

AACT Herbal Dietary Supplements SIG Abstracts Sept. 2016

1. Cushing in a Leaf: Endocrine Disruption From a Natural Remedy. Martini C, Zanchetta E, Di Ruvo M, Nalesso A, Battocchio M, Gentilin E, Degli Uberti E, Vettor R, Zatelli MC.

J Clin Endocrinol Metab. 2016 Aug;101(8):3054-60. doi: 10.1210/jc.2016-1490. Epub 2016 May 24.

BACKGROUND: Information regarding the safety of herbal drugs is often not reported. We describe the case of a 65-year-old woman referred to us for a iatrogenic hypercortisolism, who denied any previous steroid consumption. She reported only a chronic application of a phytocosmetic cream, containing ethanol extract of the *Cardiospermum halicacabum* (CH) plant. Adrenal insufficiency occurred after the cream application was stopped. CH is used in traditional and Western medicine for its documented anti-inflammatory properties. Once the presence of synthetic glucocorticoids was ruled out in the phytocosmetic product, we investigated whether and how its chronic application could have caused the iatrogenic hypercortisolism. **METHODS:** Liquid chromatography high-resolution mass spectrometry (LC-HRMS) was performed to exclude the presence of known glucocorticoids in the cream. ELISA assay and Western blot analysis were employed to assess ACTH secretion and the glucocorticoid receptor expression respectively in murine ACTH-secreting pituitary adenoma cells AtT-20/D16v-F2, treated with dexamethasone, CH tincture, and mifepristone alone or in combination. To detect specific interaction of CH extract with the glucocorticoid receptor, we performed a dual-luciferase reporter assay in HEK293 cells. **RESULTS:** In AtT-20/D16v-F2 cells, CH extract showed to significantly reduce basal and CRH-induced ACTH secretion and the glucocorticoid receptor expression, similarly to dexamethasone; these effects were counteracted by mifepristone. In HEK293 cells, dexamethasone significantly induced luciferase activity after 24- and 36-hour treatment and CH tincture only after 36 hours; these effects were antagonized by mifepristone. **CONCLUSIONS:** CH extract displays a glucocorticoid-like activity, by means of a direct binding to the glucocorticoid receptor.

DOI: 10.1210/jc.2016-1490

PMID: 27218272 [PubMed - in process]

2. Notes from the Field: Thyrotoxicosis After Consumption of Dietary Supplements Purchased Through the Internet--Staten Island, New York, 2015. Regina A, Majlesi N.

MMWR Morb Mortal Wkly Rep. 2016 Apr 8;65(13):353-4. doi: 10.15585/mmwr.mm6513a4.

On June 18, 2015, a woman aged 30 years was brought to the Staten Island University Hospital Emergency Department (ED) in New York by her mother, who reported that the patient had become acutely confused at home, was repeating herself, and did not recognize her family members. She had a diagnosis of bipolar disorder for which she took lithium, and she had a history notable for polysubstance abuse (use of three or more addictive drugs in the past 12 months). Her other medications included risperidone (an antipsychotic), benztropine (an anticholinergic), and bupropion (an antidepressant). ED staff members learned from the patient's mother that the patient had started taking "diet pills" that contained a thyroid hormone, which the patient had purchased through the Internet 2 weeks earlier. The patient volunteered that she had doubled the dosage 1 week earlier, in an attempt to lose more weight.

DOI: 10.15585/mmwr.mm6513a4

PMID: 27054849 [PubMed - indexed for MEDLINE]

3. Caffeine toxicity in forensic practice: possible effects and under-appreciated sources.

Musgrave IF, Farrington RL, Hoban C, Byard RW.

Forensic Sci Med Pathol. 2016 Sep;12(3):299-303. doi: 10.1007/s12024-016-9786-9. Epub 2016 Jun 25.

Caffeine is considered a very safe stimulant and is widely consumed in a variety of forms, from pure caffeine to beverages and foods. Typically, death is only seen when gram quantities of caffeine are consumed, usually in suicide attempts. Even in this scenario, death is rare. However, there are special populations that need to be considered in forensic presentations, who may be at greater risk. These include poor metabolizers, people with liver disease, and people with cardiac conditions, who can die as a result of caffeine intake at levels well below what is ordinarily considered toxic. Also, caffeine intake may be hidden. For example, herbal medicines with substantial caffeine content may not disclose these concentrations on their product label. The role of caffeine in medicolegal deaths is yet to be defined, however, herbal medicines and herbal weight loss supplements may represent an underappreciated source of caffeine in this context.

DOI: 10.1007/s12024-016-9786-9

PMID: 27344159 [PubMed - in process]

4. The adverse effects of long-term l-carnitine supplementation on liver and kidney function in rats. Liu L, Zhang DM, Wang MX, Fan CY, Zhou F, Wang SJ, Kong LD.

Hum Exp Toxicol. 2015 Nov;34(11):1148-61. doi: 10.1177/0960327115571767. Epub 2015 Feb 9.

Levo-Carnitine (l-carnitine) is widely used in health and food. This study was to focus on the adverse effects of 8-week oral supplementation of l-carnitine (0.3 and 0.6 g/kg) in female and male Sprague Dawley rats. l-carnitine reduced body and fat weights, as well as serum, liver, and kidney lipid levels in rats. Simultaneously, hepatic fatty acid β -oxidation and lipid synthesis were disturbed in l-carnitine-fed rats. Moreover, l-carnitine accelerated reactive oxygen species production in serum and liver, thereby triggering hepatic NOD-like receptor 3 (NLRP3) inflammasome activation to elevate serum interleukin (IL)-1 β and IL-18 levels in rats. Alteration of serum alkaline phosphatase levels further confirmed liver dysfunction in l-carnitine-fed rats. Additionally, l-carnitine may potentially disturb kidney function by altering renal protein levels of rat organic ion transporters. These observations may provide the caution information for the safety of long-term l-carnitine supplementation.

DOI: 10.1177/0960327115571767

PMID: 25669660 [PubMed - indexed for MEDLINE]

5. Estimates of Ethanol Exposure in Children from Food not Labeled as Alcohol-Containing. Gorgus E, Hittinger M, Schrenk D.

J Anal Toxicol. 2016 Sep;40(7):537-42. doi: 10.1093/jat/bkw046. Epub 2016 Jul 11.

Ethanol is widely used in herbal medicines, e.g., for children. Furthermore, alcohol is a constituent of fermented food such as bread or yogurt and "non-fermented" food such as fruit juices. At the same time, exposure to very low levels of ethanol in children is discussed as possibly having adverse effects on psychomotoric functions. Here, we have analyzed alcohol levels in different food products from the German market. It was found that orange, apple and grape juice contain substantial amounts of ethanol (up to 0.77 g/L). Furthermore, certain packed bakery products such as burger rolls or sweet milk rolls contained more than 1.2 g ethanol/100 g. We designed a scenario for average ethanol exposure by a 6-year-old child. Consumption data for the "categories" bananas, bread and bakery products and apple juice were derived from US and German surveys. An average daily exposure of 10.3 mg ethanol/kg body weight (b.w.) was estimated. If a high (acute) consumption level was assumed for one of the "categories," exposure rose to 12.5-23.3 mg/kg b.w. This amount is almost 2-fold (average) or up to 4-fold (high) higher than the lowest

exposure from herbal medicines (6 mg/kg b.w.) suggested to require warning hints for the use in children.

DOI: 10.1093/jat/bkw046

PMID: 27405361 [PubMed - in process]

6. Total, Dietary, and Supplemental Vitamin C Intake and Risk of Incident Kidney Stones.

Ferraro PM, Curhan GC, Gambaro G, Taylor EN.

Am J Kidney Dis. 2016 Mar;67(3):400-7. doi: 10.1053/j.ajkd.2015.09.005. Epub 2015 Oct 14.

BACKGROUND: Previous studies of vitamin C and kidney stones were conducted mostly in men and either reported disparate results for supplemental and dietary vitamin C or did not examine dietary vitamin C. **STUDY DESIGN:** Prospective cohort analysis. **SETTING & PARTICIPANTS:** 156,735 women in the Nurses' Health Study (NHS) I and II and 40,536 men in the Health Professionals Follow-up Study (HPFS). **PREDICTOR:** Total, dietary, and supplemental vitamin C intake, adjusted for age, body mass index, thiazide use, and dietary factors. **OUTCOMES:** Incident kidney stones. **RESULTS:** During a median follow-up of 11.3 to 11.7 years, 6,245 incident kidney stones were identified. After multivariable adjustment, total vitamin C intake (<90 [reference], 90-249, 250-499, 500-999, and $\geq 1,000$ mg/d) was not significantly associated with risk for kidney stones among women, but was among men (HRs of 1.00 [reference], 1.19 [95% CI, 0.99-1.46], 1.15 [95% CI, 0.93-1.42], 1.29 [95% CI, 1.04-1.60], and 1.43 [95% CI, 1.15-1.79], respectively; P for trend = 0.005). Median total vitamin C intake for the 500- to 999-mg/d category was ~700 mg/d. Supplemental vitamin C intake (no use [reference], <500, 500-999, and $\geq 1,000$ mg/d) was not significantly associated with risk for kidney stones among women, but was among men (HR, 1.19 [95% CI, 1.01-1.40] for $\geq 1,000$ mg/d; P for trend = 0.001). Dietary vitamin C intake was not associated with stones among men or women, although few participants had dietary intakes > 700 mg/d. **LIMITATIONS:** Nutrient intakes derived from food-frequency questionnaires, lack of data on stone composition for all cases. **CONCLUSIONS:** Total and supplemental vitamin C intake was significantly associated with higher risk for incident kidney stones in men, but not in women.

DOI: 10.1053/j.ajkd.2015.09.005

PMCID: PMC4769668 [Available on 2017-03-01]

PMID: 26463139 [PubMed - indexed for MEDLINE]

7. Efficacy of zinc sulfate supplement on febrile seizure recurrence prevention in children with normal serum zinc level: A randomised clinical trial.

Fallah R, Sabbaghzadegan S, Karbasi SA, Binesh F.

Nutrition. 2015 Nov-Dec;31(11-12):1358-61. doi: 10.1016/j.nut.2015.05.024. Epub 2015 Jul 6.

OBJECTIVE: Serum zinc level might be related to pathogenesis of febrile seizure (FS). The purpose of this study was to evaluate efficacy and safety of oral zinc supplementation on FS recurrence prevention in non-zinc-deficient children. **MATERIALS AND METHODS:** In a randomized clinical study, one hundred 18 to 60 mo old children with normal zinc level with first simple FS were referred to Shahid Sadoughi Hospital, Yazd, Iran from May 2012 to June 2013, were randomly assigned to two groups to receive 2 mg/kg/d zinc sulfate for six consecutive months or placebo as control group and were followed up for 1 y for FS recurrence. **RESULTS:** 41 girls and 59 boys with mean age of 2.47 ± 1.01 y were evaluated. Race, mean weight, height and body fat were similar in both groups. FS recurrence occurred in 19 children (38%) in the control group [95% confidence interval (CI): 19.45%-53.95%] and in 11 children (22%) in the zinc sulfate (95% CI: 57.47%-89.13%) groups, respectively; and the zinc group had lower FS recurrence (P = 0.03). The mean serum zinc level before intervention was lower in children with FS recurrence (72.43 ± 14.58 μ g/dL versus 96.33 ± 12.69 μ g/dL, P = 0.04). Gastrointestinal side effects (vomiting

in five children, heartburn in two children and abdominal pain in one child) were seen in 16% of the zinc group and vomiting occurred in two children (4%) in control group and frequency of adverse events was similar in the two groups ($P = 0.1$). **CONCLUSION:** Zinc supplementation should be considered as effective and safe in prevention of FS recurrence.

DOI: 10.1016/j.nut.2015.05.024

PMID: 26429655 [PubMed - indexed for MEDLINE]

8. Toxicity of Botanical Medicines: An Overlooked Global Health Problem. Marcus DM, Grollman AP.

Am J Public Health. 2016 Jan;106(1):16-7. doi: 10.2105/AJPH.2015.302937. Epub 2015 Nov 12.

Commentary

DOI: 10.2105/AJPH.2015.302937

PMID: 26562106 [PubMed - indexed for MEDLINE]

9. Liver toxicity related to herbs and dietary supplements: Online table of case reports. Part 3 of 6. Brown AC.

Food Chem Toxicol. 2016 Jul 8. pii: S0278-6915(16)30221-6. doi: 10.1016/j.fct.2016.07.001. [Epub ahead of print]

BACKGROUND: No current list of potentially life-threatening, hepatotoxic herbs and dietary supplements based on PubMed case studies exists in a summarized tabular form. **METHODS:** Documented case reports of herbs or dietary supplements appearing to contribute to liver injury were used to create a "Harmful Herb and Dietary Supplement List" of potentially hepatotoxic herbs and dietary supplements (PubMed, 1966 to May, 2015, and cross-referencing). The spectrum of herbal induced liver injuries (HDSILI) researched included elevated liver enzymes, hepatitis, steatosis, cholestasis, hepatic necrosis, hepatic fibrosis, hepatic cirrhosis, veno-occlusive disease, acute liver failure requiring a liver transplant, and death. **RESULTS:** Over the past 50 years, approximately 19 herbs (minus germander and usnic acid that are no longer sold) and 13 dietary supplements (minus the six no longer sold and vitamin A & niacin due to excess) posed a possible risk for liver injuries in certain individuals. The top three herbs with the most number of reported publications (but not cases studies) in descending order, were germander, black cohosh, kava extract, and green tea extract. **CONCLUSION:** These online tables will contribute to continued Phase IV post marketing surveillance to detect possible liver toxicity cases and serve to forewarn consumers, clinicians, and corporations.

DOI: 10.1016/j.fct.2016.07.001

PMID: 27402097 [PubMed - as supplied by publisher]

10. Freshwater clam extract supplement-induced acute cholestasis. Yokomori H, Yamazaki H, Oda M.

Hepatology. 2016 Feb;63(2):665-6. doi: 10.1002/hep.28320. Epub 2015 Dec 15.

Dietary supplements are increasingly used to support health in affluent societies. Adverse hepatic reactions have been reported following their intake. Freshwater clams are a widely consumed type of shellfish in Asia. Animal studies have revealed that freshwater clams have hepatoprotective characteristics. We describe a patient who developed drug induced liver injury following the use of a freshwater clam extract (FCE) supplement.

DOI: 10.1002/hep.28320

PMID: 26517853 [PubMed - indexed for MEDLINE]

11. The characteristics and clinical outcome of drug-induced liver injury in a Chinese hospital: A retrospective cohort study. Chen SS, Yu KK, Huang C, Li N, Zheng JM, Bao SX, Chen MQ, Zhang WH.

Medicine (Baltimore). 2016 Aug;95(34):e4683. doi: 10.1097/MD.0000000000004683.

The aim of this cohort study was to determine the characteristics and clinical outcome of 287 patients with drug-induced liver injury (DILI) in a Chinese hospital. Between January 2008 and January 2013, individuals who were diagnosed with DILI were selected. The complete medical records of each case were reviewed, and factors for the outcome of patients with DILI were extracted and analysed using univariate and multivariate analysis. Two hundred eighty-seven cases identified as DILI were included in the study. A total of 105 different drugs were considered to be related to the hepatotoxicity. The main causative group of drugs was Chinese herb (n=111). Liver failure developed in 9 (3.1%) patients, and 2 died (0.7%). Overall, complete recovery occurred in 92 (32.1%) patients. Univariate analysis and binary logistic regression analysis identified the digestive symptoms, jaundice, total bilirubin (TBIL), and direct bilirubin (DBIL) as independent factors for the non-recovery of DILI. Then the prediction model, including digestive symptoms, jaundice, TBIL, and DBIL, was built by using binary logistic regression analysis again. Receiver operating characteristic curve validated the strong power (area under the curve (AUC)=0.907) of prediction model for predicting the DILI non-recovery. DILI is an important cause of liver test abnormalities, and Chinese herb represented the most common drug group. The factors such as digestive symptoms, jaundice, TBIL, and DBIL have effect on DILI outcomes. The prediction model, including digestive symptoms, jaundice, TBIL, and DBIL, established in this study is really an excellent predictive tool for non-recovery of DILI patients.

DOI: 10.1097/MD.0000000000004683

PMID: 27559976 [PubMed - in process]

12. Hepatotoxicity by combination treatment of temozolomide, artesunate and Chinese herbs in a glioblastoma multiforme patient: case report review of the literature. Efferth T, Schöttler U, Krishna S, Schmiedek P, Wenz F, Giordano FA.

Arch Toxicol. 2016 Aug 12. [Epub ahead of print]

Glioblastoma multiforme (GBM) represents an aggressive tumor type with poor prognosis. The majority of GBM patients cannot be cured. There is high willingness among patients for the compassionate use of non-approved medications, which might occasionally lead to profound toxicity. A 65-year-old patient with glioblastoma multiforme (GBM) has been treated with radiochemotherapy including temozolomide (TMZ) after surgery. The treatment outcome was evaluated as stable disease with a tendency to slow tumor progression. In addition to standard medication (ondansetron, valproic acid, levetiracetam, lorazepam, clobazam), the patient took the antimalarial drug artesunate (ART) and a decoction of Chinese herbs (*Coptis chinensis*, *Siegesbeckia orientalis*, *Artemisia scoparia*, *Dictamnus dasycarpus*). In consequence, the clinical status deteriorated. Elevated liver enzymes were noted with peak values of 238 U/L (GPT/ALAT), 226 U/L (GOT/ASAT), and 347 U/L (γ -GT), respectively. After cessation of ART and Chinese herbs, the values returned back to normal and the patient felt well again. In the literature, hepatotoxicity is well documented for TMZ, but is very rare for ART. Among the Chinese herbs used, *Dictamnus dasycarpus* has been reported to induce liver injury. Additional medication included valproic acid and levetiracetam, which are also reported to exert hepatotoxicity. While all drugs alone may bear a minor risk for hepatotoxicity, the combination treatment might have caused increased liver enzyme activities. It can be speculated that the combination of these drugs caused liver injury. We conclude that the compassionate use of ART and Chinese herbs is not recommended during standard radiochemotherapy with TMZ for GBM.

DOI: 10.1007/s00204-016-1810-z

PMID: 27519711 [PubMed - as supplied by publisher]

13. Fulminant liver failure and transplantation after use of dietary supplements. Smith RJ, Bertilone C, Robertson AG.

Med J Aust. 2016 Jan 18;204(1):30-2.

Over 900 drugs and herbs have been reported to cause hepatotoxicity. In the United States, the use of herbal and dietary supplements is the second most common cause of idiosyncratic drug induced liver injury (DILI), after antimicrobial therapy. Of the herbal and dietary supplements, weight loss and body building supplements are most commonly implicated. In addition, contamination and adulteration of herbal supplements is common, with reported contaminants including undeclared antimicrobials, pharmaceuticals and heavy metals. Diagnosis of DILI is complicated by the tendency for herbal supplements to contain multiple ingredients, many of which are poorly characterised and could act synergistically. The protein supplement ingested by the patient in this case contained many ingredients, including green tea (*Camellia sinensis*) extract, green coffee extract, African mango extract, guarana, whey protein, and various vitamins and minerals. This, combined with his ingestion of a second supplement containing *G. cambogia* (active ingredient hydroxycitric acid), prohibits definitive identification of the causative agent or agents.

PMID: 26763816 [PubMed - indexed for MEDLINE]

14. Drug-induced liver injury associated with Complementary and Alternative Medicine: a review of adverse event reports in an Asian community from 2009 to 2014. Teo DC, Ng PS, Tan SH, Lim AT, Toh DS, Chan SY, Cheong HH.

BMC Complement Altern Med. 2016 Jul 7;16:192. doi: 10.1186/s12906-016-1168-z.

BACKGROUND: The use of Complementary and Alternative Medicine (CAM) has been increasing over the years. A recent review of adverse event reports (AERs) associated with CAM in Singapore found a notable number of AERs submitted. The objectives of this study are to analyse hepatotoxicity cases associated with CAM in Singapore based on spontaneous adverse event reporting to the Health Sciences Authority (HSA), and to highlight safety signals for specific herbal ingredients. **METHODS:** AERs associated with CAM and hepatotoxicity submitted to the Vigilance and Compliance Branch (VCB) of the HSA from 2009 to 2014 were compiled. The following information was extracted and analysed: Demographic information; time to onset; hospitalisation status; outcome; type of hepatotoxicity; ingredients of CAM, and the total daily doses (TDD); concurrent western medicines and health supplements; and reporter details. **RESULTS:** Fifty-seven reports were eligible for analysis. Thirty-five (61.4 %) cases involved Traditional Chinese Medicine (TCM). The Roussel Uclaf Causality Assessment Method was applied in 29 (82.9 %) of these cases, and the median score was 4 (range: 1-8). Chai Hu (*Radix bupleuri*) was suspected in 11 (31.4 %) cases. TDDs of most ingredients were within recommended doses of the Chinese Pharmacopoeia. **CONCLUSIONS:** Drug-induced liver injury is still poorly understood and more objective assessments are warranted. Reporting of adverse events should be strongly advocated to facilitate future analyses and the understanding of risk-benefit profiles of CAM.

DOI: 10.1186/s12906-016-1168-z

PMCID: PMC4937524

PMID: 27389194 [PubMed - in process]

15. Acute Hepatitis after Ingestion of a Preparation of Chinese Skullcap and Black Catechu for Joint Pain. Papafragkakis C, Ona MA, Reddy M, Anand S.

Case Reports Hepatol. 2016;2016:4356749. doi: 10.1155/2016/4356749. Epub 2016 Apr 10.

Many herbal preparations are routinely used and have been occasionally associated with a wide range of side effects, from mild to severe. Chinese skullcap and black catechu are herbal medications commonly used for their hepatoprotective and other properties. We report a case of acute toxic hepatitis associated with ingestion of Chinese skullcap and black catechu in one preparation for the alleviation of joint pain.

DOI: 10.1155/2016/4356749

PMCID: PMC4842037

PMID: 27144042 [PubMed]

16. Hidden Risks of Alternative Medicines: A Case of Boldo-Induced Hepatotoxicity. Ribeiro RJ, Silvestre C, Duarte C.

J Diet Suppl. 2016 Aug 30;1-5. [Epub ahead of print]

The alternative medicines are commonly used, especially herbal ones. Among them, boldo is traditionally used for symptomatic treatment of dyspepsia and mild gastrointestinal spasmodic disorders. Nevertheless, the number of reported cases of possible hepatotoxicity of some of these products has increased, including one report of boldo-induced hepatitis. We present the case of a 72-year-old female patient who has developed jaundice and increased serum levels of liver enzymes, after repeated consumption of boldo leaves infusion, during 2 weeks. After exclusion of common causes of hepatobiliary pathology, boldo-induced hepatotoxicity was considered probable. Interrupting of ingestion led to clinical and laboratorial recovery. This case proves the value of research in the alternative medicines' use. Ingestion of boldo, particularly in elderly patients with biliary tract disorders, may be the cause of otherwise unexplained jaundice or abnormal values of liver enzymes.

DOI: 10.1080/19390211.2016.1207123

PMID: 27576017 [PubMed - as supplied by publisher]

17. Case of acute lead toxicity associated with Ayurvedic supplements. Breyre A, Green-McKenzie J.

BMJ Case Rep. 2016 Jun 30;2016. pii: bcr2016215041. doi: 10.1136/bcr-2016-215041.

Use of traditional folkloric remedies not disclosed to the physician may be difficult to identify as a source of lead toxicity. This report illustrates the presentation of a 26-year-old man who, during his 1 month vacation in India, was treated for low back pain with Ayurvedic herbal medicine. On his return to the USA, he presented to the emergency department with epigastric pain, weight loss, dark stools, nausea and vomiting. He was admitted and noted to be anaemic with a blood lead level (BLL) of 94.8 $\mu\text{g/dL}$. Peripheral blood smear demonstrated basophilic stippling. Chelation therapy with succimer was initiated. The patient became asymptomatic within months. Three years later, he remained asymptomatic with BLL <20 $\mu\text{g/dL}$. Physicians should be cognisant of potential toxicity from these Ayurvedic medications and have a heightened level of suspicion for lead toxicity in the face of anaemia and abdominal pain without obvious cause.

DOI: 10.1136/bcr-2016-215041

PMID: 27364782 [PubMed - in process]

18. Adverse Effects of Grape Seed Extract Supplement: A Clinical Case and Long-Term Follow-Up. Berry AC, Nakshabendi R, Abidali H, Atchaneeyasakul K, Dholaria K, Johnson C, Kishore VA, Baltz AC.

J Diet Suppl. 2016;13(2):232-5. doi: 10.3109/19390211.2015.1008617. Epub 2015 Feb 17.

Grape seed extract (GSE) supplement use is becoming more popular today for its potential chemopreventive and chemotherapeutic role. We report a 49-year-old male who presented with recurrent nausea, vomiting, diarrhea, and acute weakness following GSE use. A thorough medical workup ensued and no causes were identified clinically, procedurally, or with imaging. Symptoms resolved after GSE discontinuation and the patient remained symptom-free 5 years later. This case illustrates the paucity of documented detailed clinical cases and lack of controlled trials detailing a thorough and reproducible adverse effect profile of GSE supplement.

DOI: 10.3109/19390211.2015.1008617

PMID: 25688637 [PubMed - indexed for MEDLINE]

19. Adulteration of herbal sexual enhancers and slimmers: The wish for better sexual well-being and perfect body can be risky. Skalicka-Woźniak K, Georgiev MI, Orhan IE.

Food Chem Toxicol. 2016 Jun 20. pii: S0278-6915(16)30199-5. doi: 10.1016/j.fct.2016.06.018. [Epub ahead of print]

The popularity of herbal medicines and dietary supplements is increasing all over the world due to the many side-effects assigned to synthetic drugs. Herbal remedies should be considered as safe, with no side-effects, but unfortunately, even if they are labelled as natural, large numbers of adulterants, not only with toxic heavy metals but also with undeclared synthetic substances, have been detected up to date. In this review, the most frequent instances of adulteration of herbal medicines and dietary supplements acting as sexual enhancers and slimming products are thoroughly discussed. The great success of synthetic phosphodiesterase type-5 (PDE-5) inhibitory drugs like sildenafil, vardenafil and tadalafil, used for the treatment of erectile dysfunction has made them, as well as their unapproved analogues, popular as adulterants in herbal dietary supplements. The second group among blockbuster products are herbal preparations for slimming purpose, as obesity and gaining weight are major problems worldwide. Here, sibutramine hydrochloride monohydrate, an anti-obesity drug which inhibits serotonergic and noradrenergic reuptake, seems to be the most common adulterant. Together with large numbers of its analogues, thyroid hormones, anorexigens, diuretics, stimulants, and laxative agents are also detected in most of tested diet supplements.

DOI: 10.1016/j.fct.2016.06.018

PMID: 27338710 [PubMed - as supplied by publisher]

20. Use of complementary and alternative medicines in haemodialysis patients: a cross-sectional study from Palestine. Zyoud SH, Al-Jabi SW, Sweileh WM, Tabeeb GH, Ayaseh NA, Sawafta MN, Khdeir RL, Mezyed DO, Daraghme DN, Awang R.

BMC Complement Altern Med. 2016 Jul 11;16:204. doi: 10.1186/s12906-016-1196-8.

BACKGROUND: Complementary and alternative medicine (CAM), and herbal therapies, are accepted worldwide, and have been important from medical, sociological and economic perspectives, among haemodialysis (HD) patients. The primary aim of this study was to evaluate the use of CAM among patients with end-stage renal disease (ESRD) who are undergoing HD.

METHODS: Face-to-face interviews of patients with ESRD undergoing HD from ten outpatient renal departments at a national level in Palestine were conducted from June 2014 to January 2015. A survey questionnaire, which included questions on socio-demographic and clinical characteristics, and on the CAM therapies that were used, was administered. **RESULTS:** Out of 267 patients interviewed, 172 patients used at least one type of CAM in the last month prior to the interview, and thus the utilisation rate was 64.4 %. Forty one (15.4 %) patients reported using one type of CAMs, while 18.7 % used two different CAMs and 30.3 % used more than two types of CAMs for their health status. Of the patients who used CAM, herbal therapies were used most often (43.5 %), followed by honey (35.6 %), diet (22.8 %), and exorcism in Islam (16.9 %). The herbal therapies mentioned most often were *Nigella sativa* L. (18.7 %), followed by *Salvia officinalis* L. (16.9 %), and *Pimpinella anisum* L. (10.5 %). **CONCLUSIONS:** In conclusion, the prevalence of CAM is relatively high in the selected population. Most patients used biological therapies such as herbal remedies, thus highlighting a greater need for patient education regarding CAM therapies and possible herb-drug interactions. Health care providers must be aware of the potential benefits and risks related to CAM use. There is a need for more clinical research pertaining to CAM to reach stronger evidence regarding potential benefits and risks related to CAM use.

DOI: 10.1186/s12906-016-1196-8

PMCID: PMC4940841

PMID: 27400742 [PubMed - in process]

21. Comparison of toxic heavy metals concentration in medicinal plants and their respective branded herbal formulations commonly available in Khyber Pakhtunkhwa. Shah WA, Zakiullah, Khuda F, Khan F, Saeed M.

Pak J Pharm Sci. 2016 Jul;29(4):1251-6.

The present study was conducted on fifteen medicinal plants and their respective branded formulations, commonly used in Khyber Pakhtunkhwa, for the evaluation of toxic heavy metals. The purpose of the study was to assess the toxic profile of the crude medicinal plants with respect to the worldwide permissible limits of metal concentrations and to correlate it with their respective herbal formulations available on the market. Chromium (Cr), Copper (Cu), Lead (Pb), Manganese (Mn) and Nickel (Ni) content were evaluated using wet digestion and Atomic Absorption Spectrophotometry technique. The results exhibited that in 100% of the analyzed medicinal plants Cr and Ni are present in excess of the maximum limits, Cu and Pb in 73% and 60% respectively, while Mn is in the normal range. Likewise in the respective branded formulations Cr and Ni exceed the normal limit in 100% of the products, Cu and Pb in 27% and 20% of the products respectively, while Mn is in the normal range. It indicates that majority of people in Pakistan who frequently use herbal drugs in various forms are exposed to the hazardous elements, which may pose serious health effects. Regulatory measures should therefore be taken to protect the general public from their hazardous health effects.

PMID: 27393438 [PubMed - in process]

22. Acute Disseminated Encephalomyelitis after Oral Therapy with Herbal Extracts: A Case Report. Kaymakamzade B, Karabudak R, Kurne AT, Nurlu G.

Balkan Med J. 2016 May;33(3):366-9. doi: 10.5152/balkanmedj.2016.140420. Epub 2016 May 1.

BACKGROUND: Acute disseminated encephalomyelitis (ADEM) is a rare demyelinating disease of the central nervous system, commonly attributed to infections or vaccinations. Toxic or allergenic compounds can also trigger a response in the immune system and may cause demyelination. We present a case with ADEM after using oral herbal medications. **CASE REPORT:** A 25 year-old male developed bilateral central facial palsy and severe quadriparesis after taking herbal drugs (containing echinacea and many other herbal ingredients) for two weeks. He had used the extract

to increase his potency and reproductivity. He had no past history of recent immunization or viral infection. The clinical findings, cerebrospinal fluid (CSF) analysis and brain magnetic resonance imaging (MRI) were compatible with ADEM. The neurological findings were improved after seven doses of pulse methylprednisolone treatment. To our knowledge, this is the third report in the literature that links herbal therapy and demyelinating disease. **CONCLUSION:** Most of the ADEM cases related to herbal therapy in the literature similarly used echinacea. It is our opinion that other ingredients of the herbal extract used by our case, besides echinacea, could have the potential to cause a trigger in the immune system. Further studies are needed to clarify the immunological effects of different kinds of herbal compounds, as well as the effects of different parts of the plants and the results of various dosages. Moreover, ingredients should also be tested for toxicity, adverse effects and drug interactions.

DOI: 10.5152/balkanmedj.2016.140420

PMCID: PMC4899001

PMID: 27308086 [PubMed]

23. Padma 28 for intermittent claudication. Stewart M, Morling JR, Maxwell H.

Cochrane Database Syst Rev. 2016 Mar 29;3:CD007371. doi: 10.1002/14651858.CD007371.pub3.

BACKGROUND: Intermittent claudication (IC) is pain caused by chronic occlusive arterial disease that develops in a limb during exercise and is relieved with rest. Most drug treatments of IC have a limited effect in improving walking distance. Padma 28, a Tibetan herbal preparation, has been used to treat IC, but there is debate as to whether Padma 28 produces a clinical benefit beyond the placebo effect. This is an update of a review first published in 2013.

AUTHORS' CONCLUSIONS: Some evidence exists from individual trials to suggest that Padma 28 may be effective in increasing walking distances, at least in the short term (four months), in people with IC. Side effects do not appear to be a problem. However, the longer term effects of treatment are unknown and the clinical significance of the improvements in walking distance are questionable. Moreover, the quality of the evidence is limited by the small sample size of the available trials, limited reporting of statistical analyses that compared treatment groups, and relatively high withdrawal rates that were linked to the outcome. That is, patients were withdrawn if they failed to improve walking distance. There was also evidence of publication bias. We therefore feel there is currently insufficient evidence to draw conclusions regards the effectiveness of Padma 28 in the routine management of IC. Further well-designed research would be required to determine the true effects of this herbal preparation.

DOI: 10.1002/14651858.CD007371.pub3

PMID: 27021597 [PubMed - indexed for MEDLINE]

24. Chinese herbal medicine for menopausal symptoms. Zhu X, Liew Y, Liu ZL.

Cochrane Database Syst Rev. 2016 Mar 15;3:CD009023. doi:10.1002/14651858.CD009023.pub2.

BACKGROUND: Chinese herbal medicine (CHM) usage is expected to increase as women suffering from menopausal symptoms are seeking alternative therapy due to concerns from the adverse effects (AEs) associated with hormone therapy (HT). Scientific evidence for their effectiveness and safety is needed.

AUTHORS' CONCLUSIONS: We found insufficient evidence that Chinese herbal medicines were any more or less effective than placebo or HT for the relief of vasomotor symptoms. Effects on safety were inconclusive. The quality of the evidence ranged from very low to moderate; there is a need for well-designed randomised controlled studies.

DOI: 10.1002/14651858.CD009023.pub2
PMCID: PMC4951187 [Available on 2017-03-15]
PMID: 26976671 [PubMed - indexed for MEDLINE]

25. Vitamin supplementation for preventing miscarriage. Balogun OO, da Silva Lopes K, Ota E, Takemoto Y, Rumbold A, Takegata M, Mori R.

Cochrane Database Syst Rev. 2016 May 6;(5):CD004073. doi:10.1002/14651858.CD004073.pub4.

Update of Cochrane Database Syst Rev. 2011;(1):CD004073.

BACKGROUND: Miscarriage is a common complication of pregnancy that can be caused by a wide range of factors. Poor dietary intake of vitamins has been associated with an increased risk of miscarriage, therefore supplementing women with vitamins either prior to or in early pregnancy may help prevent miscarriage.

AUTHORS' CONCLUSIONS: Taking any vitamin supplements prior to pregnancy or in early pregnancy does not prevent women experiencing miscarriage. However, evidence showed that women receiving multivitamins plus iron and folic acid had reduced risk for stillbirth. There is insufficient evidence to examine the effects of different combinations of vitamins on miscarriage and miscarriage-related outcomes.

DOI: 10.1002/14651858.CD004073.pub4
PMID: 27150280 [PubMed - indexed for MEDLINE]