

# AACT Herbal Dietary Supplement Section

## Abstracts July 2022

**1. Vitamin, Mineral, and Multivitamin Supplementation to Prevent Cardiovascular Disease and Cancer: US Preventive Services Task Force Recommendation Statement.** US Preventive Services Task Force, Mangione CM, Barry MJ, Nicholson WK, Cabana M, Chelmow D, Coker TR, Davis EM, Donahue KE, Doubeni CA, Jaén CR, Kubik M, Li L, Ogedegbe G, Pbert L, Ruiz JM, Stevermer J, Wong JB.

JAMA. 2022 Jun 21;327(23):2326-2333. doi: 10.1001/jama.2022.8970.

Vitamin, Mineral, and Multivitamin Supplementation to Prevent Cardiovascular Disease and Cancer: US Preventive Services Task Force Recommendation Statement. **IMPORTANCE:** According to National Health and Nutrition Examination Survey data, 52% of surveyed US adults reported using at least 1 dietary supplement in the prior 30 days and 31% reported using a multivitamin-mineral supplement. The most commonly cited reason for using supplements is for overall health and wellness and to fill nutrient gaps in the diet. Cardiovascular disease and cancer are the 2 leading causes of death and combined account for approximately half of all deaths in the US annually. Inflammation and oxidative stress have been shown to have a role in both cardiovascular disease and cancer, and dietary supplements may have anti-inflammatory and antioxidative effects. **OBJECTIVE:** To update its 2014 recommendation, the US Preventive Services Task Force (USPSTF) commissioned a review of the evidence on the efficacy of supplementation with single nutrients, functionally related nutrient pairs, or multivitamins for reducing the risk of cardiovascular disease, cancer, and mortality in the general adult population, as well as the harms of supplementation. **POPULATION:** Community-dwelling, nonpregnant adults. **EVIDENCE ASSESSMENT:** The USPSTF concludes with moderate certainty that the harms of beta carotene supplementation outweigh the benefits for the prevention of cardiovascular disease or cancer. The USPSTF also concludes with moderate certainty that there is no net benefit of supplementation with vitamin E for the prevention of cardiovascular disease or cancer. The USPSTF concludes that the evidence is insufficient to determine the balance of benefits and harms of supplementation with multivitamins for the prevention of cardiovascular disease or cancer. Evidence is lacking and the balance of benefits and harms cannot be determined. The USPSTF concludes that the evidence is insufficient to determine the balance of benefits and harms of supplementation with single or paired nutrients (other than beta carotene and vitamin E) for the prevention of cardiovascular disease or cancer. Evidence is lacking and the balance of benefits and harms cannot be determined. **RECOMMENDATION:** The USPSTF recommends against the use of beta carotene or vitamin E supplements for the prevention of cardiovascular disease or cancer. (D recommendation) The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the use of multivitamin supplements for the prevention of cardiovascular disease or cancer. (I statement) The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the use of single- or paired-nutrient supplements (other than beta carotene and vitamin E) for the prevention of cardiovascular disease or cancer. (I statement).

DOI: 10.1001/jama.2022.8970

PMID: 35727271 [Indexed for MEDLINE]

**2. Multivitamins and Supplements-Benign Prevention or Potentially Harmful Distraction?** Jia J, Cameron NA, Linder JA.

JAMA. 2022 Jun 21;327(23):2294-2295. doi: 10.1001/jama.2022.9167.

DOI: 10.1001/jama.2022.9167

PMID: 35727292 [Indexed for MEDLINE]

**3. Survey of Lifestyle, Past Medical History and Complementary and Alternative Medicine Use Among Adult Patients Participating in the National Cancer Institute's Exceptional Responders Initiative.**

Olaku O, Conley BA, Ivy SP, McShane LM, Staudt LM, King SM, Sansevere M, Kim B, White JD.

Transl Oncol. 2022 Aug 6;25:101484. doi: 10.1016/j.tranon.2022.101484. Online ahead of print.

**INTRODUCTION:** The Exceptional Responders Initiative (ERI) at the National Cancer Institute attempts to correlate unusually good outcomes in patients with cancer with genetic targets in tumors and the therapies the patients received. It is not known if other factors might contribute to exceptional responses or outcomes. We explored aspects of the medical history, lifestyle changes, complementary and alternative medicine (CAM) use and communication between health care practitioners and patients who experienced an exceptional response following cancer treatment. **METHODS:** All subjects whose case was submitted to the ERI were eligible to participate in the survey. A 121-question survey questionnaire was developed to assess aspects of the subject's past medical history, lifestyle (e.g., diet, exercise, spirituality) and use of CAM. **RESULTS:** Thirty subjects completed and returned the questionnaire from approximately 88 patients invited to participate (approximate response rate = 34%). Approximately 68% were female and 32% were male. Fifty percent of subjects changed their diet after their cancer diagnosis. Eighteen patients (60%) reported using a CAM therapy (not including oral vitamins/minerals or spiritual practices) during their Exceptional Response (ER). **CONCLUSION:** Multiple factors, including features of the tumor itself, the patient, or the environment, could affect tumor response or patient survival, either solely or in combination with the treatments received. Many patients use other medications, change their diet or physical activity or use CAM interventions after their cancer diagnosis. Investigators attempting to understand the exceptional response phenomenon should acquire rich data sets of their subjects that include information about these factors.

DOI: 10.1016/j.tranon.2022.101484  
PMID: 35944413

#### **4. Differences in clinical characteristics among 726 patients with Chinese herbal medicine- or Western medicine-induced liver injury.** Tan K, Yang W, Pang L, Hou F.

Medicine (Baltimore). 2022 Aug 12;101(32):e29909. doi: 10.1097/MD.0000000000029909.

The differences between Chinese herbal medicine (CHM)- and Western medicine (WM)-induced liver injury have rarely been reported. Our aim was to investigate the clinical features of patients with drug-induced liver injury (DILI) caused by CHM or WM. The medical records of 726 DILI patients were retrospectively collected at Peking University First Hospital from January 1995 through August 2019. The number of inpatients with DILI in our hospital showed an increasing trend over time. The incidence of DILI caused by CHM exhibited a linear trend toward an increase with time ( $P = .0012$ ). Of the 726 DILI patients, females accounted for 65.8%. There were 353 cases (48.6%) caused by CHM and 225 cases (40.0%) caused by WM. The 3 most common causative CHMs were Polygonum multiflorum (38 cases), Fructus Psoraleae (35 cases), and Epimedium (26 cases). The proportions of female patients, alanine aminotransferase (ALT) levels, aspartate aminotransferase (AST) levels, total bilirubin (TBIL) levels and antinuclear antibody (ANA) positivity rates among cases caused by CHM were higher than those of cases caused by WM ( $P < .05$ ). There were more patients with severe cases caused by CHM than with severe cases caused by WM ( $P < .05$ ). The clinical characteristics of DILI caused by CHM differ from those caused by WM. The incidence of DILI caused by CHM is increasing yearly. The medication time of DILI caused by CHM is longer than that of DILI caused by WM, and the severity is greater. Therefore, it is necessary to scientifically and rationally use traditional CHM and monitor liver function. For DILI caused by CHM, the CHM prescription should be recorded in detail to provide detailed clinical data for scientific research on the liver toxicity of CHM.

DOI: 10.1097/MD.0000000000029909  
PMCID: PMC9371566  
PMID: 35960048 [Indexed for MEDLINE]

#### **5. The banned herbal medicine induced liver injury in Taiwan.** Lin HC, Yen CM, Chen KF, Kung YY, Hsieh YH, Chang CM.

Hepatol Int. 2022 Jun;16(3):730-731. doi: 10.1007/s12072-022-10341-8. Epub 2022 Apr 28.

Comment on Hepatol Int. 2021 Dec;15(6):1456-1465.

DOI: 10.1007/s12072-022-10341-8  
PMID: 35482275 [Indexed for MEDLINE]

#### **6. High doses of eugenol cause structural and functional damage to the rat liver.** Carvalho RPR, Ribeiro FCD, Lima TI, Ervilha LOG, de Oliveira EL, Faustino AO, Lima GDA, Machado-Neves M.

Life Sci. 2022 Jun 6:120696. doi: 10.1016/j.lfs.2022.120696. Online ahead of print.

Eugenol is a phenolic compound found in clove extract and extensively used in traditional medicine. It is unclear whether its intake can cause positive or negative effects on liver morphology and physiology in healthy individuals. Thus, we aimed to evaluate liver parameters of rats treated with 10, 20, and 40 mg kg<sup>-1</sup> eugenol. After 60 days of treatment, liver samples were collected and analyzed by biometric, histological, biochemical, and oxidative analyses. Our results showed that 10, 20, and 40 mg kg<sup>-1</sup> eugenol did not alter body and liver weights, serum and hepatic ALT levels and catalase, glutathione-s-transferase, total, Ca<sup>2+</sup>, and Mg<sup>2+</sup> ATPases activities in treated animals. However, 20 and 40 mg kg<sup>-1</sup> eugenol reduced Na<sup>+</sup>/K<sup>+</sup> ATPase pump activity and blood glucose levels. They also increased hepatic glycogen content, superoxide dismutase activity, ferric reducing antioxidant power, and nitric oxide and malondialdehyde levels. Still, 20 and 40 mg kg<sup>-1</sup> eugenol caused structural and functional damage to the liver tissue of eugenol-treated rats. We concluded that 10 mg kg<sup>-1</sup> eugenol is a safe dose for consumption in long-term treatment for rats. Doses higher than 20 mg kg<sup>-1</sup> lead to hepatic damage that can impair vital processes of liver functionality.

DOI: 10.1016/j.lfs.2022.120696

PMID: 35679916

### **7. Liver injury and dietary supplements: Does hydroxycitric acid trigger hepatotoxicity?**

Zovi A, Langella R, Nisic A, Vitiello A, Musazzi UM.

J Integr Med. 2022 May 30:S2095-4964(22)00066-8. doi: 10.1016/j.joim.2022.05.003. Online ahead of print.

Rising rates of obesity has increased the global use of herbal supplements intended to control weight. However, taking these preparations without appropriate medical supervision could increase the risk of manifestation of side effects, especially at the hepatic level. In literature, different cases of acute liver injury consequent to the use of food supplements containing *Garcinia cambogia* and hydroxycitric acid are reported. This letter aims to review the most recent literature that analysed the herb-induced liver disease due to the use of hydroxycitric acid, from the first alert coming from the European Food and Drug Administration in 2009, to the last recent European food alerts from 2020 to 2021. It is noteworthy that in some cases it demonstrated the relationship between hydroxycitric acid and hepatotoxicity. Therefore, there is a need to draw more attention to the relationship between a safe use and a more awareness in the intake of these supplements, to preserve the safety of the consumers who increasingly purchase food supplements, products that have only nutritive properties and are never curative.

DOI: 10.1016/j.joim.2022.05.003

PMID: 35710615

### **8. Recent Advances in *Garcinia cambogia* Nutraceuticals in Relation to Its Hydroxy Citric Acid Level. A Comprehensive Review of Its Bioactive Production, Formulation, and Analysis with Future Perspectives.** H Baky M, Fahmy H, Farag MA.

ACS Omega. 2022 Jul 19;7(30):25948-25957. doi: 10.1021/acsomega.2c02838. eCollection 2022 Aug 2.

*Garcinia cambogia* (Gaertn.) Desr. (known as Malabar tamarind) is a popular traditional herbal medicine and is one of the well-known folk medicines reported for the treatment of obesity and incorporated in several nutraceuticals worldwide. These effects are mediated by a myriad of bioactive compounds with most effects attributed to its hydroxy citric acid (HCA) content. This review aims to present a holistic overview on novel trends in the production of *G. cambogia* bioactive components and how extraction optimization is important to ensure best product quality with its reported nanoformulations with particular emphasis on HCA content. Further, an overview of the different analytical approaches used for quality control assessment of *G. cambogia* plant and its nutraceuticals is presented highlighting both advantages and limitations. Moreover, analytical approaches for detecting *G. cambogia* metabolites in biological fluids with emphasis on HCA level to determine its pharmacokinetics and proof of efficacy are presented for the first time.

DOI: 10.1021/acsomega.2c02838

PMCID: PMC9352243

PMID: 35936438

## **9. Recalls, Availability, and Content of Dietary Supplements Following FDA Warning Letters.**

Cohen PA, Avula B, Katragunta K, Khan I.

JAMA. 2022 Jul 26;328(4):393-395. doi: 10.1001/jama.2022.9734.

DOI: 10.1001/jama.2022.9734

PMID: 35881132 [Indexed for MEDLINE]

## **10. The efficacy of Shenghua Decoction supplementation after early medical abortion:**

**A meta-analysis of randomized controlled trials.** Li HF, Chen WM, Shen HL, Feng ZF, Yang Y, Shen QH.

Complement Ther Med. 2022 Oct;69:102848. doi: 10.1016/j.ctim.2022.102848. Epub 2022 Jun 30.

AIMS: Shenghua Decoction (SHD) is a well-known classic herbal formula documented in traditional Chinese medicine (TCM) that has been widely applied during the postpartum period in Chinese communities for several years. We conducted this systematic review and meta-analysis to explore the influence of SHD as an adjuvant treatment for early medical abortion using a combination of mifepristone followed by misoprostol. METHODS: This systematic review and meta-analysis was reported using 2020 PRISMA guidelines. Eight databases were searched from their establishment to February 28, 2022, for randomized controlled trials (RCTs): PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure, the Chinese BioMedical database, the Chinese Scientific Journal Database, and the Wanfang database. The Grading of Recommendations Assessment, Development, and Evaluation estimated the quality of evidence. RESULTS: Sixteen RCTs involving 3016 patients were included in the meta-analysis. Overall, compared with no treatment as the control group after early medical abortion, patients treated with SHD were associated with a higher complete abortion rate (RR: 1.14; 95% CI: 1.10 - 1.18;  $P < 0.01$ ,  $I^2 = 26\%$ , moderate quality), lower incomplete abortion rate (RR: 0.31; 95% CI: 0.24 - 0.41;  $P < 0.01$ ,  $I^2 = 0\%$ , moderate quality), and lower viable pregnancy rate (RR: 0.26; 95% CI: 0.11 - 0.62;  $P < 0.01$ ,  $I^2 = 0\%$ , moderate quality). Additionally, SHD supplementation was associated with reduced the induction-abortion time, duration of vaginal bleeding and menstrual recovery time. CONCLUSION: Our findings suggest that SHD supplementation may be beneficial for women seeking a medical abortion before the 7-week gestational period and no adverse events in the experimental group were reported. However, the methodological quality of the included RCTs was unsatisfactory, and therefore it is necessary to further verify the effectiveness of SHD using standardized studies of rigorous design.

DOI: 10.1016/j.ctim.2022.102848

PMID: 35779783 [Indexed for MEDLINE]

## **11. Toxicity of oxidized fish oil in pregnancy - a dose response study in rats.** Satokar VV, Vickers MH, Reynolds CM, Ponnampalam AP, Firth EC, Garg ML, Bridge-Comer PE, Cutfield WS, Albert BB.

Am J Physiol Regul Integr Comp Physiol. 2022 Jun 21. doi: 10.1152/ajpregu.00042.2022. Online ahead of print.

INTRODUCTION: Fish oil (FO) supplements are consumed during pregnancy to increase dietary omega-3. However, FO is often oxidized past recommended limits. In rats, a large dose of highly oxidized FO substantially increased newborn mortality, but the effects of human-relevant doses of less oxidized oil are unknown. A dose-response study in rats was conducted to estimate the safe level of oxidation during pregnancy. METHODOLOGY: Sprague-Dawley rat dams were mated, then individually housed and provided with a gel treatment on each day of pregnancy. Treatment groups differed only in the FO content of the gel; control (no oil), PV5, PV10, and PV40 (0.05ml of FO oxidized to a peroxide value (PV) of 5, 10, or 40meq/kg), or PV40(1ml) (1ml of PV40). A subset of dams was culled on gestational day 20 to enable sampling, and the remainder were allowed to give birth. Newborn mortality was recorded. Offspring were sampled at postnatal days 2 and 21, and dams at day 21. RESULTS: There were no signs of unwellness during pregnancy. However, there was markedly increased neonatal mortality affecting the PV40(1ml) (12.8%) and PV40 (6.3%) groups, but not the control, PV5, or PV10 groups (1-1.4%). Dietary oxidized FO altered the expression of placental genes involved in antioxidant pathways and the production of free radicals. Conclusions Highly oxidized FO was toxic in rat pregnancy leading to a marked increase in mortality even at a human-relevant dose. We observed no toxic effects of FOs with  $PV \leq 10$ meq/kg, suggesting that this is an appropriate maximum limit.

DOI: 10.1152/ajpregu.00042.2022  
PMID: 35726870

**12. Potency and Therapeutic THC and CBD Ratios: U.S. Cannabis Markets Overshoot.** Pennypacker SD, Cunnane K, Cash MC, Romero-Sandoval EA.

Front Pharmacol. 2022 Jun 6;13:921493. doi: 10.3389/fphar.2022.921493. eCollection 2022.

Background and aims: The effects exerted by cannabis are a result of the cannabinoids trans- $\Delta^9$ -tetrahydrocannabinol (THC) and cannabidiol (CBD), and is dependent upon their pharmacological interaction and linked to the two cannabinoids' concentrations and ratios. Based on current literature and trends of increasing cannabis potency, we postulate that most medical cannabis products with THC and CBD have ratios capable of producing significant acute intoxication and are similar to recreational products. We will test this by organizing products into clinically distinct categories according to THC:CBD ratios, evaluating the data in terms of therapeutic potential, and comparing the data obtained from medical and recreational programs and from states with differing market policies. Methods: We utilized data encompassing online herbal dispensary product offerings from nine U.S. states. The products were analyzed after being divided into four clinically significant THC:CBD ratio categories identified based on the literature: CBD can enhance THC effects (THC:CBD ratios  $\geq 1:1$ ), CBD has no significant effect on THC effects (ratios  $\sim 1:2$ ), CBD can either have no effect or can mitigate THC effects (ratios  $1:>2 < 6$ ), or CBD is protective against THC effects (ratios  $\leq 1:6$ ). Results: A significant number of products (58.5%) did not contain any information on CBD content. Across all states sampled, the majority (72-100%) of both medical and recreational products with CBD ( $>0\%$ ) fall into the most intoxicating ratio category ( $\geq 1:1$  THC:CBD), with CBD likely enhancing THC's acute effects. The least intoxicating categories ( $1:>2 < 6$  and  $\leq 1:6$  THC:CBD) provided the smallest number of products. Similarly, the majority of products without CBD (0%) contained highly potent amounts of THC ( $>15\%$ ). These results were consistent, regardless of differing market policies in place. Conclusions: Despite the distinct goals of medical and recreational cannabis users, medical and recreational program product offerings are nearly identical. Patients seeking therapeutic benefits from herbal cannabis products are therefore at a substantial risk of unwanted side effects, regardless of whether they obtain products from medical or recreational programs. Efforts are needed to better inform patients of the risks associated with high potency cannabis and the interaction between THC and CBD, and to help shape policies that promote more therapeutic options.

DOI: 10.3389/fphar.2022.921493  
PMCID: PMC9207456  
PMID: 35734402

**13. Poisonous Plants of the Indian Himalaya: An Overview.** Jamloki A, Trivedi VL, Nautiyal MC, Semwal P, Cruz-Martins N.

Metabolites. 2022 Jun 13;12(6):540. doi: 10.3390/metabo12060540.

Indian Himalayan region (IHR) supports a wide diversity of plants and most of them are known for their medicinal value. Humankind has been using medicinal plants since the inception of civilization. Various types of bioactive compounds are found in plants, which are directly and indirectly beneficial for plants as well as humans. These bioactive compounds are highly useful and being used as a strong source of medicines, pharmaceuticals, agrochemicals, food additives, fragrances, and flavoring agents. Apart from this, several plant species contain some toxic compounds that affect the health of many forms of life as well as cause their death. These plants are known as poisonous plants, because of their toxicity to both humans and animals. Therefore, it is necessary to know in what quantity they should be taken so that it does not have a negative impact on health. Recent studies on poisonous plants have raised awareness among people who are at risk of plant toxicity in different parts of the world. The main aim of this review article is to explore the current knowledge about the poisonous plants of the Indian Himalayas along with the importance of these poisonous plants to treat different ailments. The findings of the present review will be helpful to different pharmaceutical industries, the scientific community and researchers around the world.

DOI: 10.3390/metabo12060540  
PMCID: PMC9229149

PMID: 35736473

**14. The dark side of miracle plant-Aloe vera: a review.** Jangra A, Sharma G, Sihag S, Chhokar V.

Mol Biol Rep. 2022 Jun;49(6):5029-5040. doi: 10.1007/s11033-022-07176-9. Epub 2022 Jan 29.

**BACKGROUND:** Aloe vera (*Aloe barbadensis* Miller), commonly known as Ghritkumari/Gwarpatha, is a member of the Liliaceae family, used in the traditional medicine system for ages. Aloe vera has made its importance as a therapeutic agent, acting as a cure for various diseases such as skin problems, lungs, and heart disorders, diabetes, ulcers, various microbial infections, and asthma. Despite its tremendous health benefits, the dark side of the plant is a reason of concern as there are several active compounds present in the plant, raising questions on its safe oral consumption and application. **METHODS AND RESULTS:** The literature review was compiled from information resourced from various national and international journals available at Google Scholar and curated with Mendeley. The data mining was carried out during the period of January to May 2021. This study explored and summarized the dark side of Aloe vera, subjected to various secondary metabolites present in it. Aloin, the most active compound of Aloe vera, is a type of anthraquinone metabolized by human gut microflora, resulting in the formation of aloe-emodin anthraquinone, later being associated with several harmful effects such as carcinogenicity, genotoxicity, nephrotoxicity, and purgative. Besides this, several alkaloids and polysaccharides present in the plant are reported to cause hepatotoxicity and male infertility, respectively. **CONCLUSIONS:** The harmful effects of the plants are not adequately discovered yet; hence there is a need to come up with some mechanism to understand and suppress the formation of such toxic compounds completely. This review examined the botany, active compounds, and adverse clinical effects in the range of metabolites associated with this herb - "Aloe vera".

DOI: 10.1007/s11033-022-07176-9

PMID: 35092563 [Indexed for MEDLINE]

**15. Identification of phosphodiesterase type-5 (PDE-5) inhibitors in herbal supplements using a tiered approach and associated consumer risk.** Akuamoah F, Bovee TFH, van Dam R, Maro L, Wesseling S, Vervoort J, Rietjens IMCM, Hoogenboom RLAP.

Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2022 Jun;39(6):1021-1032. doi: 10.1080/19440049.2022.2052972. Epub 2022 Mar 24.

The use of herbal supplements for improved sexual performance is a common practice amongst the youth and some senior citizens in Ghana. These products are considered 'natural' and greatly preferred over synthetic alternatives due to the assurance of little to no adverse effects by producers. However, the high rate of adulteration often compromises their safety. Forty herbal supplements, of which 25 were previously shown to result in medium to high intake of phosphodiesterase type-5 (PDE-5) inhibitors using a PDE-Glo bioassay, were further investigated using liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis to examine the reliability of the bioassay and whether the observed higher responses could be ascribed to inherent plant constituents or adulterants. Results showed significant amounts of vardenafil, tadalafil and especially sildenafil, in 2, 1 and 10 samples, respectively, with total concentration levels resulting in estimated daily intakes (EDIs) above 25 mg sildenafil equivalents with six supplements even having EDIs above 100 mg sildenafil equivalents. Only one sample contained a natural ingredient (icariin), but its concentration (0.013 mg g<sup>-1</sup>) was too low to explain the observed potency in the bioassay. The estimated concentrations of PDE-5 inhibitors in 35 supplements, according to the bioassay, were in line with those of the LC-MS/MS analysis. However, discrepancies were observed for five supplements. Further examination of one of the latter supplements using the PDE-Glo bioassay to select the positive fraction and further examination with LC-MS/MS and 1H-NMR revealed the presence of hydroxythiohomosildenafil, a sildenafil analogue not yet included in the liquid chromatography-mass spectrometry reference library. This study demonstrates the significance of applying a tiered approach, where the use of a bioassay is followed by chemical analysis of bioactive samples in order to identify unknown bioactive compounds.

DOI: 10.1080/19440049.2022.2052972

PMID: 35323088 [Indexed for MEDLINE]

**16. St. John's Wort (*Hypericum perforatum*)-Related Acute Kidney Injury.** Adibelli Z, Karacay I, Demir M, Duran C.

Blood Purif. 2022;51(6):520-522. doi: 10.1159/000518349. Epub 2021 Aug 24.

Some herbal products were reported to cause nephrotoxicity through different mechanisms. This case report defines an acute kidney injury (AKI) in a patient who used *Hypericum perforatum* tea as a sleep disorder remedy. The patient developed AKI after ingestion of tea prepared from *Hypericum perforatum* and underwent hemodialysis because of acute kidney failure. After 1 week, the kidney recovered, and she was discharged with normal kidney function. This is the first case reported having acute kidney failure caused by ingestion of *Hypericum perforatum*.

DOI: 10.1159/000518349

PMID: 34515077 [Indexed for MEDLINE]

**17. Vulvar allergic contact dermatitis caused by *Magnolia officinalis* bark extract.** Amat-Samaranch V, López-Sánchez C, Tubau C, Puig L, Serra-Baldrich E.

Contact Dermatitis. 2022 Jul;87(1):96-97. doi: 10.1111/cod.14101. Epub 2022 Mar 29.

DOI: 10.1111/cod.14101

PMID: 35277988 [Indexed for MEDLINE]

**18. Suspected cholinergic toxicity due to cevimeline hydrochloride and *Bacopa monnieri* interaction: a case report.** Acquarulo B, Tandon P, Macica CM.

J Med Case Rep. 2022 Jun 29;16(1):253. doi: 10.1186/s13256-022-03479-4.

**BACKGROUND:** Muscarinic agonists are indicated for the treatment of many conditions including ileus, urinary retention, glaucoma, and Sjögren's syndrome. Due to their lack of tissue specificity, these drugs can lead to undesirable side effects at off-target sites and may be potentiated by supplements that impact the half-life of these drugs. **CASE PRESENTATION:** A 58-year-old Caucasian female with history of Sjögren's syndrome, who was being managed with cevimeline, presented to the primary care office with reported hyperhidrosis, malaise, nausea, and tachycardia. She reported taking an herbal supplement containing *B. monnieri* and phosphatidylserine the previous night. It has been previously demonstrated that *B. monnieri* alters cytochrome P450 enzymes. Electrocardiogram showed no acute ST-T changes. Clinical improvement occurred with hydration and discontinuation of the supplement. **CONCLUSIONS:** To our knowledge, there has only been one other documented cevimeline overdose, and it was not associated with an herbal supplementation interaction. Physicians should actively elicit herbal supplement information from patients to anticipate possible drug-herb interactions. An additional consideration of clinical relevance is the known genetic variability that may affect drug responsiveness due to differences in metabolism and half-life of drugs that arise from common genetic variants of cytochrome P450 genes.

DOI: 10.1186/s13256-022-03479-4

PMCID: PMC9241182

PMID: 35765109 [Indexed for MEDLINE]

**19. Could herbal soup be a potentially unrecognized cause of hepatotoxicity at autopsy?**

Britza SM, Farrington R, Musgrave IF, Aboltins C, Byard RW.

Forensic Sci Med Pathol. 2022 Jun 24:1-4. doi: 10.1007/s12024-022-00490-5. Online ahead of print.

Unexpected hepatic failure with liver necrosis is sometimes encountered during a forensic autopsy. Determining the etiology may sometimes be difficult, although increasingly herbal medicines are being implicated. To determine whether such effects might also be caused by foodstuffs, the following in vitro study was undertaken. Four formulations of traditional herbal soup advertised as bak kut teh were prepared and added to cultures of liver carcinoma cells (HepG2). Cell viability was assessed using an MTT colorimetric assay at 48 h demonstrating that all formulations had significant toxicity prior to dilution ( $p < 0.05$ ). Formulation #1 showed 21% cell death ( $p = 0.023$ ), Formulation #2 30% ( $p = 0.009$ ), and Formulation #3 41% ( $p < 0.0001$ ). Formulations #1-3 showed no significant toxicity once diluted ( $p > 0.05$ ). Formulation 4 showed approximately 83% cell death before dilution ( $p < 0.0001$ ) and persistent toxicity even with dilutions at 1:10 ( $15\% \pm 3.7$ ,  $p = 0.023$ ) and 1:1000 ( $14\% \pm 3.8$ ,  $p = 0.024$ ). This study has shown that herbal foodstuffs such as bak kut teh may be responsible for variable degrees of in vitro hepatotoxicity, thus

extending the range of herbal products that may be potentially injurious to the liver. If unexpected liver damage is encountered at autopsy, information on possible recent ingestion of herbal food preparations should be sought, as routine toxicology screening will not identify the active components. Liver damage may therefore be caused not only by herbal medicines but possibly by herbal products contained in food.

DOI: 10.1007/s12024-022-00490-5

PMCID: PMC9226283

PMID: 35749044

**20. Abdominal fullness and discomfort induced by an extract of the Japanese herbal medicine Tsumura Ninjin'yoeito: The cases of two patients with Alzheimer's disease and anorexia.** Sato S, Tamura M, Ide M, Matsuzaki A, Shiratori Y, Hisanaga A.

Psychiatry Clin Neurosci. 2022 Aug;76(8):406-407. doi: 10.1111/pcn.13431. Epub 2022 Jun 23.

DOI: 10.1111/pcn.13431

PMID: 35638555 [Indexed for MEDLINE]