AACT Herbal Dietary Supplements SIG Abstracts Jan. 2017

1. Lead intoxication due to ayurvedic medications as a cause of abdominal pain in adults. Mehta V, Midha V, Mahajan R, Narang V, Wander P, Sood R, Sood A.

Clin Toxicol (Phila). 2016 Dec 13:1-5. [Epub ahead of print]

BACKGROUND: Though a majority of cases of lead intoxication come from occupational exposures, traditional and folk remedies have also been reported to contain toxic amounts of lead. We present a large series of patients with lead poisoning due to intake of Ayurvedic medicines, all of whom presented with unexplained abdominal pain. METHODOLOGY: This was a retrospective, observational case series from a tertiary care center in India. The charts of patients who underwent blood lead level (BLL) testing as a part of workup for unexplained abdominal pain between 2005 and 2013 were reviewed. The patients with lead intoxication (BLLs >25 μg/dl) were identified and demographics, history, possible risk factors, clinical presentation and investigations were reviewed. Treatment details, duration, time to symptomatic recovery, laboratory follow-up and adverse events during therapy were recorded. RESULTS: BLLs were tested in 786 patients with unexplained abdominal pain and high levels were identified in 75 (9.5%) patients, of which a majority (73 patients, 9.3%) had history of Ayurvedic medication intake and only two had occupational exposure. Five randomly chosen Ayurvedic medications were analyzed and lead levels were impermissibly high (14-34,950 ppm) in all of them. Besides pain in abdomen, other presenting complaints were constipation, hypertension, neurological symptoms and acute kidney injury. Anemia and abnormal liver biochemical tests were observed in all the 73 patients. Discontinuing the Ayurvedic medicines and chelation with d-penicillamine led to improvement in symptoms and reduction in BLLs in all patients within 3-4 months. CONCLUSION: The patients presenting with severe recurrent abdominal pain, anemia and history of use of Ayurvedic medicines should be evaluated for lead toxicity. Early diagnosis in such cases can prevent unnecessary investigations and interventions, and permits early commencement of the treatment.

DOI: 10.1080/15563650.2016.1259474
PMID: 27957879 [PubMed - as supplied by publisher]

2. Traditional medicine preparations and health risks: time to revisit their regulatory status. De Capitani EM.

Clin Toxicol (Phila). 2016 Nov 24:1-2. [Epub ahead of print]

DOI: 10.1080/15563650.2016.1260138
PMID: 27882778 [PubMed - as supplied by publisher]

3. Herbal Medicines Induced Anticholinergic Poisoning in Hong Kong. Chan TY.

Toxins (Basel). 2016 Mar 18;8(3). pii: E80. doi: 10.3390/toxins8030080.

In the present review, the main objective was to report the incidence and causes of herbal medicines induced anticholinergic poisoning in Hong Kong during 1989-2012 and to emphasize the importance of pharmacovigilance, investigations and preventive measures. Relevant papers, official figures and unpublished data were obtained from Medline search, the Department of Health and the Drug and Poisons Information Bureau. In the New Territories East (where ~20% of the Hong Kong population lived), the incidence of herbal medicines induced anticholinergic poisoning during 1989-1993 was 0.09 per 100,000 population. There were no confirmed cases during 1994-1996. In the whole of Hong Kong, the incidence during 2000-June 2005 was 0.03 per 100,000 population. Contamination of Rhizoma Atractylodis (50%) and erroneous substitution (42%) were the main causes. The incidence during 2008-2012 was 0.06 per 100,000 population. Contamination of non-toxic herbs (50%) and erroneous substitution (41%) were the main causes. In Hong Kong, contamination of non-toxic herbs by tropane alkaloids and substitution of Flos Campsis by toxic Flos Daturae Metelis were the predominant causes of herbal medicines induced anticholinergic poisoning. Systematic studies along the supply chain are necessary to identify the likely sources of contamination. If erroneous substitution of Flos Campsis by Flos Daturae Metelis could be prevented, 40% of herbal medicines induced anticholinergic poisoning would not have occurred. Regular inspection of the retailer, continuing education for the staff in the herbal trade and repeated publicity measures will also be required. Pharmacovigilance of herbal medicines should help determine the incidence and causes of adverse reactions and monitor the effectiveness of preventive measures.

DOI: 10.3390/toxins8030080
PMCID: PMC4810225
PMID: 26999208 [PubMed - indexed for MEDLINE]St

4. St. John's wort treatment in women bears risks beyond pharmacokinetic drug interactions. Hohmann N, Maus A, Carls A, Haefeli WE, Mikus G.

Arch Toxicol. 2016 Apr;90(4):1013-5. doi: 10.1007/s00204-015-1532-7. Epub 2015 May 12.

We analyzed adverse events in a clinical phase I trial to assess dose-dependent metabolic effects of St. John's wort co-administered with rifampicin in 12 healthy volunteers. Within 3-6 days after increasing the St. John's wort dose from 300 to 600 mg TID, five of six female participants developed ambient temperature-dependent allodynia and paresthesia in sun-exposed areas (back of the hands and perioral and nasal area). Aggravation of symptoms resulted in persistence of paresthesia and phototoxic erythrodermia. None of the male participants showed any of these effects. Gender, duration of treatment, dose, and solar exposure seem to be extrinsic and host factors facilitating St. John's wort-induced neuropathy. The risk to develop this adverse effect is almost exclusively present in women.

DOI: 10.1007/s00204-015-1532-7
PMID: 25963330 [PubMed - indexed for MEDLINE]

5. Impaired Glucose Tolerance in Healthy Men Treated with St. John's Wort. Stage TB, Damkier P, Christensen MM, Nielsen LB, Højlund K, Brøsen K.

Basic Clin Pharmacol Toxicol. 2016 Mar;118(3):219-24. doi: 10.1111/bcpt.12486. Epub 2015 Oct 8.

The purpose of this study was to examine whether the over-the-counter herbal medicinal plant St. John's wort affects glucose tolerance in healthy men. To do this, we included 10 healthy men who were examined by a 2-hr oral glucose tolerance test on three occasions: A: baseline; B: after 21 days of treatment with St. John's wort; and C: at least 6 weeks after the last capsule of St. John's wort was ingested. Plasma glucose, serum insulin and C-peptide levels were measured during an oral glucose tolerance test and used for estimation of area under the concentration-time curve (AUC) as well as indices of insulin sensitivity and insulin secretion. We found that treatment with St. John's wort increased total and incremental glucose AUC and 2-hr plasma glucose levels. Surprisingly, this effect was sustained and even further increased 6 weeks after the last capsule of St. John's wort was taken. No effect on indices of insulin sensitivity was seen, but indices of insulin secretion were reduced even after adjustment for insulin sensitivity. In conclusion, this study indicates that long-term treatment with St. John's wort may impair glucose tolerance by reducing insulin secretion in young, healthy men. The unregulated use of this over-the-counter drug might be a risk factor for impaired glucose tolerance and type 2 diabetes.

DOI: 10.1111/bcpt.12486
PMID: 26346185 [PubMed - indexed for MEDLINE]

6. Pick your poison: hERG-blocking alkaloids in the emetic herbal drug ipecac. Kratz JM, Mair CE, Oettl SK, Saxena P, Scheel O, Schuster D, Hering S, Rollinger JM.

Planta Med. 2016 Dec;81(S 01):S1-S381. Epub 2016 Dec 14.

The human ether a-go-go related gene (hERG) channel is an important antitarget associated with QT interval prolongation and increased risk of fatal arrhythmias [1]. Although hERG-safety evaluation is mandatory in formal drug discovery, natural products are rarely evaluated. As botanicals continue to rise in popularity, there is an urgent need for hERG-related cardiotoxic risks assessment. Here, we implemented in silico/in vitro approaches for the fast identification of hERG-blocking constituents in highly consumed herbal remedies. Firstly, we virtually screened a multi-conformational 3D molecular natural product database with a previously validated pharmacophore model [2]. For pharmacological profiling, lead-like enhanced extracts from virtually predicted and commonly consumed botanicals (n = 55) were prepared [3] and screened in Xenopus oocytes (100 µg/mL). The combined approach revealed 32.5% hERG blockade for the Carapichea ipecacuanha root extract, and six virtually predicted blockers from the group of ipecac alkaloids. Chromatographic separation resulted in the isolation and identification of five alkaloids (emetine, cephaeline, N-methylemetine, psychotrine and O-methylpsychotrine). All compounds were virtual hits and blocked hERG currents to different extents in vitro. The underground parts of C. ipecacuanha, alkaloid-enriched organs, are extracted for producing ipecac syrup, which is used as an emetic in emergency poisoning. Major ipecac constituents, emetine and cephaeline, showed IC50 values of 21.4 and 5.3µM, respectively, in HEK293 cells. Chronic abuse of ipecac products is known to induce cardiotoxicity in patients with eating disorders. However, this is the first report on the hERG-blockage of ipecac's major alkaloids. Our findings raise further questions regarding the safety of such herbal products, especially due to their tissue accumulation [4]. If combined with drugs or dietary supplements containing hERG blockers [5] they might boost cardiotoxicity.

DOI: 10.1055/s-0036-1597035
PMID: 27976234 [PubMed - in process]

7. Ayahuasca Exposure: Descriptive Analysis of Calls to US Poison Control Centers from 2005 to 2015. Heise CW, Brooks DE.

J Med Toxicol. 2016 Nov 28. [Epub ahead of print]

BACKGROUND: Ayahuasca is a hallucinogenic plant preparation which usually contains the vine Banisteriopsis caapi and the shrub Psychotria viridis. This tea originates from the Amazon Basin where it is used in religious ceremonies. Because interest in these religious groups spreading as well as awareness of use of ayahuasca for therapeutic and recreational purposes, its use is increasing. Banisteriopsis caapi is rich in β-carbolines, especially harmine, tetrahydroharmine and harmaline, which have monoamine oxidase inhibiting (MAOI) activity. Psychotria viridis contains the 5HT2A/2C/1A receptor agonist hallucinogen N,N-dimethyltryptamine (DMT). Usual desired effects include hallucination, dissociation, mood alteration and perception change. Undesired findings previously reported are nausea, vomiting, hypertension, and tachycardia. METHODS: All human exposure calls reported to the American Association of Poison Controls Centers' (AAPCC) National Poison Data System (NPDS) between September 1,2005 and September 1, 2015 were reviewed. Cases were filtered for specific plant derived ayahuasca-related product codes. Abstracted data included the following: case age and gender, exposure reason, exposure route, clinical manifestations, treatments given, medical outcomes and fatality. RESULTS: Five hundred and thirty-eight exposures to ayahuasca botanical products were reported. The majority of the calls to poison control centers came from healthcare facilities (83%). The most common route of exposure was ingestion. Most cases were men (437, 81%, 95% CI 77.7% - 84.3%). The median age was 21 (IQR 18-29). Most exposures were acute. Three hundred thirty-seven (63%) were reported to have a major or moderate clinical effect. The most common clinical manifestations reported were hallucinations (35%), tachycardia (34%), agitation (34%), hypertension (16%), mydriasis (13%) and vomiting (6%). Benzodiazepines were commonly given (30%). There were 28 cases in the series who required endotracheal intubation (5%). Four cases were reported to have had a cardiac arrest and 7 a respiratory arrest. Twelve cases had a seizure. Reports of exposures called to poison centers appeared to increase during this period based on annual estimates. Three fatalities were reported. CONCLUSIONS: Ayahuasca use appears to be rising in the United States based on calls to poison control centers. While most use is reported to be safe and well tolerated, with possible beneficial effects, serious and life threatening adverse manifestations are possible. Most of the exposures reported to poison control centers were young people, more likely to be men and already in a healthcare facility. Further research, which includes comprehensive drug testing, will be needed to better identify the risks and effects of ayahuasca use.

DOI: 10.1007/s13181-016-0593-1
PMID: 27896660 [PubMed - as supplied by publisher]

8. In vitro toxicity evaluations of Tibetan medicine Zuota from four institutions. Li B, Li YD, Yang Z, Chen Y, Liu P, Liu Y, Zhang ZF, Lv LY, Zhang JZ, Zeng R, Li LM.

Drug Chem Toxicol. 2016;39(2):174-81. doi: 10.3109/01480545.2015.1065416. Epub 2015 Jul 21.

Zuota is regarded as the king of Tibetan medicine. However, the major starting material of Zuota is mercury, which is one very toxic heavy metal. This has aroused serious doubts on the biosafety of Zuota containing drugs. In this study, we quantified the Hg contents in four Zuota samples, monitored the release of Hg in simulated gastric/intestinal juice and evaluated their cytotoxicity to Caco-2 cells. Our results showed that the Hg contents in Zuota samples were in the range of 566-676 mg/g. Fortunately, the release of Hg from Zuota samples was very low in simulated gastric juice, and much lower in simulated intestinal juice. Direct contact of Zuota with Caco-2 cells led to dose-dependent cytotoxicity, including activity loss and membrane leakage. The toxicity was closely related to apoptosis, because the caspase 3/7 levels of Caco-2 cells increased after the exposure to Zuota. Interestingly, Zuota samples inhibited the oxidative stress at low concentrations, but the toxicity could be relived by antioxidants. The possible toxicity should be attributed to the cellular uptake of Zuota particulates. Beyond the cytotoxicity, significant differences among Zuota samples from different institutions were observed, suggesting that the preparation process of Zuota had meaningful influence of its biosafety. The implications to the safety and clinical applications of Zuota are discussed.

DOI: 10.3109/01480545.2015.1065416
PMID: 26195083 [PubMed - indexed for MEDLINE]

9. Detection of aristolochic acids I and II in "Chiniy-trèf", a traditional medicinal preparation containing caterpillars feeding on Aristolochia trilobata L. in Martinique, French West Indies. Cachet X, Langrand J, Bottai C, Dufat H, Locatelli-Jouans C, Nossin E, Boucaud-Maitre D.

Toxicon. 2016 May;114:28-30. doi: 10.1016/j.toxicon.2016.02.013. Epub 2016 Feb 12.

"Chiniy-trèf" is a traditional medicinal preparation used in Martinique, French West Indies, for the prevention of all kinds of attempted poisoning and hex. It is produced by the maceration in alcohol (mostly rum) of larvae (caterpillars) of the butterfly Battus polydamas ssp. cebriones, feeding on the leaves of Aristolochia trilobata. Aristolochic acids I and II that are well-known nephrotoxic and carcinogenic substances were identified on two samples of "chiniy-trèfl" by chromatographic methods.

DOI: 10.1016/j.toxicon.2016.02.013
PMID: 26879332 [PubMed - indexed for MEDLINE]

10. Risk assessment of plant food supplements and other herbal products containing aristolochic acids using the margin of exposure (MOE) approach. Abdullah R, Diaz LN, Wesseling S, Rietjens IM.

Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2016 Dec 16:1-10. [Epub ahead of print]

After the incidences of induction of aristolochic acid nephropathy after consumption of herbal weight loss preparations that accidentally contained aristolochic acids (AAs), several countries defined national restrictions on the presence of AAs in food, including plant food supplements (PFS) and herbal products. This study investigates whether the risks associated with exposure to AAs via PFS and herbal products are at present indeed negligible. Data reported in literature on AA levels in PFS and other herbal products and also obtained from a new series of PFS in the present study were used to calculate the estimated daily intakes (EDIs) and corresponding margins of exposure (MOEs). Available literature data revealed that 206 out of 573 samples were found to contain aristolochic acid I (AAI) and/or aristolochic acid II (AAII). The results obtained from recently collected PFS revealed that both AAI and AAII were detected in three out of 18 analysed PFS at levels up to 594.8 and 235.3 μg g(-1), respectively, being in line with the levels reported in literature. The EDIs resulting from intake of these PFS resulted in MOEs that were generally below 10,000, corroborating the priority for risk management. Although these results refer to PFS collected by targeted sampling strategies, the data reveal that AA-containing PFS are still freely available. When considering that the use of these samples may be limited to shorter periods of time, the EDIs might be lower, but MOE values would still be lower than 10,000 for more than 50% of the AA-containing PFS and herbal products. In conclusion, the presence of AAs in PFS and herbal products even several years after instalment of the legal restrictions still raises concern, especially for people who frequently use the respective PFS and herbal products.

DOI: 10.1080/19440049.2016.1266098
PMID: 27892830 [PubMed - as supplied by publisher]

11. Aristolochic Acid I Causes Testis Toxicity by Inhibiting Akt and ERK1/2 Phosphorylation. Kwak DH, Lee S.

Chem Res Toxicol. 2016 Jan 19;29(1):117-24. doi: 10.1021/acs.chemrestox.5b00467. Epub 2015 Dec 22.

Aristolochic acid (AA) is a natural bioactive substance found in Chinese herbs that induce toxicity during ovarian maturation of animals and humans. Apoptosis is induced by various types of damage and governs the progression of biological cell removal that controls the equilibrium between cell growth and death. However, the AA toxicity mechanism during testis maturation in mouse has not been elucidated and was thus the focus of the present study. This study used TM4 Sertoli cells and an ICR mouse model, both of which were injected with aristolochic acid I (AAI) for 4 weeks. Testis dimensions and weight were surveyed to define AAI cytotoxicity in the mice testis. The MTT assay was used to analyze the cytotoxicity of AAI in TM4 Sertoli cells. An apoptosis expression mediator was analyzed through Western blotting, while the measure of apoptosis-induced cell death of TM4 Sertoli cells and testis tissues was analyzed by the TUNEL assay. We found that AAI strongly inhibits survival in TM4 cells and that AAI significantly activated apoptosis-induced cell death in TM4 Sertoli cells and mice testis tissue. In addition, AAI suppressed the expression of B-cell lymphoma 2 (Bcl-2), a factor related to anti-apoptosis. It markedly improved pro-apoptotic protein expression, including Bcl-2-associated X protein, poly(ADP-ribose) polymerase, and caspase-3 and -9. Furthermore, we observed that AAI significantly reduced the size and weight of mouse testis. Moreover, germ cells and somatic cells in testis were markedly damaged by AAI. In addition, we found that AAI significantly inhibits ERK1/2 and Akt activation in TM4 Sertoli cells and testis tissue. The data obtained in this study indicate that AAI causes severe injury for the period of testis development by impeding apoptosis related to the Akt and ERK1/2 pathway.

DOI: 10.1021/acs.chemrestox.5b00467
PMID: 26656393 [PubMed - indexed for MEDLINE]

12. Plants Producing Ribosome-Inactivating Proteins in Traditional Medicine. Polito L, Bortolotti M, Maiello S, Battelli MG, Bolognesi A.

Molecules. 2016 Nov 18;21(11). pii: E1560.

Ribosome-inactivating proteins (RIPs) are enzymes that deadenylate nucleic acids and are broadly distributed in the plant kingdom. Many plants that contain RIPs are listed in the pharmacopoeias of folk medicine all over the world, mostly because of their toxicity. This review analyses the position occupied in traditional medicine by plants from which RIPs have been isolated. The overview starts from the antique age of the Mediterranean area with ancient Egypt, followed by the Greek and Roman classic period. Then, the ancient oriental civilizations of China and India are evaluated. More recently, Unani medicine and European folk medicine are examined. Finally, the African and American folk medicines are taken into consideration. In conclusion, a list of RIP-expressing plants, which have been used in folk medicine, is provided with the geographical distribution and the prescriptions that are recommended by traditional healers. Some final considerations are provided on the present utilization of such herbal treatments, both in developing and developed countries, often in the absence of scientific validation. The most promising prospect for the medicinal use of RIP-expressing plants is the conjugation of purified RIPs to antibodies that recognise tumour antigens for cancer therapy.

DOI: 10.3390/molecules21111560
PMID: 27869738 [PubMed - in process]

13. Scientific and Regulatory Perspectives in Herbal and Dietary Supplement Associated Hepatotoxicity in the United States. Avigan MI, Mozersky RP, Seeff LB.

Int J Mol Sci. 2016 Mar 3;17(3):331. doi: 10.3390/ijms17030331.

In the United States (US), the risk of hepatotoxicity linked to the widespread use of certain herbal products has gained increased attention among regulatory scientists. Based on current US law, all dietary supplements sold domestically, including botanical supplements, are regulated by the Food and Drug Administration (FDA) as a special category of foods. Under this designation, regulatory scientists do not routinely evaluate the efficacy of these products prior to their marketing, despite the content variability and phytochemical complexity that often characterizes them. Nonetheless, there has been notable progress in the development of advanced scientific methods to qualitatively and quantitatively measure ingredients and screen for contaminants and adulterants in botanical products when hepatotoxicity is recognized.

DOI: 10.3390/ijms17030331
PMCID: PMC4813193
PMID: 26950122 [PubMed - indexed for MEDLINE]

14. Mandatory disclaimers on dietary supplements do not reliably communicate the intended issues. Kesselheim AS, Connolly J, Rogers J, Avorn J.

Health Aff (Millwood). 2015 Mar;34(3):438-46. doi: 10.1377/hlthaff.2014.0515.

Some efforts by the government to regulate the promotional statements of pharmaceutical manufacturers have recently been found unconstitutional under the First Amendment, which has been interpreted to protect commercial as well as personal speech. As an alternative means of protecting patients from unreliable marketing claims, courts have proposed that the Food and Drug Administration could add disclaimers to promotional messages that discuss off-label, or unapproved, uses. We conducted a systematic review of studies of the disclaimers currently required for dietary supplements, to assess how well disclaimers inform consumers' health choices. A few small studies reported a modest impact of disclaimers on consumers' attitudes about dietary supplements, but larger and more rigorous studies generally revealed that many consumers were unaware of a disclaimer or reported that it did not affect their perceptions of a product. The available evidence indicates that replacing government restrictions on pharmaceutical marketing with potentially ineffective disclaimers will be an inadequate way of informing patients about the efficacy and safety of drugs, and it risks returning the United States to a previous era when inappropriate marketing claims about prescription drugs proliferated and contributed to the
inappropriate use of those products.

DOI: 10.1377/hlthaff.2014.0515
PMID: 25732494 [PubMed - indexed for MEDLINE]

15. An overview of herb and dietary supplement efficacy, safety and government regulations in the United States with suggested improvements. Part 1 of 5 series. Brown AC.

Food Chem Toxicol. 2016 Nov 3. pii: S0278-6915(16)30402-1. doi: 10.1016/j.fct.2016.11.001. [Epub ahead of print]

This is the first of five review articles investigating dietary supplements (DS; includes herbs) that now exceed over 50,000 in the Office of Dietary Supplement’s "Dietary Supplement Label Database." Four review articles follow summarizing published medical case reports of DS related to liver toxicity, kidney toxicity, heart toxicity, and cancer. The most popular DS were vitamin or mineral supplements (43%) followed by specialty supplements (20%), botanicals (20%; herbs), and sports supplements (16%). The 2013 Annual Report of the American Association of Poison Control Centers revealed 1692 fatalities due to drugs, and zero deaths due to DS. Less than 1 percent of Americans experience adverse events related to DS, and the majority was classified as minor, with many of these related to caffeine, yohimbe, or other stimulant ingredients. The number one adulterant in DS is drugs, followed by New Dietary Ingredients (NDI) not submitted to the FDA - both are illegal and not DS, but rather "tainted products marketed as dietary supplements." The three main categories of DS prone to medical problems are those for sexual enhancement, weight loss, and sports performance/body building. DS are regulated in the U.S. by several federal agencies with overlapping jurisdiction - the Food and Drug Administration (FDA) and the Federal Trade Commission (FTC); enforced by the State Attorneys General Offices (AGO) and Department of Justice (DOJ); and monitored (not regulated) by the Centers for Disease Control and Prevention (CDC). The FDA can remove a DS from the market for phase IV post-marketing surveillance adverse event reports, adulteration (drugs, NDI, synthetic substances), contamination, misidentification, mislabeling or false claims, and not meeting good manufacturing practices (GMP). The FTC and state AGO can also enforce laws

against deceptive marketing practices. Suggested improvements to current regulatory requirements are included along with online DS Toxic Tables in the series to forewarn consumers, clinicians, corporations, and governments of possible serious adverse events. They may also quicken the response rate during Phase IV post-marketing surveillance, in which governments could then exercise their regulatory powers.

DOI: 10.1016/j.fct.2016.11.001
PMID: 27818322 [PubMed - as supplied by publisher]

16. Herbal Medicines: challenges in the modern world. Part 5. status and current directions of complementary and alternative herbal medicine worldwide. Enioutina EY, Salis ER, Job KM, Gubarev MI, Krepkova LV, Sherwin CM.

Expert Rev Clin Pharmacol. 2016 Dec 15:1-12. [Epub ahead of print]

INTRODUCTION: Herbal medicine (HM) use is growing worldwide. Single herb preparations, ethnic and modern HM formulations are widely used as adjunct therapies or to improve consumer wellbeing. Areas covered: This final part in the publication series summarizes common tendencies in HM use as adjunct or alternative medicine, education of healthcare professionals and consumers, current and proposed guidelines regulating of production. We discuss potential HM-HM and HM-drug interactions that could lead to severe adverse events in situations where HMs are taken without proper medical professional oversight. Expert commentary: A number of serious problems have arisen with the steady global increase in HM use. HM interaction with conventional drugs (CD) may result in inadequate dosing of CD or adverse reactions; HM-HM interaction within herbal supplements could lead to toxicity of formulations. Inadequate education of clinicians and patients regarding medicinal properties of HMs must be addressed regionally and globally to ensure consumer safety.

DOI: 10.1080/17512433.2017.1268917
PMID: 27923318 [PubMed - as supplied by publisher]

17. Nutritional and sports supplement use among deployed U.S. Army soldiers in a remote, austere combat outpost in eastern Afghanistan. Paisley RD.

Mil Med. 2015 Apr;180(4):391-401. doi: 10.7205/MILMED-D-14-00334.

BACKGROUND: Nutritional and sports supplements are commonly used by soldiers, with uncertain implications for health and mission readiness. METHODS: An anonymous survey was conducted of a company of U.S. Army paratroopers deployed to eastern Afghanistan between December 2011 and October 2012. Survey questions covered supplements used, duration of use, adverse effects, and medication interactions. Exercise habits, goals for exercise and supplement use, and information and acquisition sources were also queried. RESULTS: Out of 112 surveys distributed, 100 completed surveys were returned. 77 respondents reported using at least one supplement during deployment. On average, 2.5 supplements were used per individual surveyed. Nine respondents reported adverse effects of supplement use. No respondents reported serious complications of supplement use, drug interactions, or seeking medical care for supplement adverse effects. The Internet was the most frequently reported source of information on supplement use. Most frequently, supplements were acquired by Internet mail order. CONCLUSIONS AND RELEVANCE: Supplement use occurs during deployment among paratroopers at a higher rate than reported in garrison, despite their remote and austere deployed location. These findings have profound implications for military health care providers and policy makers considering the health of deployed combat soldiers.

DOI: 10.7205/MILMED-D-14-00334
PMID: 25826344 [PubMed - indexed for MEDLINE]

18. Consumption and reasons for use of dietary supplements in an Australian university population. Barnes K, Ball L, Desbrow B, Alsharairi N, Ahmed F.

Nutrition. 2016 May;32(5):524-30. doi: 10.1016/j.nut.2015.10.022. Epub 2015 Dec 12.

OBJECTIVE: The aim of this study was to examine the association between dietary supplement use and sociodemographic factors in an Australian university population. Additionally, reasons for use of specific dietary supplements were explored. METHODS: A cross-sectional online questionnaire was completed by 1633 students and staff members of Griffith University, Queensland, Australia (76% female). The questionnaire collected information on sociodemographic characteristics, use of dietary supplements, and reasons for use of each dietary supplement reported. Multiple regression analyses were used to describe the relationship between demographic factors and dietary supplement use. Pearson $\chi(2)$ was used to identify correlations between frequency of dietary supplement use and selected demographic factors. Frequency distributions were used to explore the reasons for use of each dietary supplement reported. RESULTS: Vitamin or mineral use and use of "other" dietary supplements was reported by 69% and 63% of participants, respectively. Age, sex, ethnicity, and physical activity were independently associated with dietary supplement use. Age, sex, and income were associated with acute use of specific dietary supplements during

illness or injury. The reasons for use of specific dietary supplements were closely aligned with marketed claims. Broad reasons of health were commonly reported for use of most dietary supplements. CONCLUSIONS: Use of dietary supplements in this population reflects that of other countries. Individuals were unsure of the benefits and risks associated with dietary supplementation. Health professionals should account for dietary supplements when assessing diet. These results also warrant consideration by regulating bodies and public health officers to ensure safe practices.

DOI: 10.1016/j.nut.2015.10.022
PMID: 26819063 [PubMed - indexed for MEDLINE]

19. Herbal and Dietary Supplement-Induced Liver Injury. de Boer YS, Sherker AH.

Clin Liver Dis. 2017 Feb;21(1):135-149. doi: 10.1016/j.cld.2016.08.010. Epub 2016 Oct 14.

The increase in the use of herbal and dietary supplements (HDSs) over the last decades has been accompanied by an increase in the reports of HDS-associated hepatotoxicity. The spectrum of HDS-induced liver injury is diverse and the outcome may vary from transient liver test increases to fulminant hepatic failure resulting in death or requiring liver transplant. There are no validated standardized tools to establish the diagnosis, but some HDS products have a typical clinical signature that may help to identify HDS-induced liver injury.

DOI: 10.1016/j.cld.2016.08.010
PMCID: PMC5117680 [Available on 2018-02-01]
PMID: 27842768 [PubMed - in process]

20. Adverse drug reactions and organ damage: The liver. Licata A.

Eur J Intern Med. 2016 Mar;28:9-16. doi: 10.1016/j.ejim.2015.12.017. Epub 2016 Jan 28.

Drug-induced liver injury (DILI) is among the most challenging acute or chronic liver conditions to be handled by physicians. Despite its low incidence in the general population, DILI is a frequent cause of acute liver failure. As such, the possibility of DILI should be considered in all patients who present with acute liver damage, independent of any known pre-existing liver disease. DILI can be classified as intrinsic/dose-dependent (e.g., acetaminophen toxicity) or idiosyncratic/dose independent, with the latter form being relatively uncommon. Amoxicillin-clavulanate is the antimicrobial that is most frequently associated with idiosyncratic DILI. Large, ongoing, prospective studies in western countries have reported other drugs associated with DILI, including nonsteroidal anti-inflammatory drugs, statins, and herbal and dietary supplements. An important safety issue, DILI is one of the most frequently cited reasons for cessation of drug development during or after preclinical studies and for withdrawal of a drug from the market. This review summarizes the epidemiology, risk factors, commonly implicated drugs, clinical features, and diagnosis of DILI, with the aim of aiding physicians in the management of this debated problem. Old and new biomarkers for DILI and pharmacogenetic studies are also described.

DOI: 10.1016/j.ejim.2015.12.017
PMID: 26827101 [PubMed - indexed for MEDLINE]

21. Epidemiology and Genetic Risk Factors of Drug Hepatotoxicity. Ahmad J, Odin JA.

Clin Liver Dis. 2017 Feb;21(1):55-72. doi: 10.1016/j.cld.2016.08.004. Epub 2016 Oct 14.

Idiosyncratic drug-induced liver injury (DILI) from prescription medications and herbal and dietary supplements has an annual incidence rate of approximately 20 cases per 100,000 per year. However, the risk of DILI varies greatly according to the drug. In the United States and Europe, antimicrobials are the commonest implicated agents, with amoxicillin/clavulanate the most common, whereas in Asian countries, herbal and dietary supplements predominate. Genetic analysis of DILI is currently limited, but multiple polymorphisms of human leukocyte antigen genes and genes involved in drug metabolism and transport have been identified as risk factors for DILI.

DOI: 10.1016/j.cld.2016.08.004
PMID: 27842775 [PubMed - in process]

22. Drug-Induced Liver Injury Network Causality Assessment: Criteria and Experience in the United States. Hayashi PH.

Int J Mol Sci. 2016 Feb 4;17(2):201. doi: 10.3390/ijms17020201.

Hepatotoxicity due to drugs, herbal or dietary supplements remains largely a clinical diagnosis based on meticulous history taking and exclusion of other causes of liver injury. In 2004, the U.S. Drug-Induced Liver Injury Network (DILIN) was created under the auspices of the U.S. National Institute of Diabetes and Digestive and Kidney Diseases with the aims of establishing a large registry of cases for clinical, epidemiological and mechanistic study. From

inception, the DILIN has used an expert opinion process that incorporates consensus amongst three different DILIN hepatologists assigned to each case. It is the most well-established, well-described and vigorous expert opinion process for DILI to date, and yet it is an imperfect standard. This review will discuss the DILIN expert opinion process, its strengths and weaknesses, psychometric performance and future.

DOI: 10.3390/ijms17020201
PMCID: PMC4783935
PMID: 26861284 [PubMed - indexed for MEDLINE]

23. Drug-induced liver injury. Katarey D, Verma S.

Clin Med (Lond). 2016 Dec;16(Suppl 6):s104-s109.

Drug-induced liver injury (DILI) remains the most common cause of acute liver failure (ALF) in the western world. Excluding paracetamol overdose, nearly all DILI encountered in the clinical setting is idiosyncratic in nature because affected individuals represent only a small proportion of those treated with such drugs. In many cases, the mechanism for idiosyncrasy is immune-mediation and is often identified by genetic risk determined by human leukocyte antigen variants. In the absence of diagnostic tests and/or biomarkers, the diagnosis of DILI requires a high index of suspicion after diligently excluding other causes of abnormal liver tests. Antibiotics are the class of drugs most frequently associated with idiosyncratic DILI, although recent studies indicate that herbal and dietary supplements are an increasingly recognised cause. It is imperative that upon development of DILI the culprit drug be discontinued, especially in the presence of elevated transaminases (aspartate aminotransferase/alanine aminotransferase ratio ≥5 times the upper limit of normal) and/or jaundice. Risk factors for the development ALF include hepatocellular DILI and female gender, the treatment being supportive with some benefit of N-acetylcysteine in the early stages. In view of the poor transplant-free survival in idiosyncratic DILI, early consideration for liver transplant is mandatory.

DOI: 10.7861/clinmedicine.16-6-s104
PMID: 27956449 [PubMed - in process]

24. Analysis of Immunogenetic Factors in Idiosyncratic Drug-Induced Liver Injury in the Paediatric Population. Ocete-Hita E, Salmerón-Fernández MJ, Urrutia-Maldonado E, de Rueda PM, Salmerón-Ruiz M, Martinez-Padilla MC, Ruiz-Extremera A.

J Pediatr Gastroenterol Nutr. 2016 Dec 22. doi: 10.1097/MPG.0000000000001502.
[Epub ahead of print]

OBJECTIVE: Idiosyncratic drug-induced liver injury (DILI) is a multifactorial complex disease, in which the toxic potential of the drug, together with genetic and acquired factors and deficiencies in adaptive processes which limit the extent of damage, can determine susceptibility and make individuals unique in their development of hepatotoxicity. The aim of this study is to analyse the genetic factors (HLA, cytokine polymorphisms and KIR genotype) of children who experience an episode of drug-induced liver injury. SUBJECTS AND METHOD: Prospective multicentre case control study. The subjects included in the study were 30 paediatric patients - infants and children aged between 0 and 15 years and who presented possible liver disease associated with the intake of medicines, herbal products, drugs or toxins. As a control group, 62 subjects were selected. RESULTS AND CONCLUSIONS: Although HLAC0401 and HLADQB0603 may provide a hepatoprotective mechanism in the paediatric population, HLADQA0102 and HLA-DR*12 are more commonly found in sick children and their presence may be related to liver damage. The KIR inhibitor KIR3DL1 was not present in any child in the control group. Polymorphisms that are low producers of IL-10 occur more frequently in children who have experienced hepatotoxicity.

DOI: 10.1097/MPG.0000000000001502
PMID: 28005582 [PubMed - as supplied by publisher]

25. Acute Effusive Pericarditis due to Horse Chestnut Consumption. Edem E, Kahyaoğlu B, Çakar MA.

Am J Case Rep. 2016 May 4;17:305-8.

BACKGROUND: There are many well-known causes of pericardial effusion, such as cancer metastasis, bacterial or viral pericarditis, and uremic pericarditis; however, no reports exist in the literature demonstrating a pericardial effusion that led to cardiac tamponade following consumption of an herbal remedy. CASE REPORT: A 32-year-old male patient was referred to our cardiology outpatient clinic with a complaint of dyspnea. The patient's medical history was unremarkable; however, he had consumed 3 boxes of horse chestnut (Aesculus hippocastanum L) paste over the previous 1.5 months. His chest x-ray examination revealed an enlarged cardiac shadow and bilateral pleural effusion. On transthoracic echocardiographic examination, his ejection fraction was found to be 55% with circumferentially extended pericardial effusion that reached 3.9 cm at its maximal thickness. No growth had been detected in the pericardial and pleural biopsies or blood samples; there was no evidence of an infectious process in the physical examination. Based on this information, we diagnosed pericarditis resulting from the use of herbal remedies. This is the

first report to demonstrate that herbal remedy consumption may cause this type of clinical condition. CONCLUSIONS: Besides other well-known causes, pericardial effusion related to the consumption of herbal remedies should always be considered when treating patients with pericardial effusion caused by unclear etiologies.

PMCID: PMC4913740
PMID: 27141926 [PubMed - indexed for MEDLINE]

26. A Case of Strychnine Poisoning from a Southeast Asian Herbal Remedy. Singhapricha T, Pomerleau AC.

J Emerg Med. 2016 Nov 14. pii: S0736-4679(16)30882-4. doi: 10.1016/j.jemermed.2016.10.007. [Epub ahead of print]

BACKGROUND: Strychnine is a highly toxic alkaloid found in both naturally occurring compounds and commercial products. Extracts of fruits from the strychnine plant have been used in Southeast Asia as remedies for various illnesses. We describe strychnine poisoning from ingestion of a Southeast Asian herbal supplement quantitatively confirmed by serum and urine analysis. CASE REPORT: A 40-year-old Cambodian woman presented to the emergency department with a complaint of jaw pain and spasms. The patient was staying with a relative and drank 2 oz from an unmarked bottle that she thought contained vodka. She then developed trismus and abdominal cramping, after which a family member said the bottle contained a compound called "slang nut." Her vital signs were as follows: heart rate 102 beats/min, blood pressure 142/72 mm Hg, respiratory rate 20 breaths/min, and oxygen level 100%. The physical examination revealed no significant abnormalities. Serum toxicologic screens were negative except for strychnine levels that revealed a serum concentration of 350 ng/mL and a urine concentration >200 ng/mL. The patient was observed for 2.5 h and discharged with no long-term complications. WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?: Strychnine is a well-known compound that has been used in poisons, rodenticides, and performance enhancing drugs for years. In the Western world, strychnine is a much less common poisoning given that its use has been restricted because of the potential for severe toxicity; however, given its potentially high mortality, it is important to be aware of other sources of exposure, including those from herbal and homeopathic remedies.

DOI: 10.1016/j.jemermed.2016.10.007
PMID: 27856027 [PubMed - as supplied by publisher]

27. A rare chemical burn due to Ranunculus arvensis: three case reports. Kocak AO, Saritemur M, Atac K, Guclu S, Ozlu I.

Ann Saudi Med. 2016 Jan-Feb;36(1):89-91. doi: 10.5144/0256-4947.2016.89.

Ranunculus arvensis, a plant that is a member of Ranunculaceae family, generally used for local treatment of joint pain, muscle pain, burns, lacerations, edema, abscess drainage, hemorrhoids, and warts among the population. In this case report, we presented three patients who developed chemical skin burns after using R. arvensis plant locally for knee pain. The destructive effect of the plant has been reported previously to be more in fresh plants and less in dried plants. Although protoanemonin, which is considered as the main toxic substance, was reported to be absent in dried or boiled plants, the plant was boiled, cooled, and wrapped over the region with pain in our cases. Therefore, we thought that protoanemonin may be considered to be heat resistant. Also, the burn management proceeded up to surgery by using the flap technique in one of our patients in contrast to the cases found in published reports who were treated by antibiotics and dressings.

DOI: 10.5144/0256-4947.2016.89
PMID: 26922695 [PubMed - indexed for MEDLINE]

28. Hepatotoxicity due to red bush tea consumption: a case report. Reddy S, Mishra P, Qureshi S, Nair S, Straker T.

J Clin Anesth. 2016 Dec;35:96-98. doi: 10.1016/j.jclinane.2016.07.027. Epub 2016 Aug 9.

Many conventional drugs used today, including isoniazid, dapsone, and acetaminophen, are well recognized culprits of hepatotoxicity. With increasing use of complementary and alternative medical therapies, several herbal medicines, such as Ma-Huang, kava, and chaparral leaf, have been implicated as hepatotoxins. Hepatotoxicity may be the most frequent adverse reaction to these herbal remedies when taken in excessive quantities. A myriad of liver dysfunctions may occur including transient liver enzyme abnormalities due to acute and chronic hepatitis. These herbal products are often overlooked as the causal etiologic agent during the evaluation of a patient with elevated liver function tests. We describe a case of hepatotoxicity due to ingestion of red bush tea diagnosed during preoperative assessment of a patient scheduled for laparoscopic appendectomy. Elevated liver enzymes and thrombocytopenia detected in the patient's laboratory work up confounded the initial diagnosis of acute appendicitis and additional investigations were required to rule out cholecystitis and other causes of hepatitis. Open appendectomy was done uneventfully under spinal anesthesia without any further deterioration of hepatic function.

DOI: 10.1016/j.jclinane.2016.07.027
PMID: 27871602 [PubMed - in process]

29. Severe liver injury due to a homemade flower pollen preparation in a patient with high CYP3A enzyme activity: a case report. Rollason V, Spahr L, Escher M.

Eur J Clin Pharmacol. 2016 Apr;72(4):507-8. doi: 10.1007/s00228-015-1986-9. Epub 2016 Jan 8.

DOI: 10.1007/s00228-015-1986-9
PMID: 26746721 [PubMed - indexed for MEDLINE]

30. A Comprehensive Review of Recent Studies on Herb-Drug Interaction: A Focus on Pharmacodynamic Interaction. Choi JG, Eom SM, Kim J, Kim SH, Huh E, Kim H, Lee Y, Lee H, Oh MS.

J Altern Complement Med. 2016 Apr;22(4):262-79. doi: 10.1089/acm.2015.0235. Epub 2016 Mar 22.

OBJECTIVES: The concomitant use of herbal and conventional drugs accelerates the possibility of clinically significant herb-drug interactions (HDIs). This paper aims to analyze the current status of HDI studies worldwide and to review studies on HDI-induced pharmacodynamic (PD) interactions. METHODS: HDI studies published from 2000 to 2014 and indexed in PubMed were categorized according to publication year, area/country, study methods and objectives, and disease categories. The reviewed studies focused on HDI-induced PD; each PD interaction with concurrent use of approximately 100 herbal drugs and 70 conventional drugs was summarized. All PD-related articles were categorized according to four characteristics: herbal drugs, conventional drugs, types of PD interaction, and type of study. Among them, 17 well-designed clinical studies were evaluated by using the Jadad Quality Assessment Scale. RESULTS: The number of HDI reports has gradually increased since 2000, with a primary focus on neoplasms and diseases of the circulatory system. Most of these investigated pharmacokinetic reactions, such as cytochrome P450 enzyme metabolism, with fewer reports investigating PD. Most PD interaction studies investigated warfarin, ginkgo leaves, and St. John's wort. An evaluation of 17 studies revealed a generally positive view of PD effects involving synergism or reduced toxicity and a high average quality score (>3 points on a 0-5 scale). CONCLUSIONS: These results demonstrate that most HDI studies so far have examined PK interactions and have been limited to very few conventional drugs and herbal drugs. This suggests that more studies focusing on PD are necessary to understand interactions between commonly used herbal and conventional drugs.

DOI: 10.1089/acm.2015.0235
PMID: 27003511 [PubMed - indexed for MEDLINE]

31. Dehydropyrrolizidine Alkaloid Toxicity, Cytotoxicity, and Carcinogenicity. Stegelmeier BL, Colegate SM, Brown AW.

Toxins (Basel). 2016 Nov 29;8(12). pii: E356.

Dehydropyrrolizidine alkaloid (DHPA)-producing plants have a worldwide distribution amongst flowering plants and commonly cause poisoning of livestock, wildlife, and humans. Previous work has produced considerable understanding of DHPA metabolism, toxicity, species susceptibility, conditions, and routes of exposure, and pathogenesis of acute poisoning. Intoxication is generally caused by contaminated grains, feed, flour, and breads that result in acute, high-dose, short-duration poisoning. Acute poisoning produces hepatic necrosis that is usually confirmed histologically, epidemiologically, and chemically. Less is known about chronic poisoning that may result when plant populations are sporadic, used as tisanes or herbal preparations, or when DHPAs contaminate milk, honey, pollen, or other animal-derived products. Such subclinical exposures may contribute to the development of chronic disease in humans or may be cumulative and probably slowly progress until liver failure. Recent work using rodent models suggest increased neoplastic incidence even with very low DHPA doses of short durations. These concerns have moved some governments to prohibit or limit human exposure to DHPAs. The purpose of this review is to summarize some recent DHPA research, including in vitro and in vivo DHPA toxicity and carcinogenicity reports, and the implications of these findings with respect to diagnosis and prognosis for human and animal health.

DOI: 10.3390/toxins8120356
PMID: 27916846 [PubMed - in process]

32. Metabolic activation of furan moiety makes Diosbulbin B hepatotoxic. Li W, Lin D, Gao H, Xu Y, Meng D, Smith CV, Peng Y, Zheng J.

Arch Toxicol. 2016 Apr;90(4):863-72. doi: 10.1007/s00204-015-1495-8. Epub 2015 Apr 8.

Diosbulbin B (DIOB), a furanoid, is a major constituent of herbal medicine Dioscorea bulbifera L. Exposure to DIOB caused liver injury in humans and experimental animals. The mechanisms of DIOB-induced hepatotoxicities remain unknown. The present study demonstrated that DIOB induced hepatotoxicities in a time- and dose-dependent manner in mice. H&E stained histopathologic image showed the occurrence of necrosis in the liver obtained from the mice treated with DIOB at dose of 200 mg/kg. Pretreatment with KTC protected the animals from hepatotoxicities and hepatic GSH

depletion induced by DIOB, increased area under the concentration-time curve of blood DIOB, decreased urinary excretion of GSH conjugates derived from DIOB, and increased urinary excretion of parent drug. Pretreatment with BSO exacerbated DIOB-induced hepatotoxicities. In order to define the role of furan moiety in DIOB-induced liver toxicities, we replaced the furan of DIOB with a tetrahydrofuran group by chemical hydrogenation of the furan ring of DIOB. No liver injury was observed in the animals given the same doses of tetrahydro-DIOB. The furan moiety was essential for DIOB-induced hepatotoxicities. The results implicate the cis-enedial reactive metabolite of DIOB was responsible for the observed toxicities. The observed modest depletion of hepatic GSH in DIOB-treated animals suggests the actions of one or more reactive metabolites, and the hepatic injury observed could be due at least in part to reactions of these metabolites with crucial biomolecules. Cytochrome P450 3A enzymes are implicated in DIOB-induced hepatotoxicities by catalyzing the formation of the reactive metabolite of DIOB.

DOI: 10.1007/s00204-015-1495-8
PMID: 25851819 [PubMed - indexed for MEDLINE]

33. Plant species forbidden in health food and their toxic constituents, toxicology and detoxification. Xu XL, Shang Y, Jiang JG.

Food Funct. 2016 Feb;7(2):643-64. doi: 10.1039/c5fo00995b.

Many plants with pharmacological efficacies are widely used as ingredients in so-called "health foods", but many of them are toxic. In order to ensure the safety of "health food", the Chinese Ministry of Health has listed 59 materials that are forbidden from being used in health food and are called health food forbidden species (HFFS). This review focuses on 47 plants among the HFFS to discuss research regarding their pharmacology, toxicology, and detoxification methods. According to the literature published in the last 2 decades, the main constituents and the pharmacology of such plants are described here, especially their toxic constituents and toxicology. The toxicity mechanisms of several typical toxic components from the 47 plants are outlined and some effective detoxification methods are introduced. Although all HFFS are poisonous, they are considered to be useful in the treatment of many diseases. How to keep their pharmacological effects and at the same time decrease their toxicity is a great challenge. In the future, more attention should be paid to the application of modern science and technology in the exploration of the toxicology and detoxification of HFFS.

DOI: 10.1039/c5fo00995b
PMID: 26674019 [PubMed - indexed for MEDLINE]

34. Contact dermatitis as an adverse reaction to some topically used European herbal medicinal products - Part 3: Mentha × piperita - Solanum dulcamara. Calapai G, Minciullo PL, Miroddi M, Chinou I, Gangemi S, Schmidt RJ.

Contact Dermatitis. 2016 Mar;74(3):131-44. doi: 10.1111/cod.12483. Epub 2015 Nov 13.

This review focuses on contact dermatitis as an adverse effect of a selection of topically used herbal medicinal products for which the European Medicines Agency has completed an evaluation up to the end of November 2013 and for which a Community herbal monograph - now (since 2015)(†) called a European Union herbal monograph - has been produced. Part 3: Mentha × piperita L.-Solanum dulcamara L.

DOI: 10.1111/cod.12483
PMID: 26563681 [PubMed - indexed for MEDLINE]

35. Allergy-Like Immediate Reactions with Herbal Medicines: A Retrospective Study Using Data from VigiBase®. Pokladnikova J, Meyboom RH, Meincke R, Niedrig D, Russmann S.

Drug Saf. 2016 May;39(5):455-64. doi: 10.1007/s40264-016-0401-5.

INTRODUCTION: Herbal medicines are used worldwide and with an increasing popularity in Western countries. Although often perceived as 'naturally safe', herbals may cause severe adverse drug reactions (ADRs), with immediate allergic reactions being particularly life threatening. OBJECTIVES: The aim of this study was to analyse immediate allergy-like ADRs to herbals documented in VigiBase®, the WHO international pharmacovigilance database. METHODS: The documentation of all suspected ADRs in association with herbal exposure reported to VigiBase® from 1969 to August 2014 was retrieved. Among all reports in which WHO-ART reaction terms were indicative of acute allergic reactions, those classified as 'suspect' with a documented causality assessment and latency time of ≤1 day were selected. For the most frequent specific herbal-ADR combinations, the information component (IC) as a measure of disproportionality based on Bayesian statistics was calculated. RESULTS: We identified 757 reports out of 1039 ADRs. Products with mixed herbals (36.0 %) as well as those administered orally (63.2 %) were predominant. The most frequent reactions were urticaria and rash (49.2 %). Anaphylactic reactions accounted for 9.5 %. Disproportionally frequent reporting of mouth edema (IC = 1.81) and anaphylactic reactions (IC = 1.24) to Phleum pretense were noted. CONCLUSION: Our findings indicate that herbal medicines for oral use carry a risk of causing immediate allergy-like ADRs. Studies using the Vigibase® database can identify specific combinations of particular herbs and adverse

reactions. Healthcare professionals and patients should be aware of these risks and report any serious adverse experiences.

DOI: 10.1007/s40264-016-0401-5
PMID: 26936182 [PubMed - indexed for MEDLINE]