

Herbal Dietary Supplement SIG AACT March 2016 Abstracts

1. Reliability of causality assessment for drug, herbal and dietary supplement hepatotoxicity in the Drug-Induced Liver Injury Network (DILIN). Hayashi PH, Barnhart HX, Fontana RJ, Chalasani N, Davern TJ, Talwalkar JA, Reddy KR, Stolz AA, Hoofnagle JH, Rockey DC.

Liver Int. 2015 May;35(5):1623-32. doi: 10.1111/liv.12540. Epub 2014 Apr 16.

Abstract:

BACKGROUND & AIMS: Because of the lack of objective tests to diagnose drug-induced liver injury (DILI), causality assessment is a matter of debate. Expert opinion is often used in research and industry, but its test-retest reliability is unknown. To determine the test-retest reliability of the expert opinion process used by the Drug-Induced Liver Injury Network (DILIN). **METHODS:** Three DILIN hepatologists adjudicate suspected hepatotoxicity cases to one of five categories representing levels of likelihood of DILI. Adjudication is based on retrospective assessment of gathered case data that include prospective follow-up information. One hundred randomly selected DILIN cases were re-assessed using the same processes for initial assessment but by three different reviewers in 92% of cases. **RESULTS:** The median time between assessments was 938 days (range 140-2352). Thirty-one cases involved >1 agent. Weighted kappa statistics for overall case and individual agent category agreement were 0.60 (95% CI: 0.50-0.71) and 0.60 (0.52-0.68) respectively. Overall case adjudications were within one category of each other 93% of the time, while 5% differed by two categories and 2% differed by three categories. Fourteen per cent crossed the 50% threshold of likelihood owing to competing diagnoses or atypical timing between drug exposure and injury. **CONCLUSIONS:** The DILIN expert opinion causality assessment method has moderate interobserver reliability but very good agreement within one category. A small but important proportion of cases could not be reliably diagnosed as $\geq 50\%$ likely to be DILI.

PMCID: PMC4305346 [Available on 2016-05-01]

PMID: 24661785 [PubMed - indexed for MEDLINE]

2. 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). pii: E201. doi: 10.3390/ijms17020201.

Abstract: 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 or 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.

PMID: 26861284 [PubMed - in process]

3. RUCAM in Drug and Herb Induced Liver Injury: The Update. Danan G, Teschke R.

Int J Mol Sci. 2015 Dec 24;17(1). pii: E14. doi: 10.3390/ijms17010014.

Abstract: RUCAM (Roussel Uclaf Causality Assessment Method) or its previous synonym CIOMS (Council for International Organizations of Medical Sciences) is a well established tool in common use to quantitatively assess causality in cases of suspected drug induced liver injury (DILI) and herb induced

liver injury (HILI). Historical background and the original work confirm the use of RUCAM as single term for future cases, dismissing now the term CIOMS for reasons of simplicity and clarity. RUCAM represents a structured, standardized, validated, and hepatotoxicity specific diagnostic approach that attributes scores to individual key items, providing final quantitative gradings of causality for each suspect drug/herb in a case report. Experts from Europe and the United States had previously established in consensus meetings the first criteria of RUCAM to meet the requirements of clinicians and practitioners in care for their patients with suspected DILI and HILI. RUCAM was completed by additional criteria and validated, assisting to establish the timely diagnosis with a high degree of certainty. In many countries and for more than two decades, physicians, regulatory agencies, case report authors, and pharmaceutical companies successfully applied RUCAM for suspected DILI and HILI. Their practical experience, emerging new data on DILI and HILI characteristics, and few ambiguous questions in domains such alcohol use and exclusions of non-drug causes led to the present update of RUCAM. The aim was to reduce interobserver and intraobserver variability, to provide accurately defined, objective core elements, and to simplify the handling of the items. We now present the update of the well accepted original RUCAM scale and recommend its use for clinical, regulatory, publication, and expert purposes to validly establish causality in cases of suspected DILI and HILI, facilitating a straightforward application and an internationally harmonized approach of causality assessment as a common basic tool.

PMCID: PMC4730261

PMID: 26712744 [PubMed - in process]

4. Herb-Induced Liver Injury in the Berlin Case-Control Surveillance Study. Douros A, Bronder E, Andersohn F, Klimpel A, Kreutz R, Garbe E, Bolbrinker J.

Int J Mol Sci. 2016 Jan 15;17(1). pii: E114. doi: 10.3390/ijms17010114.

Abstract:Herb-induced liver injury (HILI) has recently attracted attention due to increasing reports of hepatotoxicity associated with use of phytotherapeutics. Here, we present data on HILI from the Berlin Case-Control Surveillance Study. The study was initiated in 2000 to investigate the serious toxicity of drugs including herbal medicines. Potential cases of liver injury were ascertained in more than 180 Departments of all 51 Berlin hospitals from October 2002 to December 2011. Drug or herb intake was assessed through a standardized face-to-face interview. Drug or herbal aetiology was assessed based on the updated Council for International Organizations of Medical Sciences scale. In ten of all 198 cases of hepatotoxicity included in the study, herbal aetiology was assessed as probable (once ayurvedic herb) or possible (Valeriana five times, Mentha piperita once, Pelargonium sidoides once, Hypericum perforatum once, Eucalyptus globulus once). Mean age was 56.4 ± 9.7 years, and the predominant pattern of liver injury was hepatocellular. No cases of acute liver failure or death were observed. This case series corroborates known risks for ayurvedic herbs, supports the suspected association between Valeriana use and liver injury, and indicates a hepatotoxic potential for herbs such as Pelargonium sidoides, Hypericum perforatum or Mentha piperita that were rarely associated with liver injury before. However, given that possible causality does not prove clinical significance, further studies in this field are needed.

PMCID: PMC4730355

PMID: 26784183 [PubMed - in process]

5. Energy Drinks: Implications for the Breastfeeding Mother. Thorlton J, Ahmed A, Colby DA.

MCN Am J Matern Child Nurs. 2016 Feb 23. [Epub ahead of print]

Abstract: Breastfeeding women may experience disrupted sleep schedules and be tempted to turn to popular energy drinks to reduce fatigue and enhance alertness, prompting the question: What are the maternal and child health implications for breastfeeding mothers consuming energy drinks? Caffeine and vitamin-rich energy drinks contain a variety of herbal ingredients and vitamins; however, ingredient

amounts may not be clearly disclosed on product labels. Interactions between herbal ingredients and caffeine are understudied and not well defined in the literature. Some infants can be sensitive to caffeine and display increased irritability and sleep disturbances when exposed to caffeine from breastmilk. Breastfeeding women who consume energy drinks may be ingesting herbal ingredients that have not undergone scientific evaluation, and if taking prenatal vitamins, may unknowingly exceed the recommended daily intake. Caffeinated products are marketed in newer ways, fueling concerns about health consequences of caffeine exposure. We present implications associated with consumption of caffeine and vitamin-rich energy drinks among breastfeeding women. Product safety, labeling, common ingredients, potential interactions, and clinical implications are discussed. Healthcare providers should encourage breastfeeding women to read product labels for ingredients, carbohydrate content, serving size, and to discourage consumption of energy drinks when breastfeeding and/or taking prenatal vitamins, to avoid potential vitamin toxicity.

PMID: 26909852 [PubMed - as supplied by publisher]

6. Proton NMR for detection, identification and quantification of adulterants in 160 herbal food supplements marketed for weight loss. Hachem R, Assemet G, Martins N, Balayssac S, Gilard V, Martino R, Malet-Martino M.

J Pharm Biomed Anal. 2016 Feb 22;124:34-47. doi: 10.1016/j.jpba.2016.02.022. [Epub ahead of print]

Abstract: One hundred and sixty food supplements (FS) marketed for weight loss and mainly purchased on the Internet were analyzed. All the FS were claimed as 100% natural containing only natural compounds, plant extracts and/or vitamins and the presence of an active pharmaceutical ingredient (API) was never mentioned. (1)H NMR spectroscopy was used for detecting the presence of adulterants and for their identification and quantification. Mass spectrometry was used as a complementary method for supporting their identification. Among the 164 samples considered because capsules from 5 different blisters of the same FS were analyzed, 56% were tainted with six API. Forty three contained sibutramine as single adulterant (26%), 9 phenolphthalein (6%) and 23 a mixture of these API (14%) that were both withdrawn from the market several years ago because of toxicity concerns. Sildenafil was found in 12 samples, either as a single adulterant (n=5) or in combination with sibutramine (n=3), phenolphthalein (n=3) and both sibutramine and phenolphthalein (n=1). Fluoxetine was present in 4 formulations, alone (n=3) or in combination with sibutramine and orlistat (n=1). At last, lorcaserine was detected in one FS. The content of sibutramine per dosage unit was comprised between 0.1 and 22mg and that of phenolphthalein between 0.05 and 56mg. The study also highlights poor manufacturing practices as evidenced for instance by the variability of API in capsules from different blisters of the same box. This paper demonstrates the need for more effective quality control of weight loss FS and the efficiency of (1)H NMR spectroscopy for the detection of tainted FS.

PMID: 26928212 [PubMed - as supplied by publisher]

7. Seasonal Variations of Mercury Levels in Selected Medicinal Plants Originating from Poland. Ordak M, Wesolowski M, Radecka I, Muszynska E, Bujalska-Zazdrozny M.

Biol Trace Elem Res. 2016 Feb 29. [Epub ahead of print]

Abstract: The presence of mercury in the living cells may be caused by environmental pollution with this element, which is referred to as a toxic xenobiotic. Many literature reports have provided evidence for toxic effects of low levels of mercury in the human body. Therefore, it seems essential to investigate mercury content in food and in natural environment, particularly its seasonal variations. The objective of this study was to determine trace amounts of mercury in 45 samples of 20 medicinal plant species collected in northern Poland, in various seasons of the year, i.e., in autumn 2012 and then spring 2013. The results obtained showed that the levels of mercury in the herbs were lower in spring (3.66-34.89 ng/g) than in autumn (4.55-81.54 ng/g). The statistically significant correlation ($p < 0.05$) between the levels

of mercury in herbs collected in spring and autumn indicates hazardous accumulation of the element in plants in autumn. The highest levels of mercury were found in leaves and plants growing in the vicinity of busy streets. Perennials plants have a significantly higher mercury levels as compared to those of monocarpic plants. Furthermore, commonly used herbal plants have a significantly higher mercury levels as compared to those less common.

PMID: 26923864 [PubMed - as supplied by publisher]

8. Adverse Effects of Plant Food Supplements Self-Reported by Consumers in the PlantLIBRA Survey Involving Six European Countries. Restani P, Di Lorenzo C, Garcia-Alvarez A, Badea M, Ceschi A, Egan B, Dima L, Lüde S, Maggi FM, Marculescu A, Milà-Villarroel R, Raats MM, Ribas-Barba L, Uusitalo L, Serra-Majem L.

PLoS One. 2016 Feb 29;11(2):e0150089. doi: 10.1371/journal.pone.0150089. eCollection 2016.

Abstract: BACKGROUND: The use of food supplements containing botanicals is increasing in European markets. Although intended to maintain the health status, several cases of adverse effects to Plant Food Supplements (PFS) have been described. OBJECTIVES: To describe the self-reported adverse effects collected during the European PlantLIBRA PFS Consumer Survey 2011-2012, with a critical evaluation of the plausibility of the symptomatology reported using data from the literature and from the PlantLIBRA Poisons Centers' survey. SUBJECTS/SETTING: From the total sample of 2359 consumers involved in the consumers' survey, 82 subjects reported adverse effects due to a total of 87 PFS. RESULTS: Cases were self-reported, therefore causality was not classified on the basis of clinical evidence, but by using the frequency/strength of adverse effects described in scientific papers: 52 out of 87 cases were defined as possible (59.8%) and 4 as probable (4.6%). Considering the most frequently cited botanicals, eight cases were due to *Valeriana officinalis* (garden valerian); seven to *Camellia sinensis* (tea); six to *Ginkgo biloba* (Maidenhair tree) and *Paullinia cupana* (guarana). Most adverse events related to the gastrointestinal tract, nervous and cardiovascular systems. CONCLUSIONS: Comparing the data from this study with those published in scientific papers and obtained by the PlantLIBRA Poisons Centers' survey, some important conclusions can be drawn: severe adverse effects to PFS are quite rare, although mild or moderate adverse symptoms can be present. Data reported in this paper can help health professionals (and in particular family doctors) to become aware of possible new problems associated with the increasing use of food supplements containing botanicals.

PMID: 26928206 [PubMed - in process]

9. Assessing Natural Product-Drug Interactions: An End-to-End Safety Framework. Roe AL, Paine MF, Gurley BJ, Brouwer KR, Jordan S, Griffiths JC.

Regul Toxicol Pharmacol. 2016 Jan 9;76:1-6. doi: 10.1016/j.yrtph.2016.01.004. [Epub ahead of print]

Abstract: The use of natural products (NPs), including herbal medicines and other dietary supplements, by North Americans continues to increase across all age groups. This population has access to conventional medications, with significant polypharmacy observed in older adults. Thus, the safety of the interactions between multi-ingredient NPs and drugs is a topic of paramount importance. Considerations such as history of safe use, literature data from animal toxicity and human clinical studies, and NP constituent characterization would provide guidance on whether to assess NP-drug interactions experimentally. The literature is replete with reports of various NP extracts and constituents as potent inhibitors of drug metabolizing enzymes, and transporters. However, without standard methods for NP characterization or in vitro testing, extrapolating these reports to clinically-relevant NP-drug interactions is difficult. This lack of a clear definition of risk precludes clinicians and consumers from making informed decisions about the safety of taking NPs with conventional medications. A framework is needed that describes an integrated robust approach for assessing NP-drug interactions; and, translation of the data into formulation alterations, dose adjustment, labelling, and/or post-marketing surveillance strategies. A

session was held at the 41st Annual Summer Meeting of the Toxicology Forum in Colorado Springs, CO, to highlight the challenges and critical components that should be included in a framework approach.

PMID: 26776752 [PubMed - as supplied by publisher]

10. Inhibition of CYP2B6 by Medicinal Plant Extracts: Implication for Use of Efavirenz and Nevirapine-Based Highly Active Anti-Retroviral Therapy (HAART) in Resource-Limited Settings.

Thomford NE, Awortwe C, Dzobo K, Adu F, Chopera D, Wonkam A, Skelton M, Blackhurst D, Dandara C.

Molecules. 2016 Feb 16;21(2). pii: E211. doi: 10.3390/molecules21020211.

Abstract: Highly active antiretroviral therapy (HAART) has greatly improved health parameters of HIV infected individuals. However, there are several challenges associated with the chronic nature of HAART administration. For populations in health transition, dual use of medicinal plant extracts and conventional medicine poses a significant challenge. There is need to evaluate interactions between commonly used medicinal plant extracts and antiretroviral drugs used against HIV/AIDS. Efavirenz (EFV) and nevirapine (NVP) are the major components of HAART both metabolized by CYP2B6, an enzyme that can potentially be inhibited or induced by compounds found in medicinal plant extracts. The purpose of this study was to evaluate the effects of extracts of selected commonly used medicinal plants on CYP2B6 enzyme activity. Recombinant human CYP2B6 was used to evaluate inhibition, allowing the assessment of herb-drug interactions (HDI) of medicinal plants *Hyptis suaveolens*, *Myrothamnus flabellifolius*, *Launaea taraxacifolia*, *Boerhavia diffusa* and *Newbouldia laevis*. The potential of these medicinal extracts to cause HDI was ranked accordingly for reversible inhibition and also classified as potential time-dependent inhibitor (TDI) candidates. The most potent inhibitor for CYP2B6 was *Hyptis suaveolens* extract ($IC_{50} = 19.09 \pm 1.16 \mu\text{g/mL}$), followed by *Myrothamnus flabellifolius* extract ($IC_{50} = 23.66 \pm 4.86 \mu\text{g/mL}$), *Launaea taraxacifolia* extract ($IC_{50} = 33.87 \pm 1.54 \mu\text{g/mL}$), and *Boerhavia diffusa* extract ($IC_{50} = 34.93 \pm 1.06 \mu\text{g/mL}$). *Newbouldia laevis* extract, however, exhibited weak inhibitory effects ($IC_{50} = 100 \pm 8.71 \mu\text{g/mL}$) on CYP2B6. *Lanai taraxacifolia* exhibited a TDI (3.17) effect on CYP2B6 and showed a high concentration of known CYP450 inhibitory phenolic compounds, chlorogenic acid and caffeic acid. The implication for these observations is that drugs that are metabolized by CYP2B6 when co-administered with these herbal medicines and when adequate amounts of the extracts reach the liver, there is a high likelihood of standard doses affecting drug plasma concentrations which could lead to toxicity.

PMID: 26891286 [PubMed - in process]

11. Drug-induced liver injury: A 2-year retrospective study of 1169 hospitalized patients in a single medical center. Woo HJ, Kim HY, Choi ES, Cho YH, Kim Y, Lee JH, Jang E.

Phytomedicine. 2015 Dec 1;22(13):1201-5. doi: 10.1016/j.phymed.2015.10.002. Epub 2015 Oct 20.

Abstract: BACKGROUND: Although herbal medicines (HMs) are widely used in Asian and Western countries, medicinal information concerning their hepatic toxicity or interaction with conventional medicines (CMs) is sparse. PURPOSE: The aim of our study was to estimate the prevalence of drug-induced liver injury (DILI) among total inpatients prescribed HMs or CMs. Furthermore, we noted all medications suspected to be associated with hepatotoxicity in the liver injury group during the period of hospitalization. STUDY DESIGN: We retrospectively observed medical records of 1169 inpatients in a single medical center from January 2012 to July 2014. METHODS: Based on a database of the 1169 inpatients at a single medical center, we researched the occurrence rate and type of liver injury according to the criteria of the Council for International Organization of Medical Science (CIOMS). We also utilized a simplified Roussel Uclaf Causality Assessment Method (RUCAM) score for probable causality assessment between drugs and liver injury. RESULTS: Among a total of 1169 inpatients, 13 cases whose baseline LFTs had been in the normal range at admission had abnormal liver parameters at the time of follow-up, and 11 of them (0.94%) were attributed to drugs: 0.43% (5 of 1169) to HMs, 0.43% (5 of 1169) to CMs, and 0.09% (1 of 1169) to combined drug classes. Two of them were found to have liver injury

because of pneumonia and sepsis. As for liver injury type, 8 cases were hepatocellular, 2 were cholestatic, and 1 was of mixed pattern. The common causative HMs for hepatotoxicity were Ephedrae Herb and Scutellariae Radix, while CMs included antidepressants, antihistamines, and antibacterials. CONCLUSIONS: We investigated approximate incidence rates and analyzed suspicious drugs associated with liver damage, which revealed a low frequency of liver injury induced by HMs. However, further study, based on a well-designed, long-term, multicenter prospective study, will be required to determine the safety of HMs.

PMID: 26598920 [PubMed - indexed for MEDLINE]

12. Herbal Medicine in Mexico: A Cause of Hepatotoxicity. A Critical Review. Valdivia-Correa B, Gómez-Gutiérrez C, Uribe M, Méndez-Sánchez N.

Int J Mol Sci. 2016 Feb 15;17(2). pii: E235. doi: 10.3390/ijms17020235.

Abstract: In Mexico, herbal products are commonly used as therapeutic tools. The analysis of several publications reveals that there are dozens of different herbs and herbal products used for different reasons, some of which have been implicated in causing toxic liver disease. However, methodological aspects limit the attribution of causality, and the precise incidence and clinical manifestations of herb-induced liver injury have not been well characterized. This review outlines the history of traditional herbal medicine in Mexico, critically summarizes the mechanisms and adverse effects of commonly used herbal plants, and examines the regulatory issues regarding the legal use of these products.

PMID: 26891292 [PubMed - in process]

13. A Case of Hepatotoxicity Related to Kombucha Tea Consumption. Gedela M, Potu KC, Gali VL, Alyamany K, Jha LK.

S D Med. 2016 Jan;69(1):26-8.

Abstract: The use of herbal and dietary supplements (HDSs) is widespread and growing due to the popular notion that these products are of natural origins and safe. Kombucha (or "mushroom") tea is one HDS that is consumed by people for various perceived health benefits. Kombucha tea is a well-known health beverage made by fermenting sweet black tea with a round, flat, gray fungus for a week or longer. There is concern, however, from the evidence of a few case reports currently available, that it may pose life-threatening and/or adverse effects for users.

PMID: 26882579 [PubMed - in process]

14. Echinacea-associated acute cholestatic hepatitis. Gabranis I, Koufakis T, Papakrivos I, Batala S.

J Postgrad Med. 2015 Jul-Sep;61(3):211-2. doi: 10.4103/0022-3859.159430.

No abstract.

PMID: 26119446 [PubMed - indexed for MEDLINE]

15. Cases of liver failure linked to "fat-burning" supplement. Wong LL.

J Fam Pract. 2015 Sep;64(9):519.

No abstract.

PMID: 26546949 [PubMed - indexed for MEDLINE]

16. Silymarin as a Natural Antioxidant: An Overview of the Current Evidence and Perspectives. Surai PF.

Antioxidants (Basel). 2015 Mar 20;4(1):204-47. doi: 10.3390/antiox4010204.

Abstract: Silymarin (SM), an extract from the *Silybum marianum* (milk thistle) plant containing various flavonolignans (with silybin being the major one), has received a tremendous amount of attention over the last decade as a herbal remedy for liver treatment. In many cases, the antioxidant properties of SM are considered to be responsible for its protective actions. Possible antioxidant mechanisms of SM are evaluated in this review. (1) Direct scavenging free radicals and chelating free Fe and Cu are mainly effective in the gut. (2) Preventing free radical formation by inhibiting specific ROS-producing enzymes, or improving an integrity of mitochondria in stress conditions, are of great importance. (3) Maintaining an optimal redox balance in the cell by activating a range of antioxidant enzymes and non-enzymatic antioxidants, mainly via Nrf2 activation is probably the main driving force of antioxidant (AO) action of SM. (4) Decreasing inflammatory responses by inhibiting NF- κ B pathways is an emerging mechanism of SM protective effects in liver toxicity and various liver diseases. (5) Activating vitagenes, responsible for synthesis of protective molecules, including heat shock proteins (HSPs), thioredoxin and sirtuins and providing additional protection in stress conditions deserves more attention. (6) Affecting the microenvironment of the gut, including SM-bacteria interactions, awaits future investigations. (7) In animal nutrition and disease prevention strategy, SM alone, or in combination with other hepato-active compounds (carnitine, betaine, vitamin B12, etc.), might have similar hepatoprotective effects as described in human nutrition.

PMCID: PMC4665566

PMID: 26785346 [PubMed]

17. Progress on mechanism of Tripterygium wilfordii-induced liver injury and detoxification mechanism of licorice. Cao LJ, Yan M, Li HD, Zhang BK, Fang PF.

Zhongguo Zhong Yao Za Zhi. 2015 Jul;40(13):2537-41.

Abstract: Tripterygium wilfordii has exhibited multiple pharmacological activities, such as anti-inflammatory, immune modulation, anti-tumor and anti-fertility. T. wilfordii have been used for the therapy of inflammation and autoimmune diseases including rheumatoid arthritis, immune complex nephritis and systemic lupus erythematosus clinically. However, it is well known that T. wilfordii has small margin between the therapeutic and toxic doses and could cause serious injury on digestive, reproductive and urogenital systems. Among all the organs, liver is one of the most remarkable targets of T. wilfordii-induced toxicities, and the damage is more serious than others. It is generally accepted that T. wilfordii-induced liver injury is a result of the combined effects of toxic elements of T. wilfordii. It is reported in several studies that the mechanism of T. wilfordii-induced liver injury may be related to lipid peroxidation, cell apoptosis and immune damage, and so on. Licorice is one of the most commonly used Chinese herbal medicine, with effects of heat-clearing and detoxicating, anti-inflammatory and hepatoprotective, reconciling various drugs, and so on. Licorice often accompany T. wilfordii in clinical application which can significantly reduce the liver injury induced by T. wilfordii. The attenuated effect is exact, but the mechanism is still a lack of in-depth study. This paper reviews the studies on T. wilfordii-induced liver injury and the related mechanism as well as licorice and other traditional Chinese medicine accompany T. wilfordii to reduce the injury in recent years, so as to provide reference for related research in the future.

PMID: 26697674 [PubMed - indexed for MEDLINE]

18. Fatal kavalactone intoxication by suicidal intravenous injection. Ketola RA, Viinamäki J, Rasanen I, Pelander A, Goebeler S.

Forensic Sci Int. 2015 Apr;249:e7-11. doi: 10.1016/j.forsciint.2015.01.032. Epub 2015 Feb 2.

Abstract: Kavalactones are a group of compounds found in kava, a beverage or extract prepared from the rhizome of the kava plant (*Piper methysticum*). Traditionally kava extracts have been used for their anxiolytic and sedative properties. Sales of kava extracts were severely restricted or prohibited in European countries in 2002 following several cases of serious hepatotoxicity. Here we report a case where high concentrations of kavalactones and ethanol were detected in post mortem femoral blood. An injection needle with a 10-mL syringe containing 7.5 mL of slightly yellowish liquid was found next to the victim, and there were numerous needle prints on both lower arms following the venous tracks. No evidence of other cause of death was found in the medico-legal investigation. The case was therefore classified as suicide using an injection of kavalactones intravenously together with alcohol poisoning.

PMID: 25684328 [PubMed - indexed for MEDLINE]

19. 'Herbal' but potentially hazardous: an analysis of the constituents and smoke emissions of tobacco-free waterpipe products and the air quality in the cafés where they are served. Hammal F, Chappell A, Wild TC, Kindzierski W, Shihadeh A, Vanderhoek A, Huynh CK, Plateel G, Finegan BA.

Tob Control. 2015 May;24(3):290-7. doi: 10.1136/tobaccocontrol-2013-051169. Epub 2013 Oct 15.

Abstract: BACKGROUND: There are limited data on the composition and smoke emissions of 'herbal' shisha products and the air quality of establishments where they are smoked. METHODS: Three studies of 'herbal' shisha were conducted: (1) samples of 'herbal' shisha products were chemically analysed; (2) 'herbal' and tobacco shisha were burned in a waterpipe smoking machine and main and sidestream smoke analysed by standard methods and (3) the air quality of six waterpipe cafés was assessed by measurement of CO, particulate and nicotine vapour content. RESULTS: We found considerable variation in heavy metal content between the three products sampled, one being particularly high in lead, chromium, nickel and arsenic. A similar pattern emerged for polycyclic aromatic hydrocarbons. Smoke emission analyses indicated that toxic byproducts produced by the combustion of 'herbal' shisha were equivalent or greater than those produced by tobacco shisha. The results of our air quality assessment demonstrated that mean PM_{2.5} levels and CO content were significantly higher in waterpipe establishments compared to a casino where cigarette smoking was permitted. Nicotine vapour was detected in one of the waterpipe cafés. CONCLUSIONS: 'Herbal' shisha products tested contained toxic trace metals and PAHs levels equivalent to, or in excess of, that found in cigarettes. Their mainstream and sidestream smoke emissions contained carcinogens equivalent to, or in excess of, those of tobacco products. The content of the air in the waterpipe cafés tested was potentially hazardous. These data, in aggregate, suggest that smoking 'herbal' shisha may well be dangerous to health.

PMID: 24128428 [PubMed - indexed for MEDLINE]

20. Knowledge, attitudes and behaviours on doping and supplements in young football players in Italy. Giraldi G, Unim B, Masala D, Miccoli S, La Torre G.

Public Health. 2015 Jul;129(7):1007-9. doi: 10.1016/j.puhe.2015.05.008. Epub 2015 Jun 26.

No abstract.

PMID: 26119988 [PubMed - indexed for MEDLINE]

21. The risk of copper deficiency in patients prescribed zinc supplements. Duncan A, Yacoubian C, Watson N, Morrison I.

J Clin Pathol. 2015 Sep;68(9):723-5. doi: 10.1136/jclinpath-2014-202837. Epub 2015 Jun 17.

Abstract: AIMS: In high doses zinc may cause copper deficiency, a diagnosis that is often missed resulting in anaemia, neutropenia and irreversible neurological symptoms. The aim of this study was to assess if zinc deficiency is erroneously diagnosed by misinterpretation of plasma zinc concentrations and whether copper deficiency is induced in patients prescribed zinc. METHODS: Casenotes of 70 patients prescribed zinc were scrutinised. Plasma concentrations of zinc, copper, C reactive protein and albumin were recorded from the laboratory database. RESULTS: 62% of patients were prescribed zinc at doses sufficient to cause copper deficiency. In 48% of the patients, plasma zinc concentrations were low as a probable result of hypoalbuminaemia or the systemic inflammatory response rather than deficiency. Awareness of copper deficiency was lacking; it was only documented as a possible side effect in one patient and plasma copper was measured in only two patients prescribed zinc. 9% of patients developed unexplained anaemia and 7% developed neurological symptoms typical of copper deficiency. CONCLUSIONS: Zinc deficiency is frequently misdiagnosed on the basis of low plasma zinc concentrations. The potential risk of copper deficiency developing in patients prescribed high doses of zinc is apparently infrequently considered. It is probable that a significant minority of patients prescribed with high doses of zinc develop iatrogenic copper deficiency.

PMID: 26085547 [PubMed - indexed for MEDLINE]

22. Pitfalls in the diagnostic evaluation of subacute combined degeneration. Ulrich A, Müller D, Linnebank M, Tarnutzer AA.

BMJ Case Rep. 2015 May 14;2015. pii: bcr2014208622. doi: 10.1136/bcr-2014-208622.

Abstract: We report a case of a 43-year-old man presenting with a 2-week history of painless ascending sensory disturbances, suspected to be suffering from acute inflammatory polyneuropathy. On clinical examination, deep tendon reflexes were preserved and muscle strength was 5/5 everywhere. Gait was ataxic with positive Romberg test. Lumbar puncture was normal and electroneurography demonstrated demyelination. With spinal cord involvement centred on the posterior tracts on MRI, differential diagnosis focused on cobalamin deficiency. Initial laboratory work up showed nearly normal holotranscobalamin (43 pmol/L, normal >50) suggesting no vitamin B12 deficiency. Surprisingly, further testing including methylmalonic acid (3732 nmol/L, normal <271) and homocysteine (48.5 µmol/L, normal <10) showed an impairment of vitamin B12-dependent metabolism leading to the diagnosis of subacute combined degeneration. Only after repeated history taking did the patient remember having taken tablets containing cobalamin for 3 days before hospitalisation. In case of B12 deficiency, holotranscobalamin can rapidly normalise during supplementation, whereas methylmalonic acid and homocysteine might help to detect B12 deficiency in patients who recently started supplementation.

PMID: 25976195 [PubMed - indexed for MEDLINE]

23. Plasma Cell Gingivitis: An Occasional Case Report. Mishra MB, Sharma S, Sharma A.

N Y State Dent J. 2015 Aug-Sep;81(5):57-60.

Abstract: Plasma cell gingivitis, an infrequently observed oral condition, has been clinically characterized by diffuse gingival enlargement, erythema and sometimes desquamation. These lesions are usually asymptomatic, but invariably the patient will complain of a burning sensation in the gingiva and bleeding from the mouth. The diagnosis requires hematological screening in addition to clinical and histopathological examinations. This case report outlines one such case of plasma cell gingivitis in a 15-year-old female caused by use of an herbal, homemade toothpowder. The case presented here highlights the adverse effects and irrational use of herbal agents in dentifrices. At the same time, it emphasizes the need for comprehensive history taking, careful clinical examination and appropriate diagnostic tests in order to arrive at a definitive diagnosis and treatment plan for gingival conditions that are refractory to conventional therapy and to exclude certain malignancies and oral manifestations of systemic diseases.

PMID: 26521330 [PubMed - indexed for MEDLINE]