemia, or electrolyte alterations.

   DOI: 10.1111/bcp.16079 / PMID: 38657592

7. **Investigation of the drug-drug interaction and incompatibility mechanism between Aconitum carmichaelii Debx and Pinellia ternata (Thunb.)** Breit. Ge M, Ouyang H, Shang Y, Biu AM, Wu X, Li C, Zuo F, Zhu Y, Xue Z, Hao J, He J.

   J Ethnopharmacol. 2024 Aug 10;330:118212. doi: 10.1016/j.jep.2024.118212. Epub 2024 Apr 16.

   ETHNOPHARMACOLOGICAL RELEVANCE: The combination of Aconitum carmichaelii Debx (Chuanwu, CW) and Pinellia ternata (Thunb.) Breit (Banxia, BX) forms an herbal pair within the eighteen incompatible medicaments (EIM), indicating that BX and CW are incompatible. However, the scientific understanding of this incompatibility mechanism, especially the corresponding drug-drug interaction (DDI), remains complex and unclear.AIM OF THE STUDY: This study aims to explain the DDI and potential incompatibility mechanism between CW and BX based on pharmacokinetics and cocktail approach.
   MATERIALS AND METHODS: Ultraperformance liquid chromatography-tandem mass spectrometry methods were established for pharmacokinetics and cocktail studies. To explore the DDI between BX and CW, in the pharmacokinetics study, 10 compounds were determined in rat plasma after administering CW and BX-CW herbal pair extracts. In the cocktail assay, the pharmacokinetic parameters of five probe substrates were utilized to assess the influence of BX on cytochrome P450 (CYP) isoenzyme (dapsone for CYP3A4, phenacetin for CYP1A2, dextromethorphan for CYP2D6, tolbutamide for CYP2C9, and omeprazole for CYP2C19). Finally, the DDI and incompatibility mechanism of CW and BX were integrated to explain the rationality of EIM theory.
   RESULTS: BX not only enhances the absorption of aconitine and benzoylaconine but also accelerates the metabolism of mesaconitine, benzoylmesaconine, songorine, and fuziline. Moreover, BX affects the activity of CYP enzymes, which regulate the metabolism of toxic compounds.
   CONCLUSIONS: BX altered the activity of CYP enzymes, consequently affecting the metabolism of toxic compounds from CW. This incompatibility mechanism may be related to the increased absorption ofthese toxic compounds in vivo.

   DOI: 10.1016/j.jep.2024.118212
   PMID: 38636577 [Indexed for MEDLINE]

8. **Cycasin derivative: a potential embryotoxic component of Atractylodes macrocephala rhizome for limb malformation.** Xie H, Zhang A, Li J, Mou X, He T, Yeung TC, Lau CBS, Zuo Z, Li P, Kennelly EJ, Leung PC, Tang Y, Fan X, Wang CC, Li L.

   Toxicol Res (Camb). 2024 Apr 13;13(2):tfae057. doi: 10.1093/toxres/tfae057. eCollection 2024 Apr.

   OBJECTIVE: The rhizome of Atractylodes macrocephala Koidz. (Asteraceae), called Atractylodes macrocephala rhizome (AMR) and known by its traditional name Bai Zhu, is a prominent Chinese herbal medicine employed for preventing miscarriage. However, our previous study revealed that high dosages of AMR administered during pregnancy could cause embryotoxicity but the specific embryotoxic components and their underlying

mechanisms remain unclear. This study aimed to screen and identify the potential embryotoxic components of AMR.
METHODS: The AMR extracts and sub-fractions were analyzed by thin layer chromatography and subsequently screened by in vitro mouse limb bud micromass and mouse whole embryo culture bioassays. The embryotoxic fractions from AMR were further evaluated in vivo using a pregnant mouse model. The structures of the potential embryotoxic components were analyzed using matrix-assisted laser desorption/ionization tandem time-of-flight mass spectrometry (MALDI-TOF/TOF-MS).
RESULTS: In vitro and in vivo bioassays revealed that AMR glycoside-enriched sub-fractions (AMR-A-IIa and AMR-A-IIb) exhibited potential embryotoxicity. These sub-fractions, when administered to pregnant animals, increased the incidence of stillbirth and congenital limb malformations. MS pectrometry analysis identified cycasin derivatives in both sub-fractions, suggesting their possible role in the observed limb malformations. However, further experiments are necessary to validate this hypothesis and to elucidate the underlying mechanisms.
CONCLUSIONS: Our study provides significant scientific evidence on the pharmacotoxicity of AMR, which is important for the safe clinical application of commonly used Chinese herbal medicines uring pregnancy.

DOI: 10.1093/toxres/tfae057
PMCID: PMC11015991
PMID: 38623091

9. **Cannabis and Cannabinoids in Adults With Cancer: ASCO Guideline.** Braun IM, Bohlke K, Abrams DI, Anderson H, Balneaves LG, Bar-Sela G, Bowles DW, Chai PR, Damani A, Gupta A, Hallmeyer S, Subbiah IM, Twelves C, Wallace MS, Roeland EJ.

J Clin Oncol. 2024 May 1;42(13):1575-1593. doi: 10.1200/JCO.23.02596. Epub 2024 Mar 13.

PURPOSE: To guide clinicians, adults with cancer, caregivers, researchers, and oncology institutions on the medical use of cannabis and cannabinoids, including synthetic cannabinoids and herbal cannabis derivatives; single, purified cannabinoids; combinations of cannabis ingredients; and full-spectrum cannabis.
METHODS: A systematic literature review identified systematic reviews, randomized controlled trials (RCTs), and cohort studies on the efficacy and safety of cannabis and cannabinoids when used by adults with cancer. Outcomes of interest included antineoplastic effects, cancer treatment toxicity, symptoms, and quality of life. PubMed and the Cochrane Library were searched from database inception to January 27, 2023. ASCO convened an Expert Panel to review the evidence and formulate recommendations.
RESULTS: The evidence base consisted of 13 systematic reviews and five additional primary studies (four RCTs and one cohort study). The certainty of evidence for most outcomes was low or very low.
RECOMMENDATIONS: Cannabis and/or cannabinoid access and use by adults with cancer has outpaced the science supporting their clinical use. This guideline provides strategies for open, nonjudgmental communication between clinicians and adults with cancer about the use of cannabis and/or cannabinoids. Clinicians should recommend against using cannabis or

cannabinoids as a cancer-directed treatment unless within the context of a clinical trial. Cannabis and/or cannabinoids may improve refractory, chemotherapy-induced nausea and vomiting when added to guideline-concordant antiemetic regimens. Whether cannabis and/or cannabinoids can improve other supportive care outcomes remains uncertain. This guideline also highlights the critical need for more cannabis and/or cannabinoid research. Additional information is available at www.asco.org/supportive-care-guidelines.

DOI: 10.1200/JCO.23.02596
PMID: 38478773 [Indexed for MEDLINE]

10. **Mycotoxin detection in selected medicinal plants using chromatographic techniques.** Haq IU, Taj R, Nafees M, Hussain A.

Biomed Chromatogr. 2024 Apr;38(4):e5831. doi: 10.1002/bmc.5831. Epub 2024 Jan 30.

Mycotoxins are toxic mycological products that when consumed, absorbed or inhaled cause sickness or even the death of humans. Therefore, the present study aimed to evaluate the contamination levels of mycotoxins (aflatoxins, AFB1, AFB2 , AFG1 , AFG2 , and ochratoxin A, OTA) in selected medicinal herbs and shrubs using thin-layer chromatography (TLC) and high-performance liquid chromatography (HPLC). A total of 15 samples of medicinal herbs and shrubs were selected. Among them, four samples were aflatoxin contaminated while two samples were ochratoxin A contaminated. The highest level of aflatoxin was detected in Justicia adhathoda (4,704.94 ppb) through HPLC (153.4 ppb) and through TLC, while the lowest level of aflatoxin was detected in Pegnum harmala (205.1 ppb) through HPLC. Similarly, the highest level of OTA was detected in Dodonia viscosa (0.53 ppb) through HPLC (0.5 ppb) and through TLC, while the lowest level was detected in J. adhathoda (O.11 ppb) through HPLC (0.4 ppb) and through TLC. The OTA concentration was very low, being negligible and below permissible limits. The present study concludes that there is a potential risk for the consumption of herbal decoctions. Therefore, regular monitoring and proper management of mycotoxins, including aflatoxins and OTA, in herbal medicines are needed to ensure the safety of herbal drugs to protect consumers.

DOI: 10.1002/bmc.5831
PMID: 38291628 [Indexed for MEDLINE]

11. **Hawthorne root (Crataegus mexicana) toxicity.** Espinosa J, Bassett R, Lucerna A, Finn D.

Am J Emerg Med. 2024 Apr;78:242.e5-242.e6. doi: 10.1016/j.ajem.2023.10.046. Epub 2023 Nov 3.

Here we present the case of a patient who purchased a Hawthorne root (Crataegus mexicana) product, Raiz de Tejocote, for weight loss purposes. She presented with diffuse myalgias, dizziness and a heart rate of 52 beats per minute. At triage and at initial evaluation, the patient denied taking any medications, but on iterative questioning concerning over-the-counter, over-the-internet and herbal medications, she reported taking Hawthorne root tablets in the three days prior to the emergency department (ED) visit for the purpose of weight loss. The product was purchashed through the internet. Her plasma digoxin concentration was 0.4 ng/ml the

patient's constellation of symptoms, as well as the detectable plasma digoxin concentration, were consistent with hawthorne root toxicity. Hawthorne root has intrinsic cardiac glycoside activity. In addition, Hawthorne root may cause a range of toxicity. Mild symptoms can include flu-like syndrome with significant myalgias. However, in the more severe exposures the cardiac glycoside effects can result in bradycardia and hemodynamic instability. Symptoms resolved with ED observation. The heart rate normalized. This case reinforces the importance of asking a patient about all medications, including over-the-counter, over-the-internet and herbal medications.

DOI: 10.1016/j.ajem.2023.10.046
PMID: 37973470

12. **Herbal and dietary supplement induced liver injury leading to hepatitis-associated severe aplastic anemia: A case report.** Mercedes R, Harpavat S, Hertel PM, Sasa G, Kirk S, Patel K, Mysore KR.

JPGN Rep. 2024 Feb 12;5(2):208-212. doi: 10.1002/jpr3.12041. eCollection 2024 May.

Herbal and dietary supplements (HDS) are a common etiology of drug induced liver injury and, specifically, Herbalife® supplements have been implicated. Hepatitis associated aplastic anemia (HAAA) is a rare and potentially fatal complication after acute hepatitis characterized by pancytopenia. While there have been rare cases of HDS leading to HAAA, no cases of Herbalife® induced liver injury leading to HAAA have been reported from this specific HDS. We report a unique case of severe aplastic anemia developing after sub-fulminant liver failure associated with chronic HDS use. This case illustrates the importance of warning the public about HDS as their use continues to increase. It is not only important to recognize HDS as etiology, but also for healthcare providers to carefully monitor these patients after resolution of liver injury for the development of HAAA.

DOI: 10.1002/jpr3.12041
PMCID: PMC11093934
PMID: 38756121

13. **Atropine Toxicity From Ashwaganda Herbal Product.** Gorodetsky R, Howell A, Fogarty M, Kress D, Wiegand T.

2024 ACMT Annual Scientific Meeting Abstracts – Washington, DC. Journal of Medical Toxicology. 2024;20(2):86-192. doi:10.1007/s13181-024-00990-6

Background: Ashwagandha, an herbal product marketed as an adaptogen, is used for various complaints. Despite being a member of the nightshade family, it has not been found to contain atropine and no anticholinergic effects from ashwagandha have been reported. Adulteration and contamination of herbal products, however, is a well-documented problem. Hypothesis: Unexpected toxicity from an herbal product may be related to an adulterant. Methods: This is a single patient case report with bedside toxicology consultation and confirmatory laboratory testing. A 50-year-old man presented to the Emergency Department (ED) as a stroke alert

after being found altered on the bathroom floor at his place of work. His symptoms included agitated delirium, foccillation, tachycardia, dry skin and mucous membranes, and urinary retention. Stroke workup was unremarkable. An ECG revealed sinus tachycardia with narrow intervals. Toxicology was consulted and recommended an expanded urine drug panel and rivastigmine based on anticholinergic toxidrome. 6 mg was given by mouth. The encephalopathy and vital signs improved within an hour of 148 Journal of Medical Toxicology (2024) 20:86–192 administration. The patient provided history that he had added a “generous tablespoon” of an ashwagandha product purchased online to a smoothie, which he drank on the morning of presentation. His home medication list did not contain medications with anticholinergic effects, and he denied use of over-the-counter drugs. The remaining ashwagandha product was obtained for testing at a commercial laboratory. Results: The urine drug panel resulted on hospital day two and revealed atropine present. It was negative for all other drugs. Results of the product testing confirmed atropine presence in the patient’s ashwagandha product but not a control. Conclusion: Herbal products are poorly regulated and not subject to approval by the Food and Drug Administration. Adulteration is a known phenomenon. Patients should be treated based on symptoms and confirmatory testing done when possible.

PMID: 38457103
DOI: 10.1007/s13181-024-00990-6

14. **Life-Threatening Subdural Hemorrhage Associated with Nattokinase.** Bassi MK, Keller J, Petrou S, Livshits Z.

2024 ACMT Annual Scientific Meeting Abstracts – Washington, DC. Journal of Medical Toxicology. 2024;20(2):86-192. doi:10.1007/s13181-024-00990-6’

Background: Nattokinase is an enzyme found in natto, traditional Japanese food made of soybeans which are fermented with the help of bacterium Bacillus subtilis ssp. natto. Nattokinase promotes fibrinolysis by degrading fbrin clot both directly and indirectly. Nattokinase is marketed as a dietary supplement to promote cardiovascular and circulatory health and is available on the internet and in stores. We present a case of life-threatening hemorrhage in a patient who was taking nattokinase. Methods: This is a single-patient case report. An 87-year-old woman with a history of atrial fibrillation who presented to the hospital with altered mental status. She was taking “Doctor's Best Nattokinase” 2000 FU (enzyme activity in fibrinolytic units) daily for two months. She was not taking additional anticoagulants. There was no reported history of trauma. Last dose of nattokinase was more than 12 hours prior to hospital arrival. Initial brain CT revealed subdural hematoma. Results: Initial laboratory analysis was notable for the following: platelets 463x109 /L, INR 1.1, PT 13 seconds, and fbrinogen concentration of 165 mg/dl. The patient was treated with one unit of cryoprecipitate with improvement of fibrinogen concentration to 403 mg/dl. The repeat brain CT was stable without additional bleeding. Conclusion: Nattokinase is an enzyme found in fermented soybean that promotes fibrinolysis. It is marketed as a dietary supplement. We describe a case of a patient who developed life-threatening brain hemorrhage while taking nattokinase in absence of other anticoagulants. Patients taking nattokinase should be counseled about its potential for bleeding adverse effects. Reversal strategy with cryoprecipitate should be considered in patients with life-threatening hemorrhage

PMID: 38457103
DOI: 10.1007/s13181-024-00990-6

15. **Carbonyl Iron Ingestion With Elevated Serum Iron Concentration.** Hardin J, Seltzer J, Galust H, Yeung K, Moriguchi R, Florescu C, Reyna R, Friedman NA, Clark RF, Lasoff D.

    2024 ACMT Annual Scientific Meeting Abstracts – Washington, DC. Journal of Medical Toxicology. 2024;20(2):86-192. doi:10.1007/s13181-024-00990-6'

    Background: Carbonyl iron is a form of6reduced elemental iron available over the counter as a dietary supplement; acute overdoses are rarely reported. Methods: Single patient case report. A 14-year-old female ingested 30 combination 65 mg carbonyl iron and 125 mg ascorbic acid tablets: a 36 mg/kg dose of elemental iron. Prior to the presentation, she had one episode of vomiting. Initial vital signs were notable only for mild tachycardia. Physical examination was normal. Abdominal radiography showed no radiopaque foreign bodies. Serum iron concentration nine hours post-ingestion was 557 mcg/dL (99.7 micromol/L). Renal and hepatic function testing were within normal limits. Iron concentrations decreased to 484 mcg/ dL, 74 mcg/dL, 34 mcg/dL at 12, 24 and 27 hours postingestion, respectively. Deferoxamine was not administered given the patient was asymptomatic and had decreasing iron concentrations. She remained asymptomatic over a 30-hour observation period and was then medically cleared for psychiatric hospitalization. Results: Carbonyl iron is used to treat iron defciency anemia. Studies in animals and humans have shown it has a favorable side efect profle relative to iron salts, such as ferrous sulfate. The LD50 for carbonyl iron is > fve g/kg compared to 319 mg/kg for ferrous sulfate. Why this patient developed elevated serum iron concentrations exceeding established toxic thresholds with minimal symptoms is not well understood. This is a scenario in which serum iron concentrations do not reflect the same potential for toxicity that is seen following an iron salt ingestion. Thus, treatments dependent on serum iron concentrations, namely chelation therapy, may be applied needlessly. Conclusion: Carbonyl iron can elevate serum iron concentrations into the toxic range without causing clear symptoms or sequelae of iron poisoning. Treatment guidelines solely based on serum iron concentrations may not apply to patients who ingest carbonyl iron.

    PMID: 38457103
    DOI: 10.1007/s13181-024-00990-6

16. **Use of herbal medication in the perioperative period: Potential adverse drug interactions.** Elvir Lazo OL, White PF, Lee C, Cruz Eng H, Matin JM, Lin C, Del Cid F, Yumul R.

    J Clin Anesth. 2024 Aug;95:111473. doi: 10.1016/j.jclinane.2024.111473. Epub 2024 Apr

    Use of herbal medications and supplements has experienced immense growth over the last two decades, with retail sales in the USA exceeding $13 billion in 2021. Since the Dietary Supplement Health and Education Act (DSHEA) of 1994 reduced FDA oversight, these products have become less regulated. Data from 2012 shows 18% of U.S. adults used non-vitamin, non-mineral natural products. Prevalence varies regionally, with higher use in

Western states. Among preoperative patients, the most commonly used herbal medications included garlic, ginseng, ginkgo, St. John's wort, and echinacea. However, 50-70% of surgical patients fail to disclose their use of herbal medications to their physicians, and most fail to discontinue them preoperatively. Since herbal medications can interact with anesthetic medications administered during surgery, the American Society of Anesthesiologists (ASA) and the American Association of Nurse Anesthetists (AANA) recommend stopping herbal medications 1-2 weeks before elective surgical procedures. Potential adverse drug effects related to preoperative use of herbal medications involve the coagulation system (e.g., increasing the risk of perioperative bleeding), the cardiovascular system (e.g., arrhythmias, hypotension, hypertension), the central nervous system (e.g., sedation, confusion, seizures), pulmonary (e.g., coughing, bronchospasm), renal (e.g., diuresis) and endocrine-metabolic (e.g., hepatic dysfunction, altered metabolism of anesthetic drugs). During the preoperative evaluation, anesthesiologists should inquire about the use of herbal medications to anticipate potential adverse drug interactions during the perioperative period.

DOI: 10.1016/j.jclinane.2024.111473
PMID: 38613937 [Indexed for MEDLINE]

17. **St. John's wort extract with a high hyperforin content does not induce P-glycoprotein activity at the human blood-brain barrier.** El Biali M, Wölfl-Duchek M, Jackwerth M, Mairinger S, Weber M, Bamminger K, Poschner S, Rausch I, Schindler N, Lozano IH, Jäger W, Nics L, Tournier N, Hacker M, Zeitlinger M, Bauer M, Langer O.

Clin Transl Sci. 2024 May;17(5):e13804. doi: 10.1111/cts.13804.

St. John's wort (SJW) extract, a herbal medicine with antidepressant effects, is a potent inducer of intestinal and/or hepatic cytochrome P450 (CYP) enzymes and P-glycoprotein (P-gp), which can cause clinically relevant drug interactions. It is currently not known whether SJW can also induce P-gp activity at the human blood-brain barrier (BBB), which may potentially lead to decreased brain exposure and efficacy of certain central nervous system (CNS)-targeted P-gp substrate drugs. In this study, we used a combination of positron emission tomography (PET) imaging and cocktail phenotyping to gain a comprehensive picture on the effect of SJW on central and peripheral P-gp and CYP activities. Before and after treatment of healthy volunteers (n = 10) with SJW extract with a high hyperforin content (3-6%) for 12-19 days (1800 mg/day), the activity of P-gp at the BBB was assessed by means of PET imaging with the P-gp substrate [11C]metoclopramide and the activity of peripheral P-gp and CYPs was assessed by administering a low-dose phenotyping cocktail (caffeine, omeprazole, dextromethorphan, and midazolam or fexofenadine). SJW significantly increased peripheral P-gp, CYP3A, and CYP2C19 activity. Conversely, no significant changes in the peripheral metabolism, brain distribution, and P-gp-mediated efflux of [11C]metoclopramide across the BBB were observed following the treatment with SJW extract. Our data suggest that SJW does not lead to significant P-gp induction at the human BBB despite its ability to induce peripheral P-gp and CYPs. Simultaneous intake of SJW with CNS-targeted P-gp substrate drugs is not expected to lead to P-gp-mediated drug interactions at the BBB.

DOI: 10.1111/cts.13804
PMCID: PMC11067874

PMID: 38700454 [Indexed for MEDLINE]

18. **A Rare Case of Tongkat Ali-Induced Liver Injury: A Case Report.** Kaliounji A, Shadid G, Saba H, Ahlawat S.

    Cureus. 2024 Mar 21;16(3):e56639. doi: 10.7759/cureus.56639. eCollection 2024 Mar.

    Drug-induced liver injury (DILI) presents a significant challenge in clinical practice, particularly with the rising popularity of herbal and dietary supplements (HDS) in the United States. Tongkat Ali (Eurycoma longifolia Jack), a Southeast Asian herb, has garnered attention for its purported health benefits, including enhancing testosterone levels. Here, we present a case of a 47-year-old male with acute liver injury following Tongkat Ali use, the first reported case of its kind in the literature. The patient exhibited worsening scleral icterus, elevated liver enzymes, and jaundice shortly after initiating Tongkat Ali supplementation, prompting hospitalization and subsequent clinical improvement upon discontinuation of the supplement. Differential diagnosis and exclusion of other etiologies were essential in establishing the causal link between Tongkat Ali consumption and liver damage, underscoring the difficulty in diagnosing HDS-induced liver injury. The rise in DILI cases parallels the expanding use of nutraceuticals, necessitating vigilance among healthcare professionals. While mechanisms of herbal-induced liver injury remain unclear, genetic predisposition and metabolic factors may be implicated. This case emphasizes the importance of heightened awareness among healthcare providers regarding the potential hepatotoxic effects of herbal supplements, particularly in individuals consuming multiple agents. Further research into the safety profile and mechanisms of Tongkat Ali-induced liver injury is warranted to inform clinical management and promote safer supplement use.

    DOI: 10.7759/cureus.56639
    PMCID: PMC11032125
    PMID: 38646387

19. **Rapid Characterization of Undeclared Pharmaceuticals in Herbal Preparations by Ambient Ionization Mass Spectrometry for Emergency Care**. Lee CW, Su H, Hsu YW, Su LZ, Wu YH, Hou CY, Shih SY, Shiea J.

    J Am Soc Mass Spectrom. 2024 May 1;35(5):960-971. doi: 10.1021/jasms.4c00016. Epub 2024 Apr 14.

    In Asia, some herbal preparations have been found to be adulterated with undeclared synthetic medicines to increase their therapeutic efficiency. Many of these adulterants were found to be toxic when overdosed and have been documented to bring about severe, even life-threatening acute poisoning events. The objective of this study is to develop a rapid and sensitive ambient ionization mass spectrometric platform to characterize the undeclared toxic adulterated ingredients in herbal preparations. Several common adulterants were spiked into different herbal preparations and human sera to simulate the clinical conditions of acute poisoning. They were then sampled with a metallic probe and analyzed by the thermal desorption-electrospray ionization mass spectrometry. The experimental parameters including sensitivity, specificity, accuracy, and turnaround time were prudently optimized in this study. Since tedious and time-consuming pretreatment of the sample is unnecessary, the toxic adulterants could be characterized within 60 s. The results can help emergency physicians to make clinical judgments and prescribe appropriate antidotes or supportive treatment in a time-sensitive manner.

DOI: 10.1021/jasms.4c00016
PMCID: PMC11066970
PMID: 38616559 [Indexed for MEDLINE]

20. **A Narrative Review of Aconite Poisoning and Management.** Lawson C, McCabe DJ, Feldman R.

    J Intensive Care Med. 2024 Apr 13:8850666241245703. doi: 10.1177/08850666241245703.

    Aconite poisoning refers to toxicity resulting from plants belonging to the Aconitum genus, which comprises over 350 different species of perennial flowering plants that grow in temperate mountainous areas of the northern hemisphere (North America, Europe, Asia). These plants contain a group of toxins known as aconite alkaloids, which encompass numerous closely related toxic compounds. Conventional teaching from toxicology textbooks has broadly classified these alkaloids based on their mechanism of action, often simplifying them as substances that prevent sodium channel inactivation. However, this is an oversimplified and sometimes inaccurate description, as some aconite alkaloids can act as sodium channel blockers. Aconite alkaloids have a long history of use as poisonous substances and have been historically employed for hunting, assassinations, traditional medicine, and self-inflicted harm. Toxicity can occur due to the consumption of traditional medicines derived from aconitum plants or the ingestion of aconite plants and their derivatives. The clinical manifestations of aconite poisoning may encompass gastrointestinal symptoms, sensory alterations, seizures, and life-threatening dysrhythmias that may not respond to standard treatments. Treatment is primarily supportive however evaluation and management of these patients should be personalized and carried out in collaboration with a toxicologist.

    DOI: 10.1177/08850666241245703
    PMID: 38613376

21. **Natural Products That Protect Against Acetaminophen Hepatotoxicity: A Call for Increased Rigor in Preclinical Studies of Dietary Supplements.** Layman AJ, Alsbrook SM, Koturbash IK, McGill MR.

    J Diet Suppl. 2024 Apr 1:1-18. doi: 10.1080/19390211.2024.2335573. Online ahead of print.

    Acetaminophen (APAP) overdose is one of the most common causes of acute liver injury. The current standard-of-care treatment for APAP hepatotoxicity, N-acetyl-l-cysteine, is highly effective when administered early after overdose, but loses efficacy in later-presenting patients. As a result, there is interest in the identification of new treatments for APAP overdose patients. Natural products are a promising source of new treatments because many are purported to have hepatoprotective effects. In fact, a great deal of research has been done to identify natural products that can protect against APAP-induced liver injury. However, serious concerns have been raised about the rigor and human relevance of these studies. Here, we systematically reviewed the APAP-natural product literature from 2013 to 2023 to determine the veracity of these concerns and the scope of the potential problem. The results substantiate the concerns that have been previously raised and point to concrete steps that can be taken to improve APAP-natural product research.

    DOI: 10.1080/19390211.2024.2335573
    PMID: 38562009

22. **Black Cohosh Interactions with Prescription Medications Associated with Serotonin Toxicity and Rhabdomyolysis: A Case Report.** Dernbach MR, Carpenter JE, Shah N, Carter GB.

J Emerg Med. 2024 Jan 10:S0736-4679(24)00003-9. doi: 10.1016/j.jemermed.2024.01.003. Online ahead of print.

BACKGROUND: Serotonin toxicity is a well-described phenomenon that is commonly attributed to a variety of drug-drug combinations. Some unregulated herbal supplements have been implicated in the onset of serotonin toxicity, however, there is currently minimal literature available on the potential for black cohosh to contribute to rhabdomyolysis and serotonin toxicity, in spite of its known serotonergic properties. CASE REPORT: A middle-aged woman presented to the emergency department with serotonin toxicity and rhabdomyolysis shortly after taking black cohosh supplements in the setting of long-term dual antidepressant use. The serotonin toxicity and rhabdomyolysis resolved with IV fluids, benzodiazepines, and discontinuation of the offending drugs. WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?: Patients are sometimes not aware of how over-the-counter supplements might interact with their prescription medications. Female patients taking black cohosh to manage hot flashes and menopausal symptoms could be at risk for developing rhabdomyolysis and serotonin toxicity if they are also taking other serotonergic agents.

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