

1. Cardiac arrest in a 21-year-old man after ingestion of 1,3-DMAA-containing workout supplement. Karnatovskaia LV, Leoni JC, Freeman ML.

Clin J Sport Med. 2015 Jan;25(1):e23-5. doi: 10.1097/JSM.0000000000000103.

Abstract:

Dietary supplements containing 1,3-dimethylamylamine (DMAA) have been determined to be illegal by the Food and Drug Administration (FDA); although banned, the products are still widely available for purchase. Adverse effects reported include cardiac arrest, hemorrhagic stroke, and death. Nonetheless, such products remain popular among young people because of advertised claims of exercise performance enhancement and fat burning. We describe a case of a young man who took such a supplement and suffered a cardiac arrest. Notably, the product consumed was not on the FDA list of substances containing DMAA. This case highlights the importance for clinicians to be aware of the potential harm of the DMAA-containing products by maintaining a high index of suspicion in otherwise healthy individuals presenting with cardiac arrest. It is of particular importance to sports medicine physicians who are most involved in education and counseling of patients potentially at risk of taking such products.

PMID: 24878759 [PubMed - indexed for MEDLINE]

2. Hemorrhagic Stroke Probably Caused by Exercise Combined With a Sports Supplement Containing β -Methylphenyl-ethylamine (BMPEA): A Case Report. Cohen PA, Zeijlon R, Nardin R, Keizers PH, Venhuis B.

Ann Intern Med. 2015 Jun 16;162(12):879-80. doi: 10.7326/L15-5101.

No abstract.

PMID: 26075771 [PubMed - indexed for MEDLINE]

3. Human Ether-à-go-go Related Gene (hERG) Channel Blocking Aporphine Alkaloids from Lotus Leaves and Their Quantitative Analysis in Dietary Weight Loss Supplements.

Grienke U, Mair CE, Saxena P, Baburin I, Scheel O, Ganzera M, Schuster D, Hering S, Rollinger JM.

J Agric Food Chem. 2015 Jun 17;63(23):5634-9. doi: 10.1021/acs.jafc.5b01901. Epub 2015 Jun 9.

Abstract:

Blockage of the human ether-à-go-go related gene (hERG) channel can result in life-threatening ventricular tachyarrhythmia. In an in vitro screening of herbal materials for hERG blockers using an automated two-microelectrode voltage clamp assay on *Xenopus* oocytes, an alkaloid fraction of *Nelumbo nucifera* Gaertn. (lotus) leaves induced ~50% of hERG current inhibition at 100 μ g/mL. Chromatographic separation resulted in the isolation and identification of (-)-asimilobine, 1, nuciferine, 2, O-nornuciferine, 3, N-nornuciferine, 4, and liensinine, 5. In agreement with in silico predicted ligand-target interactions, 2, 3, and 4 revealed distinct in vitro hERG blockages

measured in HEK293 cells with IC50 values of 2.89, 7.91, and 9.75 μ M, respectively. Because lotus leaf dietary weight loss supplements are becoming increasingly popular, the identified hERG-blocking alkaloids were quantitated in five commercially available products. Results showed pronounced differences in the content of hERG-blocking alkaloids ranging up to 992 μ g (2) in the daily recommended dose.

PMID: 26035250

4. Acute liver injury associated with a newer formulation of the herbal weight loss supplement Hydroxycut. Araujo JL, Worman HJ.

BMJ Case Rep. 2015 May 6;2015. pii: bcr2015210303. doi: 10.1136/bcr-2015-210303.

Abstract:

Despite the widespread use of herbal and dietary supplements (HDS), serious cases of hepatotoxicity have been reported. The popular herbal weight loss supplement, Hydroxycut, has previously been implicated in acute liver injury. Since its introduction, Hydroxycut has undergone successive transformations in its formulation; yet, cases of liver injury have remained an ongoing problem. We report a case of a 41-year-old Hispanic man who developed acute hepatocellular liver injury with associated nausea, vomiting, jaundice, fatigue and asterixis attributed to the use of a newer formulation of Hydroxycut, SX-7 Clean Sensory. The patient required hospitalisation and improved with supportive therapy. Despite successive transformations in its formulation, potential liver injury appears to remain an ongoing problem with Hydroxycut. Our case illustrates the importance of obtaining a thorough medication history, including HDS, regardless of new or reformulated product marketing efforts.

PMID: 25948859 [PubMed - in process]

5. Melamine contamination in nutritional supplements--Is it an alarm bell for the general consumer, athletes, and 'Weekend Warriors'? Gabriels G, Lambert M, Smith P, Wiesner L, Hiss D.

Nutr J. 2015 Jul 17;14:69. doi: 10.1186/s12937-015-0055-7.

Abstract:

BACKGROUND: Nutritional supplements are used or experimented with by consumers, notably these are; competitive and recreational athletes of all ages, and 'weekend warriors'. As a consequence the supplement industry has grown to meet the increasing demand. A Global Industry Analysts Inc. report indicates that the herbal supplement market has not declined during the worldwide recession, but in fact exhibited steady growth over the period 2008 to 2009. It is anticipated that the market will reach US\$93.15 billion by the year 2015. These supplements may contain adulterated substances that may potentially have harmful short - and long-term health consequences to the consumer. "Scrap Melamine" is such an example, which has been implicated in the kidney failure and death of several cats, dogs and pigs. In China in 2008, reports described very severe health effects in infants and young children. At the time over 294,000 infants were screened and diagnosed with urinary tract stones and sand-like calculi associated with melamine in milk products, of which 50,000 infants were hospitalised, and at least six associated deaths, recorded. The extent that melamine contamination occurs in nutritional supplements is not known. Therefore, the aim of this study was to determine whether

commercially available nutritional and traditional supplement products contain melamine, even though they are not declared by the manufacturer on the product label. **METHODS:** A total of 138 nutritional supplements products were obtained from (i) direct purchases from shops, pharmacies and outlets, (ii) directly from consumers, and (iii) from suppliers, manufacturers and distributors. The products were laboratory analysed for melamine, using Tandem Liquid Chromatography Mass Spectrometry. **RESULTS:** Forty-seven % of all the products (n = 138) tested positive for melamine. Eight-two % of the South African produced products (n = 27) tested positive and 58 % of the products imported into South Africa (n = 50) tested positive. The median concentration estimate for melamine in the products tested were, 6.0 µg/g for the 138 supplements tested, 8.9 µg/g for South African produced products, and 6.9 µg/g for products imported into South Africa. **CONCLUSION:** The melamine (undeclared on product label) levels detected in the nutritional supplements products investigated were within the Tolerable Daily intake (TDI) limit guidelines of 200 µg/g as set by WHO and others. Melamine over exposure within the context of the nutritional supplements consumption in the products investigated should not be of concern to the consumer provided the recommended guidelines of daily product use are adhered to. Further investigation is warranted to determine, (i) the link of melamine as (part) substitute for the perceived total declared protein content on the product label, (ii) cyanuric and uric acid presence in the supplement products that could form chemical-complex formation with melamine and/or analogues that could cause adverse health effects.

PMCID: PMC4504043

PMID: 26182916

6. Traditional Chinese Medicine and herbal hepatotoxicity: a tabular compilation of reported cases. Teschke R, Zhang L, Long H, Schwarzenboeck A, Schmidt-Taenzer W, Genthner A, Wolff A, Frenzel C, Schulze J, Eickhoff A.

Ann Hepatol. 2015 Jan-Feb;14(1):7-19.

Traditional Chinese Medicine (TCM) with its focus on herbal use became popular worldwide. Treatment was perceived as safe, with neglect of rare adverse reactions including liver injury. To compile worldwide cases of liver injury by herbal TCM, we undertook a selective literature search in the PubMed database and searched for the items Traditional Chinese Medicine, TCM, Traditional Asian Medicine, and Traditional Oriental Medicine, also combined with the terms herbal hepatotoxicity or herb induced liver injury. The search focused primarily on English-language case reports, case series, and clinical reviews. We identified reported hepatotoxicity cases in 77 relevant publications with 57 different herbs and herbal mixtures of TCM, which were further analyzed for causality by the Council for International Organizations of Medical Sciences (CIOMS) scale, positive reexposure test results, or both. Causality was established for 28/57 different herbs or herbal mixtures, Bai Xian Pi, Bo He, Ci Wu Jia, Chuan Lian Zi, Da Huang, Gan Cao, Ge Gen, Ho Shou Wu, Huang Qin, Hwang Geun Cho, Ji Gu Cao, Ji Xue Cao, Jin Bu Huan, Jue Ming Zi, Jiguja, Kudzu, Ling Yang Qing Fei Keli, Lu Cha, Rhen Shen, Ma Huang, Shou Wu Pian, Shan Chi, Shen Min, Syo Saiko To, Xiao Chai Hu Tang, Yin Chen Hao, Zexie, and Zhen Chu Cao. In conclusion, this compilation of liver injury cases establishes causality for 28/57 different TCM herbs and herbal mixtures, aiding diagnosis for physicians who care for patients with liver disease possibly related to herbal TCM.

PMID: 25536637 [PubMed - indexed for MEDLINE]

7. Sinusoidal obstruction syndrome (hepatic veno-occlusive disease). Fan CQ, Crawford JM.

J Clin Exp Hepatol. 2014 Dec;4(4):332-46. doi: 10.1016/j.jceh.2014.10.002. Epub 2014 Oct 30.

Abstract:

Hepatic sinusoidal obstruction syndrome (SOS) is an obliterative venulitis of the terminal hepatic venules, which in its more severe forms imparts a high risk of mortality. SOS, also known as veno-occlusive disease (VOD), occurs as a result of cytoreductive therapy prior to hematopoietic stem cell transplantation (HSCT), following oxaliplatin-containing adjuvant or neoadjuvant chemotherapy for colorectal carcinoma metastatic to the liver and treated by partial hepatectomy, in patients taking pyrrolizidine alkaloid-containing herbal remedies, and in other particular settings such as the autosomal recessive condition of veno-occlusive disease with immunodeficiency (VODI). A central pathogenic event is toxic destruction of hepatic sinusoidal endothelial cells (SEC), with sloughing and downstream occlusion of terminal hepatic venules. Contributing factors are SEC glutathione depletion, nitric oxide depletion, increased intrahepatic expression of matrix metalloproteinases and vascular endothelial growth factor (VEGF), and activation of clotting factors. The clinical presentation of SOS includes jaundice, development of right upper-quadrant pain and tender hepatomegaly, ascites, and unexplained weight gain. Owing to the potentially critical condition of these patients, transjugular biopsy may be the preferred route for liver biopsy to exclude other potential causes of liver dysfunction and to establish a diagnosis of SOS. Treatment includes rigorous fluid management so as to avoid excessive fluid overload while avoiding too rapid diuresis or pericentesis, potential use of pharmaceuticals such as defibrotide, coagulolytic agents, or methylprednisolone, and liver transplantation. Proposed strategies for prevention and prophylaxis include reduced-intensity conditioning radiation for HSCT, treatment with ursodeoxycholic acid, and inclusion of bevacizumab with oxaliplatin-based chemotherapeutic regimes. While significant progress has been made in understanding the pathogenesis of SOS and in mitigating against its adverse outcomes, this condition remains a serious complication of a selective group of medical treatments.

PMCID: PMC4298625

PMID: 25755580 [PubMed]

8. Tusanqi-Related Sinusoidal Obstruction Syndrome in China: A Systematic Review of the Literatures. Wang X, Qi X, Guo X.

Medicine (Baltimore). 2015 Jun;94(23):e942. doi: 10.1097/MD.0000000000000942.

Abstract:

In West, sinusoidal obstruction syndrome (SOS) is often complicated with hemopoietic stem cell transplantation. By comparison, in China, SOS is frequently caused by Tusanqi-containing pyrrolizidine alkaloids. A systematic review aimed to evaluate the clinical profiles, diagnostic workup, treatment, and outcomes of Tusanqi-related SOS in China. All relevant articles were searched via PubMed, China Knowledge Resource Integrated, VIP, and Wanfang databases. Case reports were defined, as the data were available in every individual patient. Otherwise, case series were defined. Overall, 106 articles were eligible. Fifty-six case reports included 84 individual patients with SOS secondary to Tusanqi alone. All of them presented with ascites, but only 1 patient presented with upper gastrointestinal bleeding. The 1-, 3-, and 6-month

cumulative survival rate was 98%, 87%, and 76%, respectively. Increased bilirubin and aspartate transaminase levels were significantly associated with poor outcome. Thirty-one case series included 402 patients with SOS secondary to Tusanqi alone. Ascites was observed in 94% of patients, but upper gastrointestinal bleeding was observed in 40% of patients. Recovery, stabilization, progression, and death were observed in 41%, 30%, 14%, and 16% of patients, respectively. Nineteen case series included 281 patients with SOS secondary to mixed etiologies. The pooled proportion of Tusanqi-related SOS was 66% (95% confidence interval: 56%-75%). Tusanqi is a major cause of SOS in China. Ascites is the most common clinical presentation of Tusanqi-related SOS. Despite a relatively good short-term outcome, further studies should be necessary to explore the long-term outcome and refine the treatment strategy.

PMID: 26061322 [PubMed - indexed for MEDLINE]

9. Safety concerns of herbal products and traditional Chinese herbal medicines: dehydropyrrolizidine alkaloids and aristolochic acid. Stegelmeier BL, Brown AW, Welch KD.

J Appl Toxicol. 2015 Jul 7. doi: 10.1002/jat.3192. [Epub ahead of print]

Abstract:

In many countries, including the United States, herbal supplements, tisanes and vegetable products, including traditional Chinese medicines, are largely unregulated and their content is not registered, monitored or verified. Consequently, potent plant toxins including dehydropyrrolizidine alkaloids and other potential carcinogens can contaminate these products. As herbal and food supplement producers are left to their own means to determine the safety and purity of their products prior to marketing, disturbingly often good marketing practices currently in place are ignored and content is largely undocumented. Historical examples of poisoning and health issues relating to plant material containing dehydropyrrolizidine alkaloids and aristolochic acids were used as examples to demonstrate the risk and potential toxicity of herbal products, food supplements, or traditional medicines. More work is needed to educate consumers of the potential risk and require the industry to be more responsible to verify the content and insure the safety of their products. This article is a U.S. Government work and is in the public domain in the USA.

PMID: 26152912

10. Detection of pyrrolizidine alkaloids in German licensed herbal medicinal teas.

Schulz M, Meins J, Diemert S, Zagermann-Muncke P, Goebel R, Schrenk D, Schubert-Zsilavecz M, Abdel-Tawab M.

Phytomedicine. 2015 Jun 1;22(6):648-56. doi: 10.1016/j.phymed.2015.03.020. Epub 2015 Apr 29.

Abstract:

BACKGROUND: Because of the hepatotoxic, mutagenic, and cancerogenic effects of pyrrolizidine alkaloids (PAs) the German Federal Institute for Risk Assessment (BfR) recommends not to exceed a daily PA intake of 0.007 $\mu\text{g/kg}$ body weight (0.42 $\mu\text{g/60 kg}$ adult). In a recent study conducted by the BfR, up to 5647 $\mu\text{g PA/kg}$ dried herbal material were detected in tea products marketed as food. **PURPOSE:** The present study aimed at elucidating whether medicinal teas licensed or registered as medicinal products contain PAs as well.

STUDY DESIGN: One hundred sixty-nine different commercially available medicinal teas, i.e. 19 nettle (*Urtica dioica* L.), 12 fennel (*Foeniculum vulgare* Mill.), 14 chamomile (*Matricaria recutita* L.), 11 melissa (*Melissa officinalis* L.) and 4 peppermint (*Mentha piperita* L.) teas as well as 109 tea mixtures were analyzed for the presence of 23 commercially available PAs. **METHOD:** LC/MS was used for the determination of the PAs. **RESULTS:** In general, the total PA contents ranging 0-5668 $\mu\text{g/kg}$. Thirty percent of the tested single-ingredient tea products and 56.9% of the tested medicinal tea mixtures were found to contain PA concentrations above the limit of quantification (LOQ) of 10 $\mu\text{g/kg}$. In 11 medicinal teas PA contents >300 $\mu\text{g/kg}$ dry herb were determined thus exceeding the recommended limit for PA intake by BfR. In addition three products of the investigated tea mixtures revealed extremely high PA contents of 4227, 5137, and 5668 $\mu\text{g/kg}$. Generally, single-ingredient tea products contained much less or even no detectable amounts of PAs when compared to the tea mixtures. PAs in the range between 13 and 1080 $\mu\text{g/kg}$ were also detected in five analyzed aqueous herbal infusions of the medicinal tea mixture products with the highest PA content. Two out of the five investigated herbal infusions exceeded the recommended BfR limit for PA intake. **CONCLUSION:** This study demonstrates clearly that also medicinal teas licensed as medicinal products may partly contain high amounts of PAs exceeding current recommendations. For that reason manufacturers are advised to carry out more rigorous quality control tests devoted to the detection of PAs. This is very important to minimize PAs in medicinal teas accounting for possible additional exposure of the consumer to PAs from other food sources (e.g. honey).

PMID: 26055130 [PubMed - in process]

11. Pro-toxic dehydropyrrolizidine alkaloids in the traditional Andean herbal medicine "asmachilca". Colegate SM, Boppré M, Monzón J, Betz JM.

J Ethnopharmacol. 2015 Aug 22;172:179-94. doi: 10.1016/j.jep.2015.06.012. Epub 2015 Jun 16.

Abstract:

ETHNOPHARMACOLOGICAL RELEVANCE: Asmachilca is a Peruvian medicinal herb preparation ostensibly derived from *Aristeguietia gayana* (Wedd.) R.M. King & H. Rob. (Asteraceae: Eupatorieae). Decoctions of the plant have a reported bronchodilation effect that is purported to be useful in the treatment of respiratory allergies, common cold and bronchial asthma. However, its attractiveness to pyrrolizidine alkaloid-pharmacophagous insects indicated a potential for toxicity for human consumers. **AIM OF THE STUDY:** To determine if commercial asmachilca samples, including fully processed herbal teas, contain potentially toxic 1,2-dehydropyrrolizidine alkaloids. **MATERIALS AND METHODS:** Two brands of "Asmachilca" herbal tea bags and four other commercial samples of botanical materials for preparing asmachilca medicine were extracted and analyzed using HPLC-esi(+)MS and MS/MS for the characteristic retention times and mass spectra of known dehydropyrrolizidine alkaloids. Other suspected dehydropyrrolizidine alkaloids were tentatively identified based on MS/MS profiles and high resolution molecular weight determinations. Further structure elucidation of isolated alkaloids was based on 1D and 2D NMR spectroscopy. **RESULTS:** Asmachilca attracted many species of moths which are known to pharmacophagously gather dehydropyrrolizidine alkaloids. Analysis of 5 of the asmachilca samples revealed the major presence of the dehydropyrrolizidine alkaloid monoesters rinderine and supinine, and their N-oxides. The 6th sample was very similar but did not contain supinine or its N-oxide. Small quantities of other dehydropyrrolizidine alkaloid monoesters, including echinatine and intermedine, were also detected. In addition, two major metabolites, previously undescribed, were isolated and

identified as dehydropyrrolizidine alkaloid monoesters with two "head-to-tail" linked viridifloric and/or trachelanthic acids. Estimates of total pyrrolizidine alkaloid and N-oxide content in the botanical components of *asmachilca* varied from 0.4% to 0.9% (w/dw, dry weight) based on equivalents of lycopsamine. The mean pyrrolizidine alkaloid content of a hot water infusion of a commercial *asmachilca* herbal tea bag was 2.2 ± 0.5 mg lycopsamine equivalents. Morphological and chemical evidence showed that *asmachilca* is prepared from different plant species. CONCLUSIONS: All *asmachilca* samples and the herbal tea infusions contained toxicologically-relevant concentrations of pro-toxic 1,2-dehydropyrrolizidine alkaloid esters and, therefore, present a risk to the health of humans. This raises questions concerning the ongoing unrestricted availability of such products on the Peruvian and international market. In addition to medical surveys of consumers of *asmachilca*, in the context of chronic disease potentially associated with ingestion of the dehydropyrrolizidine alkaloids, the botanical origins of *asmachilca* preparations require detailed elucidation.

PMCID: PMC4523498 [Available on 2016-08-22]

PMID: 26087231

12. Hepatotoxicity of green tea: an update. Mazzanti G, Di Sotto A, Vitalone A.

Arch Toxicol. 2015 Aug;89(8):1175-91. doi: 10.1007/s00204-015-1521-x. Epub 2015 May 16.

Abstract:

Green tea (GT), obtained from the leaves of *Camellia sinensis* (L.) Kuntze (Fam. Theaceae), is largely used for its potential health benefits such as reduction in risk of cardiovascular diseases and weight loss. Nevertheless, it is suspected to induce liver damage. Present work reviews the hepatic adverse reactions associated with GT-based herbal supplements, published by the end of 2008 to March 2015. A systematic research was carried out on PubMed, MedlinePlus, Scopus and Google Scholar databases, without any language restriction. Moreover, some accessible databases on pharmacovigilance or phytovigilance were consulted. The causality assessment was performed using the CIOMS/RUCAM score. Nineteen cases of hepatotoxicity related to the consumption of herbal products containing GT were identified. The hepatic reactions involved mostly women (16/19); the kind of liver damage was generally classified as hepatocellular (16/19). The causality assessment between consumption of herbal preparation and hepatic reaction resulted as probable in eight cases and as possible in eleven cases. In seven cases, patients used preparations containing only GT, while twelve reactions involved patients who took multicomponent preparations (MC). The reactions induced by GT had a generally long latency (179.1 ± 58.95 days), and the outcome was always resolution, with recovery time of 64.6 ± 17.78 days. On the contrary, liver injury associated with MC had a shorter latency (44.7 ± 13.85 days) and was more serious in four cases that required liver transplantation and, when resolution occurred, the recovery time was longer (118.9 ± 38.79). MC preparations contained numerous other components, many of which are suspected to induce liver damage, so it is difficult to ascribe the toxicity to one specific component, e.g., GT. Present data confirm a certain safety concern with GT, even if the number of hepatic reactions reported is low considering the great extent of use of this supplement. The mechanism of GT hepatotoxicity remains unclear, but factors related to the patient are becoming predominant. A major safety concern exists when GT is associated with other ingredients that can interact between them and with GT, enhancing the risk of liver damage. Patients should be discouraged from using herbal or dietary supplements containing complex mixtures and should be

encouraged to use herbal and dietary supplement possibly under supervision of healthcare professionals.

PMID: 25975988 [PubMed - in process]

13. An integrated system for identifying the hidden assassins in traditional medicines containing aristolochic acids.

Wu L, Sun W, Wang B, Zhao H, Li Y, Cai S, Xiang L, Zhu Y, Yao H, Song J, Cheng YC, Chen S.

Sci Rep. 2015 Aug 13;5:11318. doi: 10.1038/srep11318.

Abstract:

Traditional herbal medicines adulterated and contaminated with plant materials from the Aristolochiaceae family, which contain aristolochic acids (AAs), cause aristolochic acid nephropathy. Approximately 256 traditional Chinese patent medicines, containing Aristolochiaceae materials, are still being sold in Chinese markets today. In order to protect consumers from health risks due to AAs, the hidden assassins, efficient methods to differentiate Aristolochiaceae herbs from their putative substitutes need to be established. In this study, 158 Aristolochiaceae samples representing 46 species and four genera as well as 131 non-Aristolochiaceae samples representing 33 species, 20 genera and 12 families were analyzed using DNA barcodes based on the ITS2 and psbA-trnH sequences. Aristolochiaceae materials and their non-Aristolochiaceae substitutes were successfully identified using BLAST1, the nearest distance method and the neighbor-joining (NJ) tree. In addition, based on sequence information of ITS2, we developed a Real-Time PCR assay which successfully identified herbal material from the Aristolochiaceae family. Using Ultra High Performance Liquid Chromatography-Mass Spectrometer (UHPLC-HR-MS), we demonstrated that most representatives from the Aristolochiaceae family contain toxic AAs. Therefore, integrated DNA barcodes, Real-Time PCR assays using TaqMan probes and UHPLC-HR-MS system provides an efficient and reliable authentication system to protect consumers from health risks due to the hidden assassins (AAs).

PMCID: PMC4535178

PMID: 26270958 [PubMed - in process]

14. Do cinnamon supplements cause acute hepatitis? Brancheau D, Patel B, Zughaib M.

Am J Case Rep. 2015 Apr 29;16:250-4. doi: 10.12659/AJCR.892804.

Abstract:

BACKGROUND: The use of herbal medications to treat various diseases is on the rise. Cinnamon has been reported to improve glycolated hemoglobin and serum glucose levels. When patients consider the benefit of such substances, they are often not aware of potential adverse effects and drug interactions. Cinnamon, via coumarin, can cause liver toxicity. Therefore, its concomitant use with hepatotoxic drugs should be avoided. **CASE REPORT:** A 73-year-old woman was seen in the Emergency Department complaining of abdominal pain associated with vomiting and diarrhea after she started taking cinnamon supplements for about 1 week. The patient had been taking statin for coronary artery disease for many months. The laboratory workup and imaging studies confirmed the diagnosis of hepatitis. The detail workup did not reveal any specific cause. Cinnamon and statin were held. A few weeks after discharge,

the statin was resumed without any further complications. This led to a diagnosis of cinnamon-statin combination-induced hepatitis. **CONCLUSIONS:** A combination of cinnamon supplement and statin can cause hepatitis, and it should be discouraged.

PMCID: PMC4423171

PMID: 25923145 [PubMed - in process]

15. Three cases of liver toxicity with a dietary supplement intended to stop hair loss. Fernández J, Navascués C, Albines G, Franco L, Pipa M, Rodríguez M.

Rev Esp Enferm Dig. 2014 Dec;106(8):552-5.

Abstract:

Liver toxicity associated with herbal remedies and dietary supplements is an increasing concern. Several toxic hepatitis cases have been reported in the literature in association with products intended for weight loss where green tea extracts are an ingredient. Three hepatotoxicity cases are reported below in association with the use of Inneov masa capilar®, a dietary supplement intended to stop hair loss whose primary component is green tea catechins. In all of them, other potential causes of acute hepatitis were ruled out. We highlight the importance of awareness regarding these substances at history taking in order to identify and report hepatic adverse reactions secondary to apparently safe herbs as described in the present manuscript.

PMID: 25544415 [PubMed - in process]

16. Thyroid storm caused by a chinese herb contaminated with thyroid hormones. St-Onge M, Vandenberghe H, Thompson M.

Am J Case Rep. 2015 Feb 3;16:57-9. doi: 10.12659/AJCR.892305.

BACKGROUND: We report a case of thyroid storm caused by consuming a Chinese herb contaminated with thyroid hormones. **CASE REPORT:** A 70-year-old man presented to an emergency department after 2 days of nausea, vomiting, and weakness. Three days previously, he had started taking Cordyceps powder and "Flower Man Sang Hung" as recommended by his Chinese physician. Following admission, the patient deteriorated and was eventually diagnosed with thyroid storm complicated by rapid atrial fibrillation requiring cardioversion, intubation, and intensive care admission. The analysis of the Chinese herb "Flower Man Sang Hung" was positive for levothyroxine. The patient was extubated 11 days after admission and discharged to a rehabilitation centre after 17 days of hospitalization. The Chinese medicine physician was informed of the events. **CONCLUSIONS:** Herbal products can be the source of illness, medication interactions, and contamination. Awareness should be raised among Chinese medicine physicians, allopathic physicians, and their patients. Clinicians should also have a low threshold of suspicion to seek laboratory analysis of suspect substances when the cause of the clinical presentation is unclear.

PMCID: PMC4321408

PMID: 25644333 [PubMed - in process]

17. Postpartum hepatotoxicity due to herbal medicine *Teucrium polium*. Dag M, Öztürk Z, Aydın M, Koruk I, Kadayıfç A.

Ann Saudi Med. 2014 Nov-Dec;34(6):541-3. doi: 10.5144/0256-4947.2014.541.

Abstract:

The hepatotoxicity cases due to herbal medical products have been increased in recent years. *Teucrium polium* (TP) (mountain germander) is one of the most popular species of the Lamiaceae family and is commonly used for increasing breast milk formation and for relieving gastrointestinal complaints in the last months of pregnancy and postpartum periods. Here are presented 3 cases of serious hepatotoxicity due to TP. Three female patients aged 33, 31, and 37 years were admitted to clinic with jaundice and serious elevated liver enzymes for a period of 2 years. The patients were using TP for approximately 40 days to 3 months. Two of the 3 used TP during their previous pregnancies and were monitored for similar complaints by another center. After discontinuation of TP and supportive care, the liver function tests were decreased to normal limits within 3 months in all 3 patients. In addition to the potential hepatotoxic effect of TP, physiological changes in the postpartum period may increase the severity of hepatotoxicity. TP should be considered in differential diagnosis in patients presenting similar history and complaints, where it is used commonly.

PMID: 25971830 [PubMed - in process]

18. The Phytotherapeutic Fenugreek as Trigger of Toxic Epidermal Necrolysis. Bentele-Jaberg N, Guenova E, Mehra T, Nägeli M, Chang YT, Cozzio A, French LE, Hoetzenecker W.

Dermatology. 2015;231(2):99-102. doi: 10.1159/000433423. Epub 2015 Jul 1.

Abstract:

We describe the case of a 32-year-old woman who presented to the hospital with generalized painful exanthema, blisters and erosions 1 month after giving birth to a healthy girl. The patient's medical history was inconspicuous for comorbidities; however, it included the incidental intake of pain killers and a herbal preparation (fenugreek), which she took regularly over the last 4 weeks to improve lactation. Based on the clinical characteristics, we suspected toxic epidermal necrolysis (TEN), a severe cutaneous adverse drug reaction, which was confirmed by skin biopsy. The patient was treated with high-dose intravenous human immunoglobulins and was discharged 2 weeks after hospital admission in good condition. The allergological workup identified fenugreek as the most likely causative agent. Given the increased self-medication of freely available phytotherapeutics by patients in industrialized countries, herbal mixtures should be taken into consideration in the diagnostic workup of TEN.

PMID: 26138328 [PubMed - in process]

19. A cluster of lead poisoning among consumers of Ayurvedic medicine. Breeher L, Mikulski MA, Czczok T, Leinenkugel K, Fuortes LJ.

Int J Occup Environ Health. 2015 Apr 6:2049396715Y0000000009. [Epub ahead of print]

Abstract:

BACKGROUND: Use of alternative medications and herbal remedies is widespread in the United States and across the globe. These traditional medications can be contaminated with toxic metals. Despite several case reports of poisoning from such contamination, the epidemiological data are still limited. **OBJECTIVES:** To report on a cluster of lead and mercury toxicity cases in 2011 among a community of adherents of traditional medical practice of Ayurveda. **METHODS:** Adherents of Ayurveda were offered heavy metals screening following the identification of the index case. **RESULTS:** Forty-six of 115 participants (40%) had elevated blood lead levels (BLLs) of 10 µg/dl or above, with 9.6% of BLLs at or above 50 µg/dl. **CONCLUSIONS:** This is the largest cluster of lead and mercury toxicity following use of Ayurvedic supplements described in the literature in the US. Contamination of herbal products is a public health issue of global significance. There are few regulations addressing contamination of "natural" products or supplements.

PMID: 25843124 [PubMed - as supplied by publisher]

20. Toxic metal content in 52 frequently prescribed herbal medicines on the Korean market. Kim D, Hwang KH, Lee M, Kim JH, Jung K, Park SK.

Food Addit Contam Part B Surveill. 2015 Sep;8(3):199-206. doi: 10.1080/19393210.2015.1046405. Epub 2015 Jul 25.

Abstract:

This study was conducted to investigate the toxic metal content (Pb, As, Cd and Hg) of 52 frequently prescribed herbal medicines and to identify herbal medicines that exceed the Korea Food and Drug Administration (KFDA) maximum limits. A total of 3534 samples, including 1966 domestic samples and 1568 imported samples, were analysed using an Inductively Coupled Plasma-Mass Spectrometer (ICP-MS). Total amounts of Pb, As, Cd and Hg were significantly different between domestic (0.63 mg kg⁻¹) and imported (0.81 mg kg⁻¹) medicines (p < 0.05). Among the 52 kinds of samples, 4 kinds of herbs required quality control for Pb and 12 kinds of herbs required quality control for Cd. No sample contained As and Hg above the limits.

PMID: 26001121 [PubMed - in process]

21. Metallic mercury use by South African traditional health practitioners: perceptions and practices. Street RA, Kabera GM, Connolly C.

Environ Health. 2015 Aug 15;14(1):67. doi: 10.1186/s12940-015-0053-4.

Abstract:

BACKGROUND: Mercury is a toxic metal however its use in traditional healthcare systems remains widespread. The aim of this study was to determine the prevalence of mercury use by South African Traditional Health Practitioners (THP) and to document reasons for use and administration methods. **METHODS:** A cross-sectional study design was employed. A total of 201 THPs were enrolled from two main metropolitan areas of KwaZulu-Natal (South Africa), and 198 were included in the final analysis. Information on demographic characteristics, reasons for using or not using mercury as well as mercury administration methods were collected. **RESULTS:** Of the 198 THPs, 78 (39 %) used mercury for healing purposes and 74 (95 %) of the mercury users stated that they were taught to use it by another THP. The two main routes of

administration were oral and sub-cutaneous implantations (ukugcaba) at 85 % (n=66) and 59 % (n=46), respectively. The most common responses for mercury administration were for child birth (n=70; 90 %) and protection against guns (n=39; 50 %). **CONCLUSION:** This is the first study to describe the prevalence and practice of mercury use in South African traditional medicine. Socio-cultural mercury use is a potential source of exposure to both THPs and their patients. In light of such findings, public education messages and regulatory measures need to be effected.

PMCID: PMC4537568

PMID: 26276298

22. Mercury poisoning in two 13-year-old twin sisters. Khodashenas E, Aelami M, Balali-Mood M.

J Res Med Sci. 2015 Mar;20(3):308-11.

Abstract:

Mercury (Hg) is a toxic agent that evaporates in room temperature and its inhalation may cause poisoning. Due to the nonspecific symptoms, diagnosis is difficult in special circumstances with no initial history of Hg exposure. We report two such cases of Hg poisoning. The patients were two sisters, presenting with pain in extremities, itchy rashes, sweating, salivation, weakness, and mood changes. They have used a compound that contains mercury, for treatment of pediculosis three months before admission. This compound was purchased from a herbal shop and was applied locally on the scalps for 2 days. Their urinary mercury concentrations were 50 and 70 mg/L. They were successfully treated by D-penicillamine and gabapentin. In a patient with any kind of bone and joint pain, skin rash erythema and peripheral neuropathy, mercury poisoning should be considered as a differential diagnosis.

PMCID: PMC4468237

PMID: 26109979 [PubMed]

23. Safety assessment of mainstream smoke of herbal cigarette. Toxicol Res. 2015 Mar; 31(1):41-8. doi: 10.5487/TR.2015.31.1.041.

Bak JH, Lee SM, Lim HB.

Abstract:

Owing to the increase in price of cigarettes in Korea, herbal cigarettes have received increasing attention as a non-smoking aid; however, its safety has hardly been studied. We analyzed some of the toxic components in the mainstream smoke of herbal cigarettes, performed a mutagenicity test on smoke condensates for safety assessment, and compared the results with the corresponding values of a general cigarette with the same tar content. Herbal cigarette "A" was smoked using automatic smoking machine under ISO conditions in a manner similar to general cigarette "T". The tar content measured was higher than that inscribed on the outside of a package. The mainstream smoke of herbal cigarette "A" did not contain detectable levels of tobacco-specific nitrosamines and nicotine. Carbon monoxide and benzo(a)pyrene contents in herbal cigarette "A" were higher than those in the general cigarette "T". The phenolic contents such as hydroquinone, resorcinol, and catechol in herbal cigarette "A" were higher than those in the general cigarette "T", but cresol contents in herbal cigarette "A" were lower than those in the

general cigarette "T". The content of aromatic amines such as 4-aminobiphenyl in herbal cigarette "A" was higher than that in the general cigarette "T"; however, this difference was not statistically significant. On the other hand, 1-aminonaphthalene, 2-aminonaphthalene, and 3-aminobiphenyl contents in herbal cigarette "A" were lower than those in the general cigarette "T". The smoke condensates of herbal cigarette "A" exhibited a higher mutagenic potential than the condensates from the general cigarette "T" at the same concentration. We concluded that the mainstream smoke of herbal cigarette contains some toxic components, the smoke condensates of herbal cigarettes are mutagenic similar to general cigarette because of combustion products, and that the evaluation of the chemical and biological safety of all types of herbal cigarettes available on the market.

PMCID: PMC4395654

PMID: 25874032 [PubMed]

24. Incidence and Causes of Aconitum Alkaloid Poisoning in Hong Kong from 1989 to 2010. Chan TY.

Phytother Res. 2015 Aug;29(8):1107-11. doi: 10.1002/ptr.5370. Epub 2015 May 14.

Abstract:

Aconite roots contain Aconitum alkaloids, which are highly toxic cardiotoxins and neurotoxins. In this review, the main objective was to determine the incidence and causes of Aconitum alkaloid poisoning in Hong Kong between 1989 and 2010, based on six published reports from the territory-wide poison control units. In the New Territories East of Hong Kong, the incidence of aconite poisoning showed a sudden and sustained decrease from 0.60 (1989-1991) to 0.16 (1992-1993) and 0.17 (1996-1998) per 100 000 population, after publicity measures in late 1991 to promote awareness of the toxicity of aconite roots. In the whole of Hong Kong, the incidence of aconite poisoning was even lower in January 2000-June 2004 (0.03 per 100 000 population). However, aconite poisoning became more common again in April 2004-July 2009 and 2008-2010 (0.15 and 0.28 per 100 000 population). Overdoses and use of inadequately processed aconite roots were important causes. As from 2004 to 2009, 'hidden' aconite poisoning (toxicity caused by contaminants in other dispensed herbs) emerged as an important cause. It is important to continue the safety monitoring of potent herbs and the networking of poison control units. Further systematic studies would be required to identify the likely sources of contamination of herbs.

PMID: 25974837 [PubMed - in process]

25. Characteristics and practices of traditional Chinese medicine retail shops in London, UK: A cross-sectional study using an observational approach. Teng L, Shaw D, Barnes J.

J Ethnopharmacol. 2015 Jul 23. pii: S0378-8741(15)30044-1. doi: 10.1016/j.jep.2015.07.027. [Epub ahead of print]

Abstract:

ETHNOPHARMACOLOGICAL RELEVANCE: Traditional Chinese Medicine (TCM) is a popular form of ethnomedicine in the UK, and is accessed by Western, Chinese and other ethnic groups. The current regulatory regime does not effectively protect the public against poor-quality

and unsafe TCMs. Understanding ethnopharmacological information on how TCM is promoted and practiced may help to inform initiatives aimed at ensuring the safe use of TCMs in the UK, and put laboratory-based ethnopharmacological investigations of TCMs in a broader context. **AIM OF THE STUDY:** This study aimed to examine the characteristics and practices of TCM retail outlets in London, UK, and to identify factors relevant to the safe use of TCM in the UK. **MATERIALS AND METHODS:** TCM retail outlets ('shops') in London, UK, were identified using a systematic approach. A structured questionnaire including questions on shop business type was used to recruit participant shops. Shops consenting to participate were visited within six weeks of receiving consent. A piloted semi-structured questionnaire on shop characteristics was used for data collection following observation. The British National Formulary 53 was used to classify medical conditions/uses for TCMs promoted in the shops. Data were stored and analysed using MS Access 2003, MS Excel 2003 and SPSS 13. **RESULTS:** In total, 54 TCM shops in London were identified, of which 94% offered TCM consultations with a TCM practitioner. Detailed characteristics were described within 35/50 shops that gave consent to observing their premises. Most shops labelled and displayed over 150 Chinese Materia Medica (CMMs; crude materials, particularly herbs) for dispensing after consultations with a TCM practitioner. Medical conditions/uses and Patent Chinese Medicines (PCMs) were commonly promoted. In total, 794 occurrences of 205 different medical conditions/uses (median=32, QL=19, QU=48) were identified. These conditions/uses most commonly related to the following therapeutic systems: central nervous system (160/794, 20.2%); musculoskeletal and joint disease (133/794, 16.8%); obstetrics, gynaecology, and urinary-tract disorders (122/794, 15.4%); skin (102/794, 12.9%); gastrointestinal system (62/794, 7.8%). Specific conditions/uses that were frequently promoted included eczema (19/23 shops, 82.6%), arthritis (18/23, 78.3%), acne (17/23, 73.9%), obesity/weight loss/slimming (17/23, 73.9%) and psoriasis (17/23, 73.9%). Claimed conditions/uses included some serious medical conditions (e.g. diabetes, cancer and hypertension) and those focusing on vulnerable groups (e.g. children's diseases and pregnancy treatments). **CONCLUSIONS:** TCM shops in London, UK, typically displayed names of a wide range of medical conditions/uses for TCMs using readily understandable medical terms, implying TCM can be used to prevent or treat these conditions. However, many of these advertisements did not comply with UK regulations on medical claims for herbal medicines. Future studies should explore how these advertisements influence consumers' decisions to access TCM in the UK, practices of TCM shop staff towards the supply of TCMs in the UK, and what are the health implications at the individual and population levels.

PMID: 26212021

26. Toxic Effects of *Rhamnus alaternus*: A Rare Case Report. Ben Ghezala H, Chaouali N, Gana I, Snouda S, Nouioui A, Belwaer I, Ouali J, Kaddour M, Masri W, Ben Salah D, Amira D, Ghorbal H, Hedhili A.

Case Rep Emerg Med. 2015;2015:182951. doi: 10.1155/2015/182951. Epub 2015 Jul 1.

Abstract:

In Tunisia, there are about 478 species of plants commonly used in folk medicine. Medicinal plants and herbal remedies used are responsible for 2% of intoxications listed by Tunisian National Poison Center. Most cases are related to confusion between edible plants and toxic plants lookalikes or to an excessive consumption of therapeutic plants. We report the case of a 58-year-old man admitted to the Emergency Department of the Regional Hospital of Zaghouan (Tunisia), with renal failure and rhabdomyolysis. The patient reported having daily consumption

of a homemade tea based on Mediterranean Buckthorn roots, during the last 6 months to treat type 2 diabetes. The aim of this work was to establish an association between the consumption of the herbal remedy and the occurrence of both renal failure and rhabdomyolysis. No similar cases have been reported in recent literature.

PMCID: PMC4502303

PMID: 26229696 [PubMed]

27. Pyridoxine induced rosacea-like dermatitis. Acta Clin Croat. 2015 Mar;54(1):99-102.

Rezaković S, Mokos ZB, Paštar Z.

Abstract:

Rosacea is a common chronic inflammatory cutaneous disease of unknown etiology, characterized by remissions and exacerbations, presenting with centrofacial erythema and telangiectasias. It affects mainly adults around the age of 30 years and classically predominates in females. The pathophysiology of rosacea has not yet been fully understood. Risk factors are positive family history, very light skin phototype, sun exposure and consumption of spicy food or alcohol. Recently, there has been some evidence that some drugs or vitamins could be potential factors that can aggravate rosacea or induce rosacea-like symptoms. In this context, we present a 53-year-old female developing rosacea-like dermatitis due to a fixed combination of isoniazid and pyridoxine, which she was receiving along with rifampicin for the treatment of pulmonary tuberculosis.

PMID: 26058251 [PubMed - indexed for MEDLINE]