

AACT Herbal Dietary Supplements SIG Abstracts March 2019

1. Mushroom poisoning: A proposed new clinical classification. White J, Weinstein SA, De Haro L, Bédry R, Schaper A, Rumack BH, Zilker T.

Toxicon. 2019 Jan;157:53-65. doi: 10.1016/j.toxicon.2018.11.007. Epub 2018 Nov 12.
Comment in Toxicon. 2019 Mar 1;159:63-64.

Mushroom poisoning is a significant and increasing form of toxin-induced-disease. Existing classifications of mushroom poisoning do not include more recently described new syndromes of mushroom poisoning and this can impede the diagnostic process. We reviewed the literature on mushroom poisoning, concentrating on the period since the current major classification published in 1994, to identify all new syndromes of poisoning and organise them into a new integrated classification, supported by a new diagnostic algorithm. New syndromes were eligible for inclusion if there was sufficient detail about both causation and clinical descriptions. Criteria included: identity of mushrooms, clinical profile, epidemiology, and the distinctive features of poisoning in comparison with previously documented syndromes. We propose 6 major groups based on key clinical features relevant in distinguishing between poisoning syndromes. Some clinical features, notably gastrointestinal symptoms, are common to many mushroom poisoning syndromes. Group 1 - Cytotoxic mushroom poisoning. Syndromes with specific major internal organ pathology: (Subgroup 1.1; Primary hepatotoxicity); 1A, primary hepatotoxicity (amatoxins); (Subgroup 1.2; Primary nephrotoxicity); 1B, early primary nephrotoxicity (amino hexadienoic acid; AHDA); 1C, delayed primary nephrotoxicity (orellanines). Group 2 - Neurotoxic mushroom poisoning. Syndromes with primary neurotoxicity: 2A, hallucinogenic mushrooms (psilocybins and related toxins); 2B, autonomic-toxicity mushrooms (muscarines); 2C, CNS-toxicity mushrooms (ibotenic acid/muscimol); 2D, morel neurologic syndrome (*Morchella* spp.). Group 3 - Myotoxic mushroom poisoning. Syndromes with rhabdomyolysis as the primary feature: 3A, rapid onset (*Russula* spp.); 3B, delayed onset (*Tricholoma* spp.). Group 4 - Metabolic, endocrine and related toxicity mushroom poisoning. Syndromes with a variety of clinical presentations affecting metabolic and/or endocrine processes: 4A, GABA-blocking mushroom poisoning (gyromitrins); 4B, disulfiram-like (coprines); 4C, polyporic mushroom poisoning (polyporic acid); 4D, trichothecene mushroom poisoning (*Podostroma* spp.); 4E, hypoglycaemic mushroom poisoning (*Trogia venenata*); 4F, hyperprolactinemia mushroom poisoning (*Boletus satanas*); 4G, pancytopenic mushroom poisoning (*Ganoderma neojaponicum*). Group 5 - Gastrointestinal irritant mushroom poisoning. This group includes a wide variety of mushrooms that cause gastrointestinal effects without causing other clinically significant effects. Group 6 - Miscellaneous adverse reactions to mushrooms. Syndromes which do not fit within the previous 5 groups: 6A, Shiitake mushroom dermatitis; 6B, erythromelagic mushrooms (*Clitocybe acromelagia*); 6C, Paxillus syndrome (*Paxillus involutus*); 6D, encephalopathy syndrome (*Pleurocybella porrigens*).

DOI: 10.1016/j.toxicon.2018.11.007
PMID: 30439442 [Indexed for MEDLINE]

2. Increasing potency and price of cannabis in Europe, 2006-16. Freeman TP, Groshkova T, Cunningham A, Sedefov R, Griffiths P, Lynskey MT.

Addiction. 2018 Dec 29. doi: 10.1111/add.14525. [Epub ahead of print]

AIMS: To quantify changes in (i) potency (concentration of Δ^9 -tetrahydrocannabinol; %THC), (ii) price (euros/g of cannabis) and (iii) value (mg THC/euro) of cannabis resin and herbal cannabis in Europe. DESIGN: Repeated cross-sectional study. SETTING AND PARTICIPANTS: Data collected from 28 European Union (EU) member states, Norway and Turkey by the European Monitoring Centre for Drugs and Drug Addiction. MEASUREMENTS: Outcome variables were potency, price and value for cannabis resin and herbal cannabis in Europe, 2006-16. Inflation was estimated using the Harmonised Indices of Consumer Prices. Mixed-effects linear regression models were used to estimate linear and quadratic time trends, with a random intercept and slope fitted to account for variation across countries. FINDINGS: Resin potency increased from a mean [95% confidence interval (CI)] of 8.14% THC (6.89, 9.49) in 2006 to 17.22 (15.23, 19.25) in 2016. Resin price increased from 8.21 euros/g (7.54, 8.97) to 12.27 (10.62, 14.16). Resin increased in value, from 11.00 mg THC per euro (8.60, 13.62) to 16.39 (13.68, 19.05). Quadratic time trends for resin potency and value indicated minimal change from 2006 to 2011, followed by marked increases from 2011 to 2016. Herbal cannabis potency increased from 5.00% THC (3.91, 6.23) to 10.22 (9.01, 11.47). Herbal price increased from 7.36 euros/g (6.22, 8.53) to 12.22 (10.59, 14.03). The value of herbal cannabis did not change

from 12.65 mg of THC per euro (10.18, 15.34) to 12.72 (10.73, 14.73). All price trends persisted after adjusting for inflation. CONCLUSIONS: European cannabis resin and herbal cannabis increased in potency and price from 2006 to 2016. Cannabis resin (but not herbal cannabis) increased in the quantity of Δ^9 -tetrahydrocannabinol per euro spent. Marked increases in resin potency and value from 2011 to 2016 are consistent with the emergence of new resin production techniques in European and neighbouring drug markets.

DOI: 10.1111/add.14525
PMID: 30597667

3. Notes from the Field: Acute Poisonings from a Synthetic Cannabinoid Sold as Cannabidiol - Utah, 2017-2018. Horth RZ, Crouch B, Horowitz BZ, Prebish A, Slawson M, McNair J, Elsholz C, Gilley S, Robertson J, Risk I, Hill M, Fletcher L, Hou W, Peterson D, Adams K, Vitek D, Nakashima A, Dunn A.

MMWR Morb Mortal Wkly Rep. 2018 May 25;67(20):587-588. doi: 10.15585/mmwr.mm6720a5.

DOI: 10.15585/mmwr.mm6720a5
PMID: 29795081 [Indexed for MEDLINE]

4. Legally Lethal Kratom: A Herbal Supplement with Overdose Potential. Palasamudram Shekar S, Rojas EE, D'Angelo CC, Gillenwater SR, Martinez Galvis NP.

J Psychoactive Drugs. 2019 Jan-Mar;51(1):28-30. doi: 10.1080/02791072.2018.1562591. Epub 2019 Jan 8.

This case report describes an overdose on kratom, and elicits the potential dangers of overdose on the regulated dietary supplement. A young male presented to the emergency department intubated after being found unresponsive. He was found by his family to be unarousable and agonal breathing with minimal response to naloxone administered by Emergency Medical Services (EMS). Urine toxicology and blood alcohol content were negative. Physical exam was significant for tachycardia, hypotension, and pinpoint pupils with sluggish reactivity to light. Laboratory studies were significant for elevated liver enzymes, blood urea nitrogen, creatinine, lipase, amylase, troponins, and lactic acid. Family members revealed that the patient consumed kratom, which he obtained through an e-commerce business, and had consumed over 500 grams the previous day. Urine sample for kratom on day 3 tested positive with levels of more than 500 ng/dL. The patient received supportive care and, by day 10, pupillary reflexes returned to normal and he was extubated by day 14. Most of the medications/drugs labelled under herbal supplements by the U.S. Food and Drug Administration (FDA) are not regulated and can be purchased over the counter. The safety and side-effect profile of kratom is not well-studied, especially in an overdose scenario.

DOI: 10.1080/02791072.2018.1562591
PMID: 30620247

5. Morphine Concentrations in Human Urine Following Poppy Seed Paste Consumption. Özbunar E, Aydoğdu M, Döğler R, Bostancı Hİ, Koruyucu M, Akgür SA.

Forensic Sci Int. 2019 Feb;295:121-127. doi: 10.1016/j.forsciint.2018.11.026. Epub 2018 Dec 5.

Papaver somniferum (opium poppy) is one of the world's oldest medicinal plants which are widely used for medicinal, nutritive and scientific purposes. Turkey is one of the major legal opium poppy producer countries in the world and the seed paste of the poppies is consumed in great deal, even more than 100g per meal. The main objective of this study is to investigate the influence of poppy seed paste ingestion on urine tests for opiates whether or not could lead to opiate positive urine test results. For this purpose, a variety of poppies were used and the morphine content of white, yellow and blue-black poppies were determined as 1.9, 4.0 and 2.6mg/kg, respectively. 100g of these seed pastes were consumed in the breakfast by ten healthy adults enrolled in the study over three days and urine samples were collected before and after the breakfast. Opiate screening analysis was carried out by enzyme immunoassay method and the results were evaluated by two different cut-off values (300 and 2000ng/mL). Morphine confirmation analysis was made by GC-MS system and the chromatographic method was validated in terms of selectivity, extraction efficiency, linearity (25-2000ng/ml), intra-assay precision, accuracy, limit of detection (LOD) and limit of quantitation (LOQ) (3 and 10ng/ml), carryover, matrix effect, dilution integrity and stability. According to cut-off value 300ng/ml, opiate concentrations were found positive up to 48h. For cut-off value 2000ng/mL; this time was up to 12h in

collected urine samples after consumption of three different colored poppy seed pastes. In all urine samples, thebaine was detected while the heroin abuse metabolite 6-acetyl morphine (6-AM) was not. Urine drug testing legislation was revised on 2016 in Turkey and opiate screening cut-off values increased from 300 to 2000ng/mL. Overall results have shown that poppy seed paste as food consumption could lead to opiate positive urine test result even if increased cut off levels are used. It can also be deduced that thebaine can be taken as supportive biomarker for poppy seed paste consumption. Awareness of interpretation of urine test results and defining the procedures especially for forensic drug testing must be done in legal aspect to ensure justice for each individual (workplace, traffic, court etc.).

DOI: 10.1016/j.forsciint.2018.11.026
PMID: 30579243 [Indexed for MEDLINE]

6. Isolation and characterisation of a novel sildenafil analogue adulterant, desmethylpiperazinyl propoxysildenafil, in a dietary supplement. Lee JH, Park HN, Jung A, Mandava S, Park S, Lee J, Kang H.

Sci Justice. 2018 Nov;58(6):447-454. doi: 10.1016/j.scijus.2018.07.003. Epub 2018 Jul 17.

A new sildenafil analogue was detected during routine screening of dietary supplements suspected to be adulterated with an erectile dysfunction drug(s) using HPLC-DAD. The UV spectrum of this compound was highly similar to that of sildenafil and almost identical to that of desmethylpiperazinyl sildenafil. The analogue was purified by using semi-preparative HPLC and structurally elucidated by performing mass spectrometric and NMR spectroscopic experiments. The spectral data revealed that this sildenafil analogue bears an n-propoxy group instead of an ethoxy group and possesses no methylpiperazinyl moiety. The isolated compound, structure of which was further confirmed by spectral comparison with synthetic one, was thus named as desmethylpiperazinyl propoxysildenafil.

DOI: 10.1016/j.scijus.2018.07.003
PMID: 30446074

7. Isolation and structural characterization of a novel sibutramine analogue, chlorosipentramine, in a slimming dietary supplement, by using HPLC-PDA, LC-Q-TOF/MS, FT-IR, and NMR. Yun J, Shin KJ, Choi J, Jo CH.

Forensic Sci Int. 2018 May;286:199-207. doi: 10.1016/j.forsciint.2018.03.021. Epub 2018 Mar 17.

A novel sibutramine analogue was detected in a slimming formula by high performance liquid chromatography with a photo diode detector array (HPLC-PDA). The unknown compound exhibited an ultraviolet (UV) spectrum that was similar to that of chlorosibutramine, despite having a different HPLC retention time. Further analysis of the slimming formula by LC-quadrupole time-of-flight mass spectrometry (LC-Q-TOF/MS) showed that the unknown compound had the formula C₁₈H₂₇Cl₂N. To elucidate the structure of this new sibutramine analogue, the target compound in the slimming formula was isolated on a preparative-LC system equipped with a PDA. After analysis by fourier transform infrared (FT-IR) and nuclear magnetic resonance (NMR) spectroscopy, the unknown compound was identified as a sibutramine analogue in which the iso-butyl group on the side chain is replaced with an iso-pentyl group. This new sibutramine analogue was identified to be 1-(1-(3,4-dichlorophenyl)cyclobutyl)-N,N,4-trimethylpentan-1-amine and has been named as chlorosipentramine.

DOI: 10.1016/j.forsciint.2018.03.021
PMID: 29602147 [Indexed for MEDLINE]

8. Identification and structural elucidation of a new sildenafil analogue, dithiopropylcarbodenafil, from a premixed powder intended as a dietary supplement. Yun J, Shin KJ, Choi J, Kwon K, Jo CH.

J Chromatogr B Analyt Technol Biomed Life Sci. 2018 Jan 1;1072:273-281. doi: 10.1016/j.jchromb.2017.11.029. Epub 2017 Nov 24.

A new sildenafil analogue was detected during the monitoring of a premixed powder intended as a dietary supplement. The ultraviolet (UV) spectrum of the unknown compound was similar to that of dithiodesmethylcarbodenafil and dithiodesethylcarbodenafil, although their corresponding HPLC peaks were observed at different retention times. The chemical structure of the unknown compound was characterized by

liquid chromatography-quadrupole-time-of-flight mass spectrometry (LC-Q-TOF/MS), followed by nuclear magnetic resonance (NMR) and infrared (IR) spectroscopy. The comparison of its structure with that of dithiodesmethylcarbodenafil, revealed that the N-methyl group on the piperazine ring is replaced by a propyl group. This new sildenafil analogue was identified as 5-(2-ethoxy-5-(4-propylpiperazine-1-carbonothioyl)phenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidine-7-thione and designated as a dithiopropylcarbodenafil. To the best of our knowledge, this is the first study reporting the identification and characterization of dithiopropylcarbodenafil.

DOI: 10.1016/j.jchromb.2017.11.029

PMID: 29197303 [Indexed for MEDLINE]

9. Priapism caused by "Rhino 7 Platinum 3000" an over-the-counter male enhancement supplement.

Mittakanti HR, Elliott CS.

Int J Impot Res. 2018 Aug;30(4):190-191. doi: 10.1038/s41443-018-0033-7. Epub 2018 Jun 19

Male enhancement and erectile dysfunction supplements are typically non-Food and Drug Administration (FDA) approved and readily available for purchase by anyone. Longstanding priapism is a significant potential side effect. A 25-year-old man presented with a 48-h priapism after taking Rhino 7 Platinum 3000. He required bilateral corpo-glanular shunting to alleviate his priapism. On initial 2-week follow-up, he had significant fibrosis of the corporal bodies bilaterally and had been unable to achieve an erection. There are few studies performed and few case reports regarding the roles of various supplements in causing priapism. We are unaware of any studies regarding Rhino 7 Platinum 3000. Interestingly, since our initial contact with the FDA Safety Reporting Portal, multiple investigations of Rhino products have demonstrated that sildenafil is a non-labeled ingredient. Given the lack of FDA oversight of many other supplements similar to this one, patients must be wary that the ingredients listed may not be comprehensive and that serious side effects can occur.

DOI: 10.1038/s41443-018-0033-7

PMID: 29915255 [Indexed for MEDLINE]

10. The Risks of Using Herbal Supplements for Sexual Dysfunction Associated With Psychotropic Medications: A Case Report of ExtenZe Use and Priapism.

Lee J, Hong J, Dunn N, Gersh R, Swift R.

J Clin Psychopharmacol. 2018 Jun;38(3):274-275. doi:10.1097/JCP.0000000000000857.

DOI: 10.1097/JCP.0000000000000857

PMID: 29553994 [Indexed for MEDLINE]

11. Infectious complications following probiotic ingestion: a potentially underestimated problem? A systematic review of reports and case series.

Costa RL, Moreira J, Lorenzo A, Lamas CC.

BMC Complement Altern Med. 2018 Dec 12;18(1):329. doi: 10.1186/s12906-018-2394-3.

BACKGROUND: Little is studied about complications related to probiotic ingestion. This study proposes to present a synthesis and critical evaluation of the reports and series of cases on the infectious complications related to the ingestion of probiotics, which can raise awareness for the prescribing and use of probiotics for certain groups of patients. **METHODS:** Systematic review of reports and series of cases researched in the PubMed, SciELO and Scopus databases published until August 2018. The references of the articles were investigated manually for the search of cross references. SPSS version 23.0 was used for descriptive statistics and univariate analysis. **RESULTS:** We found 60 case reports and 7 case series, making up a total of 93 patients. Fungemia was the most common infectious complications with 35 (37.6%) cases. The genus *Saccharomyces* was the most frequent with 47 (50.6%) cases, followed by *Lactobacillus*, *Bifidobacterium*, *Bacillus*, *Pediococcus* and *Escherichia* with 26 (27.9%), 12 (12.8%), 5 (5.4%), 2 (2.2%) and 1 (1.1%) case, respectively. Adults over 60 years of age, *Clostridium difficile* colitis, antibiotic use and *Saccharomyces* infections were associated with overall mortality. HIV infections, immunosuppressive drugs, solid organ transplantation, deep intravenous lines, enteral or parenteral nutrition were not associated with death. **CONCLUSION:** The use of probiotics cannot be considered risk-free and should be carefully evaluated for some patient groups. **TRIAL REGISTRATION:** CRD42016042289.

DOI: 10.1186/s12906-018-2394-3
PMCID: PMC6292120
PMID: 30541524 [Indexed for MEDLINE]

12. Systematic review of published data on herb induced liver injury. Byeon JH, Kil JH, Ahn YC, Son CG.

J Ethnopharmacol. 2019 Apr 6;233:190-196. doi: 10.1016/j.jep.2019.01.006. Epub 2019 Jan 11.

ETHNOPHARMACOLOGICAL RELEVANCE: Herbal products have been widely used as a means of ethnomedicine worldwide. Recently, the potential hepatotoxicity of herbs has become a medical issue but comprehensive studies are limited. **AIM OF THE STUDY:** This study aims to determine the clinical features of herb induced liver injury (HILI) including its constituent ratio among liver injury case cohorts that included both HILI and drug induced liver injury (DILI). **MATERIALS AND METHODS:** A systematic review was conducted using a literature search for DILI/HILI in seven electronic databases including PubMed, Cochrane and Embase. We analyzed the DILI/HILI cases and clinical characteristics in terms of herbs, conventional drugs, concomitant, or others. **RESULTS:** Thirty-one studies met the necessary criteria and included 9 prospective and 22 retrospective studies. Among total number of overall DILI/HILI cases (7511, male 2819, female 3669 and unknown 1023), 25.0% (1874 cases) were implicated in herbs. HILI was relatively higher in females (69.8% vs. 30.2% male), compared to conventional drugs (57.3% female vs. 42.7% male, $p < 0.01$), while it was prone to induce hepatocellular injury (hepatocellular 78.8%, cholestatic 8.9%, mixed type 12.3%), contrary to conventional drugs (hepatocellular 56.7% vs. cholestatic 22.1% vs. mixed 21.2%), respectively ($p < 0.01$). The main herbs causing HILI included *Polygonum multiflorum*, *Psoralea corylifolia*, *Corydalis yanhusuo*, and *Rheum officinale*. **CONCLUSIONS:** This review created the comparative and comprehensive feature of hepatotoxicity by herbal products, which provides reference data for the clinical applications and establishing pharmacovigilance system of herbs.

DOI: 10.1016/j.jep.2019.01.006
PMID: 30639232

13. Risks associated with fat burners: A toxicological perspective. Jakopin Ž.

Food Chem Toxicol. 2019 Jan;123:205-224. doi: 10.1016/j.fct.2018.10.051. Epub 2018 Oct 26.

Dietary supplements "fat burners", freely available on the market, are intended to promote weight loss and reduce fat accumulation, either via stimulation of lipolysis or by inhibition of lipogenesis. Proponents claim that fat burners can increase fat metabolism, although their usefulness remains controversial. Fat burners are usually claimed to be of natural origin and viewed as being inherently safe. This review focuses on the most common ingredients of natural origin usually found in the fat burners, their molecular mechanisms of action and the toxicological profiles of these compounds in order to gain an insight into their safety.

DOI: 10.1016/j.fct.2018.10.051
PMID: 30401639 [Indexed for MEDLINE]

14. Evidence for the efficacy and safety of herbal weight loss preparations. Farrington R, Musgrave IF, Byard RW.

J Integr Med. 2019 Jan 30. pii: S2095-4964(19)30009-3. doi: 10.1016/j.joim.2019.01.009. [Epub ahead of print]

Rising rates of obesity across the globe have been associated with an increase in the use of herbal preparations for weight control. However, the mechanisms of action for these substances are often not known, as is the potential for interaction with other herbal preparations or prescription pharmaceutical drugs. To investigate the reported efficacy and safety of herbal weight loss preparations, we conducted a review of the literature focusing on herbs that are most commonly used in weight loss preparations, specifically, *Garcinia cambogia*, *Camellia sinensis*, *Hoodia gordonii*, *Citrus aurantium* and *Coleus forskohlii*. There was no clear evidence that the above herbal preparations would cause sustained long-term weight loss in humans in the long term. Serious illness and even death have occasionally resulted from the use of herbal weight loss preparations. Few clinical trials have been undertaken to evaluate the efficacy and/or safety of herbal weight loss preparations. In addition, potential issues of herb-herb and herb-drug interactions are often not

considered. Regulation of these products is much less rigorous than for prescription medications, despite documented cases of associated hepatotoxicity.

DOI: 10.1016/j.joim.2019.01.009

PMID: 30738773

15. Drug-induced autoimmune hepatitis associated with turmeric dietary supplement use. Lukefahr AL, McEvoy S, Alfafara C, Funk JL.

BMJ Case Rep. 2018 Sep 10;2018. pii: bcr-2018-224611. doi: 10.1136/bcr-2018-224611.

Turmeric dietary supplement sales, which accounted for US\$69 million in spending in 2016, have been increasing exponentially in the USA, making this one of the most popular botanical supplements sold in the USA. Herbal supplement use, which is generally regarded as safe by consumers, is not usually reported to healthcare providers. We reported here on a case of autoimmune hepatitis, occurring in a 71-year-old woman taking turmeric dietary supplements for the maintenance of cardiovascular health, which resolved rapidly following discontinuation of the turmeric supplements. Of particular note, turmeric use was not documented in the patient's medical records and the potential causative role of the turmeric supplementation was ultimately identified by the patient rather than the healthcare providers. To our knowledge, this is the first documented report of turmeric supplement-induced autoimmune hepatitis.

DOI: 10.1136/bcr-2018-224611

PMID: 30206065 [Indexed for MEDLINE]

16. Liver transplantation and the use of KAVA: Case report. Becker MW, Lourençone EMS, De Mello AF, Branco A, Filho EMR, Blatt CR, Mallmann CA, Schneider M, Caregnato RCA, Blatt CR.

Phytomedicine. 2018 Aug 9;56:21-26. doi: 10.1016/j.phymed.2018.08.011. [Epub ahead of print]

BACKGROUND: Self-medication and the belief that herbal products are free of health risks are common in Brazil. The kava (*Piper methysticum*), known for its anxiolytic action, has a widespread popular use. Hepatotoxicity of kava is reported, including cases of liver transplantation and death. The kava had its use prohibited or restricted in countries like Germany, France, among others. Toxicity may be related to overdosage; however, factors such as botanical characteristics of the plant, the harvesting, storage, and production process may be associated with the development of hepatotoxic substances, such as triggering idiosyncratic reactions. **HYPOTHESIS:** In this case, there is a suspicion that the toxicide is intrinsic to the drug; however, the possibility of adulterants and contaminants must be ruled out. **STUDY DESIGN:** This study reports the case of a patient who, after using the herbal kava for 52 days, evolved into acute liver failure and liver transplantation. **METHODS:** The data were collected directly with the patient and compared with their clinical records. Causality was determined through the RUCAM algorithm. In addition, a phytochemical analysis of the drug used was performed. **RESULTS:** According to the patient's report, there is no evidence of overdosage. Results from RUCAM algorithm infer causality between liver damage and the use of kava. The analysis chemical constituents did not find any possible contaminants and major changes in the active compounds. Seven months after transplantation, the patient is well and continues to be followed up by a medical team. **CONCLUSION:** Our investigation indicates that there was kava-induced hepatotoxicity at standard dosages. In Brazil, self-medication by herbal medicines is frequent and many patients and health professionals do not know the risks associated with their use. Diagnosing and notifying cases in which plants and herbal medicine induce liver damage is of paramount importance to increase the knowledge about DILI and to prevent or treat similar cases quickly.

DOI: 10.1016/j.phymed.2018.08.011

PMID: 30668342

17. Arsenic-Induced Neuropathy by Improper Use of Chinese Medicine: A Case Report. Chang RS, William Leung CY, Cheung TT, Chan CK.

Am J Ther. 2018 May/Jun;25(3):e392-e393. doi: 10.1097/MJT.0000000000000576.

No Abstract

DOI: 10.1097/MJT.0000000000000576
PMID: 28394768 [Indexed for MEDLINE]

18. The vitamin epidemic: what is the evidence for harm or value? Kennedy M.

Intern Med J. 2018 Aug;48(8):901-907. doi: 10.1111/imj.13976.

Complementary medicines are a multibillion-dollar industry of which vitamin supplements are an important component. Most of the claims of benefit are not evidenced-based, and vitamin supplements may be associated with severe adverse reactions that are uncommon but can occur with high doses of some vitamins. There is no case for vitamin supplementation in normal, healthy, non-pregnant or lactating adults who are receiving the recommended daily intake of nutrients.

DOI: 10.1111/imj.13976
PMID: 30133982 [Indexed for MEDLINE]

19. Urticaria by thiamine (vitamin B1). Rodríguez-Fernández A, Sánchez-Domínguez M, Noguero-Mellado B, Rojas-Pérez-Ezquerria P.

Allergol Int. 2018 Apr;67(2):276-277. doi: 10.1016/j.alit.2017.07.008. Epub 2017 Aug 23.

No Abstract

DOI: 10.1016/j.alit.2017.07.008
PMID: 28843441 [Indexed for MEDLINE]

20. Myasthenia gravis exacerbation after red yeast rice use. Dobremez V, Serra A, Grosset-Janin D, Dopter A, Pineau-Blondel E, Ruel JH.

Rev Neurol (Paris). 2018 Sep - Oct;174(7-8):577-578. doi: 10.1016/j.neurol.2017.08.006. Epub 2018 Jul 14.

No Abstract (French)

DOI: 10.1016/j.neurol.2017.08.006
PMID: 30017101 [Indexed for MEDLINE]

21. Chinese herbal remedy found to contain steroids and antifungals. Mose KF, Bygum A.

Lancet. 2019 Feb 2;393(10170):446. doi: 10.1016/S0140-6736(19)30116-3.

No Abstract

DOI: 10.1016/S0140-6736(19)30116-3
PMID: 30712902 [Indexed for MEDLINE]

22. An unforeseen complication of a folk remedy for joint pain. Assous MV, Schwartz Y, Ben-Chetrit E.

Med Mal Infect. 2018 Aug;48(5):374-375. doi: 10.1016/j.medmal.2018.03.004. Epub 2018 Apr 12.

No Abstract

DOI: 10.1016/j.medmal.2018.03.004
PMID: 29656840 [Indexed for MEDLINE]

23. First case of symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) due to Berberine, an over-the-counter herbal glyceemic control agent. Labadie JG, Florek AG, Croitoru A, Liu W, Kronic AL.

Int J Dermatol. 2018 Sep;57(9):e68-e70. doi: 10.1111/ijd.14059. Epub 2018 May 29.

No Abstract

DOI: 10.1111/ijd.14059

PMID: 29808929 [Indexed for MEDLINE]

24. Unwanted effects of psychotropic drug interactions with medicinal products and diet supplements containing plant extracts. Woroń J, Siwek M.

Psychiatr Pol. 2018 Dec 29;52(6):983-996. doi: 10.12740/PP/OnlineFirst/80998. Epub 2018 Dec 29.

OBJECTIVES: Assessment of adverse drug interactions with herbal preparations (HP), i.e., plant medicines and nutritional supplements which contain plant extracts. **METHODS:** Analysis of 147 cases of adverse events with clinical picture indicating probability or certainty of resulting from inclusion of HP into the applied pharmacotherapy (mostly psychotropic drugs). **RESULTS:** The most common effect of interactions between SSRI or SNRI antidepressants and HP were hemorrhagic complications associated with Japanese ginkgo biloba (27.45% of complications in this subgroup). Another common complication was serotonin syndrome (SS) (11.8%) occurring during the use of ginseng (one case of SS after the addition of bacopa). In the group of antipsychotic drugs, the highest number of interactions was observed in the case of haloperidol, and the highest number of complications (29.8%) was associated with ginseng (including 6 cases of ventricular arrhythmias in combination with haloperidol), milk thistle (including 7 cases of pancreatitis in combination with haloperidol or risperidone, 1 case of hepatotoxicity after adding aripiprazole) and rhodiola rosea. As for hypnotics and sedatives - interactions with ginseng were most frequently reported, mainly intensified sedative effects, cognitive disorders and disturbances in consciousness. In 132 cases, withdrawal of the plant preparation resulted in a decrease in the severity of the reported adverse reactions or a complete resolution of the described symptoms. **CONCLUSIONS:** HP (especially ginseng, rhodiola rosea, ginkgo biloba, milk thistle) are associated with a significant risk of pharmacokinetic and pharmacodynamic interactions with psychotropic drugs. Because of the resulting complications and side effects, any decision to include a herbal supplement should be preceded by a detailed safety analysis with benefit and risk assessment.

DOI: 10.12740/PP/OnlineFirst/80998

PMID: 30659561

25. Protective effect of berberine on aconite-induced myocardial injury and the associated mechanisms. Chen X, Guo H, Li Q, Zhang Y, Liu H, Zhang X, Xie K, Zhu Z, Miao Q, Su S.

Mol Med Rep. 2018 Nov;18(5):4468-4476. doi: 10.3892/mmr.2018.9476. Epub 2018 Sep 12.

Aconitum plants, which have analgesic, diuretic and anti-inflammatory effects, have been widely used to treat various types of disease. However, the apparent toxicity of Aconitum-derived agents, particularly in the cardiovascular system, has largely limited their clinical use. Thus, the present study investigated whether berberine (Ber), an isoquinoline alkaloid, may reduce myocardial injury induced by aconitine (AC) in rats and the underlying mechanisms. Rats (n=40) were randomly divided into four groups: Control, Chuan-wu and Chuan-wu + Ber (8 and 16 mg/kg doses). Electrocardiograms (ECG) of the rats were recorded and serum biomarkers of cardiac function [lactate dehydrogenase (LDH), creatine kinase (CK) and CK-MB] were assayed. Histopathological changes were assessed using myocardial tissue sectioning and hematoxylin and eosin staining. Additionally, the effects of Ber on AC-induced arrhythmias in rats were observed. The changes in ECG following AC perfusion were observed, and the types and onset time of arrhythmias were analyzed. Furthermore, the effects of Ber and AC on papillary muscle action potentials were observed. The results suggested that Ber ameliorated myocardial injury induced by Chuan-wu, which was indicated by reduced arrhythmias and decreased LDH, CK and CK-MB levels in serum. Furthermore, histological damage, including dilation of small veins and congestion, was also markedly attenuated by Ber. In addition, the occurrence of arrhythmias was significantly delayed, and the dosage of AC required to induce arrhythmias was also increased by Ber pretreatment. Additionally, AC-induced changes in action potential amplitude, duration of 30% repolarization and duration of 90% repolarization in the papillary muscle were attenuated by Ber. All of these results indicate that Ber had a preventive effect on acute myocardial injury induced by Chuan-wu and arrhythmias caused by AC, which may be associated with the inhibition of delayed depolarization and triggered activity caused by AC. Thus, combination treatment of Ber with Aconitum plants may be a novel strategy to prevent AC-induced myocardial injury in clinical practice.

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