

Herbal Dietary Substances SIG Abstracts Nov. 2015

1. **The supplement sleuth.** Couzin-Frankel J.

Science. 2015 Aug 21;349(6250):780-3. doi: 10.1126/science.349.6250.780.

Since 2005, when internist Pieter Cohen of the Cambridge Health Alliance in Massachusetts found that his patients were being sickened by a Brazilian weight loss supplement containing antidepressants and thyroid hormones, he has become something of a mix of Indiana Jones and Sherlock Holmes of the supplement world. With chemist colleagues in the United States, Brazil, and Europe, he hunts for drugs illegally buried in supplements. Then he goes public. Ultimately, he hopes to inspire new regulations. So far, Cohen and his collaborators have identified three hidden stimulant drugs in supplements. The discoveries also highlight a broader problem, Cohen and others contend: a dysfunctional system for policing dietary supplements.

PMID: 26293935 [PubMed - indexed for MEDLINE]

2. **Potent and untested drugs sold as "dietary supplements",** (Letter) Kimergård A, Walker C, Cowan D.

BMJ. 2015 Aug 5;351:h4181. doi: 10.1136/bmj.h4181.

A new challenge to public health has recently emerged from potent and untested drugs being sold under the guise of "dietary" supplements. 1-4 Fuelled by growing demand for products promising a better body, enhanced performance, and increased wellbeing, this trend highlights creative marketing strategies used in the illicit supply of drugs. Nine supplements suspected of containing drugs were analysed as part of an investigation for the television programme Spotlight (broadcasted 31 March 2015 by BBC Northern Ireland). The supplements were bought from high street shops and from an e-commerce site (box). Products were sold as "fat burners" or "pro-hormones," with packaging often blatantly listing chemical names of drugs

PMID: 26245332 [PubMed - indexed for MEDLINE]

3. **Emergency Department Visits for Adverse Events Related to Dietary Supplements.** Geller AI, Shehab N, Weidle NJ, Lovegrove MC, Wolpert BJ, Timbo BB, Mozersky RP, Budnitz DS.

N Engl J Med. 2015 Oct 15;373(16):1531-40. doi: 10.1056/NEJMSa1504267.

Abstract:

BACKGROUND: Dietary supplements, such as herbal or complementary nutritional products and micronutrients (vitamins and minerals), are commonly used in the United States, yet national data on adverse effects are limited. **METHODS:** We used nationally representative surveillance data from 63 emergency departments obtained from 2004 through 2013 to describe visits to U.S. emergency departments because of adverse events related to dietary supplements. **RESULTS:** On the basis of 3667 cases, we estimated that 23,005 (95% confidence interval [CI], 18,611 to 27,398) emergency department visits per year were attributed to adverse events related to dietary supplements. These visits resulted in an estimated 2154 hospitalizations (95% CI, 1342 to 2967) annually. Such visits frequently involved young adults between the ages of 20 and 34 years (28.0% of visits; 95% CI, 25.1 to 30.8) and unsupervised children (21.2% of visits; 95% CI, 18.4 to 24.0). After the exclusion of unsupervised ingestion of dietary supplements by children, 65.9% (95% CI, 63.2 to 68.5) of emergency department visits for single-supplement-related adverse events involved herbal or complementary nutritional products; 31.8% (95% CI, 29.2 to 34.3) involved micronutrients. Herbal or complementary nutritional products for weight loss (25.5%; 95% CI, 23.1 to 27.9) and increased energy (10.0%; 95% CI, 8.0 to 11.9) were commonly implicated. Weight-loss or energy products caused 71.8% (95% CI, 67.6 to 76.1) of supplement-related adverse events involving palpitations, chest pain, or tachycardia, and 58.0% (95% CI, 52.2 to 63.7) involved persons 20 to 34 years of age. Among adults 65 years of age or older, choking or pill-induced dysphagia or globus caused 37.6% (95% CI, 29.1 to 46.2) of all emergency department visits for supplement-related adverse events; micronutrients were implicated in 83.1% (95% CI, 73.3 to 92.9) of these visits. **CONCLUSIONS:** An estimated 23,000 emergency department visits in the United States every year are attributed to adverse events related to dietary supplements. Such visits commonly involve cardiovascular manifestations from weight-loss or energy products among young adults and swallowing problems, often associated with micronutrients, among older adults.

PMID: 26465986 [PubMed - indexed for MEDLINE]

4. Complementary and alternative drug therapy versus science-oriented medicine.

Anlauf M, Hein L, Hense HW, Köbberling J, Lasek R, Leidl R, Schöne-Seifert B.

Ger Med Sci. 2015 Jun 23;13:Doc05. doi: 10.3205/000209.

Abstract:

This opinion deals critically with the so-called complementary and alternative medical (CAM) therapy on the basis of current data. From the authors' perspective, CAM prescriptions and most notably the extensive current endeavours to the "integration" of CAM into conventional patient care is problematic in several respects. Thus, several CAM measures are used, although no specific effects of medicines can be proved in clinical studies. It is extensively explained that the methods used in this regard are those of evidence-based medicine, which is one of the indispensable pillars of science-oriented medicine. This standard of proof of efficacy is fundamentally independent of the requirement of being able to explain efficacy of a therapy in a manner compatible with the insights of the natural sciences, which is also essential for medical progress. Numerous CAM treatments can however never conceivably satisfy this requirement; rather they are justified with pre-scientific or unscientific paradigms. The high attractiveness of CAM measures evidenced in patients and many doctors is based on a combination of positive expectations and experiences, among other things, which are at times unjustified, at times thoroughly justified, from a science-oriented view, but which are non-specific (context effects). With a view to the latter phenomenon, the authors consider the conscious use of CAM as unrevealed therapeutic placebos to be problematic. In addition, they advocate that academic medicine should again systematically endeavour to pay more attention to medical empathy and use context effects in the service of patients to the utmost. The subsequent opinion discusses the following after an introduction to medical history: the definition of CAM; the efficacy of most common CAM procedures; CAM utilisation and costs in Germany; characteristics of science-oriented medicine; awareness of placebo research; pro and contra arguments about the use of CAM, not least of all in terms of aspects related to medical ethics.

PMCID: PMC4480118

PMID: 26161049 [PubMed - in process]

5. Comparison of dietary supplement product knowledge and confidence between

pharmacists and health food store employees. Coon SA, Stevens VW, Brown JE, Wolff SE, Wrobel MJ.

J Am Pharm Assoc (2003). 2015 Mar-Apr;55(2):161-8. doi: 10.1331/JAPhA.2015.14071.

Abstract:

OBJECTIVES: To determine pharmacists' and health food store employees' knowledge about the safety and efficacy of common, nonvitamin, nonmineral dietary supplements in a retail setting and confidence in discussing, recommending, and acquiring knowledge about complementary and alternative medicine (CAM). **DESIGN:** Cross-sectional survey. **SETTING:** Central and western New York in May and June 2012. **MAIN OUTCOME MEASURES:** Knowledge and confidence survey scores based on true/false and Likert scale responses. **RESULTS:** Pharmacists' mean knowledge score was significantly higher than that of health food store employees (8.42 vs. 6.15 items of 15 total knowledge questions). Adjusting for differences in experience, education, occupation, and confidence, knowledge scores were significantly higher for pharmacists and those with a higher total confidence score. Pharmacists were significantly less confident about the safety and efficacy of CAM comparatively (13 vs. 16 items of 20 total questions). **CONCLUSION:** Pharmacists scored significantly higher than health food store employees on a survey assessing knowledge of dietary supplements' safety and efficacy. Despite the significant difference, scores were unacceptably low for pharmacists, highlighting a knowledge deficit in subject matter.

PMID: 25699640 [PubMed - indexed for MEDLINE]

6. Drug- and herb-induced liver injury: Progress, current challenges and emerging signals of post-marketing risk.

Raschi E, De Ponti F.

World J Hepatol. 2015 Jul 8;7(13):1761-71. doi: 10.4254/wjh.v7.i13.1761.

Abstract:

Drug-induced liver injury (DILI) and herb-induced liver injury is a hot topic for clinicians, academia, drug companies and regulators, as shown by the steadily increasing number of publications in the past 15 years. This review will first provide clues for clinicians to suspect idiosyncratic (unpredictable) DILI and succeed in diagnosis. Causality assessment remains challenging and requires careful medical history as well as awareness of multifaceted aspects, especially for herbs. Drug discontinuation and therapy reconciliation remain the mainstay in patient's management to minimize occurrence of acute liver failure. The second section will address novel agents associated with liver injury in 2014 (referred to as "signals"), especially in terms of clinical, research and drug development implications. Insights will be provided into recent trends by highlighting the contribution of different post-marketing data, especially registries and spontaneous reporting systems. This literature scrutiny suggests: (1) the importance of post-marketing databases as tools of clinical evidence to detect signals of DILI risk; and (2) the need for joining efforts in improving predictivity of pre-clinical assays, continuing post-marketing surveillance and design ad hoc post-authorization safety studies. In this context, ongoing European/United States research consortia and novel pharmaco-epidemiological tools (e.g., specialist prescription event monitoring) will support innovation in this field. Direct oral anticoagulants and herbal/dietary supplements appear as key research priorities.

PMCID: PMC4491905

PMID: 26167249 [PubMed]

7. Liver Injury from Herbal, Dietary, and Weight Loss Supplements: a Review. Zheng EX, Navarro VJ.

J Clin Transl Hepatol. 2015 Jun 28;3(2):93-8. doi: 10.14218/JCTH.2015.00006. Epub 2015 Jun 15.

Abstract:

Herbal and dietary supplement usage has increased steadily over the past several years in the United States. Among the non-bodybuilding herbal and dietary supplements, weight loss supplements were among the most common type of HDS implicated in liver injury. While drug induced liver injury is rare, its consequences are significant and on the rise. The purpose of this review is to highlight case reports of weight loss products such as Hydroxycut and OxyElite Pro as one form of HDS that have hepatotoxic potential and to characterize its clinical effects as well as pattern of liver injury. We also propose future strategies in the identification and study of potentially hepatotoxic compounds in an effort to outline a diagnostic approach for identifying any drug induced liver injury.

PMCID: PMC4548352

PMID: 26357638 [PubMed]

8. Adverse Psychiatric Effects Associated with Herbal Weight-Loss Products. Bersani FS, Coviello M, Imperatori C, Francesconi M, Hough CM, Valeriani G, De Stefano G, Bolzan Mariotti Posocco F, Santacroce R, Minichino A, Corazza O.

Biomed Res Int. 2015;2015:120679. doi: 10.1155/2015/120679. Epub 2015 Sep 17.

Abstract:

Obesity and overeating are among the most prevalent health concerns worldwide and individuals are increasingly using performance and image-enhancing drugs (PIEDs) as an easy and fast way to control their weight. Among these, herbal weight-loss products (HWLPs) often attract users due to their health claims, assumed safety, easy availability, affordable price, extensive marketing, and the perceived lack of need for professional oversight. Reports suggest that certain HWLPs may lead to onset or exacerbation of psychiatric disturbances. Here we review the available evidence on psychiatric adverse effects of HWLPs due to their intrinsic toxicity and potential for interaction with psychiatric medications.

PMCID: PMC4589574

PMID: 26457296 [PubMed - in process]

9. Sibutramine, a serotonin-norepinephrine reuptake inhibitor, causes fibrosis in rats. Oberholzer HM, van der Schoor C, Bester MJ.

Environ Toxicol Pharmacol. 2015 Jul;40(1):71-6. doi: 10.1016/j.etap.2015.05.011. Epub 2015 May 22.

Abstract:

Sibutramine hydrochloride monohydrate is a weight loss agent indicated for the treatment of obesity. Although it has been banned from most markets, studies are still relevant as it is often a hidden ingredient in herbal and over the counter slimming products. Sibutramine induces liver fibrosis with steatosis in female Sprague-Dawley rats fed a high-energy diet without significant weight gain. In this study, using the same animal model, the effect of Sibutramine on lung morphology was investigated using histological evaluation of the terminal bronchiole and transmission electron microscopy evaluation of the respiratory tissue. From these results Sibutramine was found to induce lung fibrosis in Sprague-Dawley rats as increased collagen synthesis, mast cell accumulation and aggregates of Bronchus Associated Lymphoid Tissue (BALT) in the terminal bronchiole as well as increased collagen deposition in the respiratory tissue was seen.

PMID: 26070021 [PubMed - in process]

10. A comprehensive scientific overview of *Garcinia cambogia*. Semwal RB, Semwal DK, Vermaak I, Viljoen A.

Fitoterapia. 2015 Apr;102:134-48. doi: 10.1016/j.fitote.2015.02.012. Epub 2015 Feb 27.

Abstract:

The fruit rind of *Garcinia gummi-gutta*, commonly known as *Garcinia cambogia* (syn.), is extensively used traditionally as a flavourant in fish curries due to its sharp sour taste. Additional ethnobotanical uses include its use as a digestive and a traditional remedy to treat bowel complaints, intestinal parasites and rheumatism. This small fruit, reminiscent of a pumpkin in appearance, is currently most popularly used and widely advertised as a weight-loss supplement. Studies have shown that the extracts as well as (-)-hydroxycitric acid (HCA), a main organic acid component of the fruit rind, exhibited anti-obesity activity including reduced food intake and body fat gain by regulating the serotonin levels related to satiety, increased fat oxidation and decreased de novo lipogenesis. HCA is a potent inhibitor of adenosine triphosphate-citrate lyase, a catalyst for the conversion process of citrate to acetyl-coenzyme A, which plays a key role in fatty acid, cholesterol and triglycerides syntheses. The crude extract or constituents from the plant also exerted hypolipidaemic, antidiabetic, anti-inflammatory, anticancer, anthelmintic, anticholinesterase and hepatoprotective activities in in vitro and in vivo models. Phytochemical studies of various plant parts revealed the presence of mainly xanthenes (e.g. carbogiol) and benzophenones (e.g. garcinol) together with organic acids (e.g. HCA) and amino acids (e.g. gamma aminobutyric acid). Currently, a large number of *G. cambogia*/HCA dietary supplements for weight management are being sold although the possible toxicity associated with the regular use of these supplements has raised concerns. In most cases, complaints have been related to multicomponent formulations and at this stage *G. cambogia* has not been confirmed as the potentially toxic culprit. This review presents a scientific overview of *G. cambogia* with reference to relevant botanical aspects, ethnobotanical uses, phytochemistry and biological activity as well as toxicity.

PMID: 25732350 [PubMed - indexed for MEDLINE]

11. Plants used in the traditional medicine of Mesoamerica (Mexico and central America) and the Caribbean for the treatment of obesity. Alonso-Castro AJ, Domínguez F, Zapata-Morales JR, Carranza-Álvarez C.

J Ethnopharmacol. 2015 Sep 24. pii: S0378-8741(15)30154-9. doi: 10.1016/j.jep.2015.09.029. [Epub ahead of print]

Abstract:

ETHNOPHARMACOLOGICAL RELEVANCE: Obesity is a worldwide medical concern. New ethnobotanical information regarding the antiobesity effect of medicinal plants has been obtained in the last 30 years in response to socio-demographic changes and high-fat diets became common. **AIM OF THE STUDY:** This review provides a summary of medicinal plants used in Mexico, Central America and the Caribbean for the empirical treatment of obesity in terms of ethnobotany, toxicity, pharmacology, conservation status, trade and chemistry. **MATERIALS AND METHODS:** Bibliographic investigation was performed by analyzing recognized books, undergraduate and postgraduate theses and peer-reviewed scientific articles, consulting worldwide accepted scientific databases from the last four decades. Medicinal plants used for the treatment of obesity were classified in two categories: 1) plants with pharmacological evidence and 2) plants without pharmacological evidence. **RESULTS:** A total of 139 plant species, belonging to 61 families, native to Mexico, Central America and the

Caribbean that are used for the empirical treatment of obesity were recorded. From these plants, 33 were investigated in scientific studies, and 106 plants lacked scientific investigation. Medicinal plants were experimentally studied in vitro (21 plants) and in vivo (16 plants). A total of 4 compounds isolated from medicinal plants used for the empirical treatment of obesity have been tested in vitro (2 compounds) and in vivo (4 compounds) studies. No clinical trials on obese subjects (BMI>30kg/m²) have been performed using the medicinal plants cited in this review. There are no herbal-based products approved in Mexico for the treatment of obesity. CONCLUSIONS: there are a limited number of scientific studies published on medicinal plants from Mexico, Central America and the Caribbean used for the treatment of obesity. This review highlights the need to perform pharmacological, phytochemical, toxicological and ethnobotanical studies with medicinal flora to obtain new antiobesity agents.

PMID: 26410815 [PubMed - as supplied by publisher]

12. Acute hepatitis induced by a Chinese herbal product Qibao Meiran Wan: a case study. Li X, Qu C, He Q, Chen W, Zhang X, Liu X, Liu Y, Tang Y.

Int J Clin Exp Med. 2015 Jul 15;8(7):11624-7.

Abstract:

Qibao Meiran Wan is a Chinese herbal product sold as a therapy for tonifying the liver and kidney, dizziness, premature graying of hair, backache, constipation, and night sweats. It is widely available in Chinese pharmacies and drugstores and is sold without prescription. We describe a case of acute liver injury in a 26-year-old Chinese man who developed symptomatic hepatitis 1 month after starting Qibao Meiran Wan. There was no evidence of viral hepatitis, Epstein-Barr virus, cytomegalovirus, autoimmune hepatitis, or Budd-Chiari syndrome. The liver injury slowly resolved over 20 days after discontinuing the herbal product. Herbal toxicity was later confirmed by a liver biopsy. Qibao Meiran Wan contains a mixture of several plants including *Polygonum multiflorum*, which was previously associated with hepatotoxicity. To our knowledge, this is the first report of hepatotoxicity by Qibao Meiran Wan. Clinicians treating patients with acute hepatitis of unclear etiology should pay attention to the consumption of Qibao Meiran Wan.

PMCID: PMC4565378

PMID: 26379995 [PubMed]

13. A comparison of patterns of spontaneous adverse drug reaction reporting with St. John's Wort and fluoxetine during the period 2000-2013. Hoban CL, Byard RW, Musgrave IF.

Clin Exp Pharmacol Physiol. 2015 Jul;42(7):747-51. doi: 10.1111/1440-1681.12424.

Abstract:

Herbal medicines are perceived to be safe by the general public and medical practitioners, despite abundant evidence from clinical trials and case reports that show herbal preparations can have significant adverse effects. The overall impact of adverse events to herbal medicines in Australia is currently unknown. Post marketing surveillance of medications through spontaneous adverse drug reaction (ADR) reports to the Therapeutic Goods Administration (TGA) is one way to estimate this risk. The patterns of spontaneously reported ADRs provide insight to herbal dangers, especially when compared with patterns of a mechanistically similar conventional drug. The study compared the pattern of spontaneously reported ADRs to St. John's Wort (*Hypericum perforatum*), a common herbal treatment for depression which contains selective serotonin reuptake inhibitors (SSRI), to fluoxetine, a commonly prescribed synthetic SSRI antidepressant. Spontaneous ADR reports sent to the TGA between 2000-2013 for St. John's Wort (n = 84) and fluoxetine (n = 447) were obtained and analysed. The demographic information, types of interaction, severity of the ADR, and the body systems affected (using the Anatomical Therapeutic Chemical classification system) were recorded for individual ADR cases. The majority of spontaneously reported ADRs for St. John's Wort and fluoxetine were concerning females aged 26-50 years (28.6%, 22.8%). The organ systems affected by ADRs to St John's Wort and fluoxetine have a similar profile, with the majority of cases affecting the central nervous system (45.2%, 61.7%). This result demonstrates that herbal preparations can result in ADRs similar to those of prescription medications.

PMID: 25988866 [PubMed - in process]

14. **The aphrodisiac herb *Carpolobia*: A biopharmacological and phytochemical review.** Nwidi LL, Nwafor PA, Vilegas W.

Pharmacogn Rev. 2015 Jul-Dec;9(18):132-9. doi: 10.4103/0973-7847.162128.

Abstract:

Any agent with the ability to provoke sexual desire in an individual is referred to as an aphrodisiac. Aphrodisiac plants are used in the management of erectile dysfunction (ED) in men. One such plant popular in West and Central Africa among the Pygmies of Cameroon, Ipassa of Garbon, and the Yoruba, Ibo, Efik and Ijaw peoples of Nigeria is *Carpolobia*. It is an accepted and commonly utilized herbal booster of libido. It is used to cure male infertility and to boosts libido thereby augmenting male sexual functions or it is used to induce penile erection, and enhance male virility. The chewing stick prepared from the stem and root of either *Carpolobia alba* (CA) or *Carpolobia lutea* (CL) is patronized because it boosts male sexual performance. The genus *Carpolobia* has over 14 species. The leaf essential oil contains a variety of terpenoids, while polyphenols and triterpenoid saponins have been isolated from the root and leaf extracts respectively. Other ethnomedicinal uses include curing of stomach ailments, rheumatism, fever, pains, insanity, dermal infection, venereal diseases; to promote child birth; and as a taeniafuge and vermifuge. In spite of its popularity, no scientific data reviewing the biopharmacological and phytochemical activities of *Carpolobia* exist to our knowledge. The aim of this work is to collate all available published scientific reports in the literature on *Carpolobia* in a review paper. In this review, an overview of the morphology, taxonomy, ethnomedicinal claims, geographical distribution, and structurally elucidated compounds that are secondary metabolites isolated and characterized from *Carpolobia* species is established. The pharmacological assays, phytochemical screenings, and toxicological reports are also reviewed.

PMCID: PMC4557236

PMID: 26392711 [PubMed]

15. **Systematic review on herb-induced liver injury in Korea.** Lee WJ, Kim HW, Lee HY, Son CG.

Food Chem Toxicol. 2015 Oct;84:47-54. doi: 10.1016/j.fct.2015.06.004. Epub 2015 Jul 10.

Abstract:

Herbal drugs are generally regarded as safe due to their extensive clinical use especially in East Asian countries. However, the potential toxicity of herbal drugs has become an important medical issue recently, resulting in numerous reports of drug-induced liver injury (DILI). Here, we performed a systematic review of herbal medicines with the potential to cause hepatotoxicity in Korea. A literature search of six databases, including PubMed and five Korean electronic databases, was performed to identify cases of herb-induced liver injury (HILI) in Korea, yielding 31 unique reports, including 21 single herb and 10 multi-herb preparations. From these reports, we identified 97 cases of HILI (47 males, 49 females, and 1 unknown sex) consisting of 74.7% hepatocellular-type injury, 10.8% cholestatic-type injury, and 14.5% mixed-type injury. Causative agents included 21 unique herbal preparations, including 11 single species and 10 multispecies, with *Polygoni Multiflora* (39.2%) and *Dictamnus dasycarpus* (37.1%) as the most frequent agents. These analyses presented a feature of HILI, and produced a comprehensive list of herbs with a higher risk of hepatotoxicity in Korea. Further studies will be necessary to ascertain the mechanisms by which these herbs induce HILI and to determine whether these effects are specific to the Korean population.

PMID: 26165727 [PubMed - in process]

16. **To chew or not to chew: that's the question.** Yildiz H, Komuta M, Monsalve C, Starkel P, Lefebvre C.

Acta Clin Belg. 2015 Sep 16;2295333715Y0000000070. [Epub ahead of print]

Abstract:

A 25-year-old Somalian man was referred to the department of internal medicine because of nausea, vomiting and jaundice of recent onset. On physical examination, he was frankly icteric without clinical signs of chronic liver disease. Laboratory data showed evidence of acute hepatitis. Viral serologic tests for hepatitis A, B, C and E were negative. Antinuclear antibodies (ANA) were positive (titre 1 : 1280; speckled pattern, NV < 1 : 40) as well anti-actin antibodies (titre 75UA, NV < 20). A liver biopsy was performed and showed a feature compatible with toxic hepatitis. On further questioning, the patient admitted to daily chew Khat when he was living in Somalia. We

concluded to Khat-induced toxic hepatitis together with high-titre anti-nuclear antibody mimicking serologic patterns of auto-immune hepatitis.

PMID: 26374255 [PubMed - as supplied by publisher]

17. Study of renal and hepatic toxicity in rats supplemented with creatine. Baracho NC, Castro LP, Borges Nda C, Laira PB.

Acta Cir Bras. 2015 May;30(5):313-8. doi: 10.1590/S0102-865020150050000002.

Abstract:

PURPOSE: To evaluate the renal and hepatic function, through biochemical analysis after 14 days of creatine supplementation in physically inactive rats. **METHODS:** Twenty four male, adult, Wistar rats were used which were kept in individual metabolic cages and were distributed into four groups, and received the following treatments by gavage: 1) CONTROL: distilled water; 2) Creatine 0.5g/Kg/day; 3) Creatine 1g/Kg/day; 4) Creatine 2g/Kg/day. Their urinary outputs as well as food and water intake were daily measured. At the end of the experiment, the animals were euthanized and serum samples were stored for biochemical analysis. **RESULTS:** Creatine supplementation at the doses given produced no significant changes in plasma levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total protein, albumin, total cholesterol, HDL cholesterol, LDL cholesterol, VLDL cholesterol, triglycerides, glucose, creatinine, urea, and creatinine clearance, compared to control group ($p > 0.05$). Similarly, water and food intake, as well as urinary output, did not show significant changes among the four groups studied. **CONCLUSION:** At the doses used, oral creatine supplementation did not result in renal and/or hepatic toxicity.

PMID: 26016930 [PubMed - indexed for MEDLINE]

18. 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]

19. Pharmacokinetic Herb-Drug Interactions: Insight into Mechanisms and Consequences. Oga EF, Sekine S, Shitara Y, Horie T.

Eur J Drug Metab Pharmacokinet. 2015 Aug 28. [Epub ahead of print]

Abstract:

Herbal medicines are currently in high demand, and their popularity is steadily increasing. Because of their perceived effectiveness, fewer side effects and relatively low cost, they are being used for the management of numerous medical conditions. However, they are capable of affecting the pharmacokinetics and pharmacodynamics of coadministered conventional drugs. These interactions are particularly of clinical relevance when metabolizing enzymes and xenobiotic transporters, which are responsible for the fate of many drugs, are induced or inhibited, sometimes resulting in unexpected outcomes. This article discusses the general use of herbal medicines in the management of several ailments, their concurrent use with conventional therapy, mechanisms underlying herb-drug

interactions (HDIs) as well as the drawbacks of herbal remedy use. The authors also suggest means of surveillance and safety monitoring of herbal medicines. Contrary to popular belief that "herbal medicines are totally safe," we are of the view that they are capable of causing significant toxic effects and altered pharmaceutical outcomes when coadministered with conventional medicines. Due to the paucity of information as well as sometimes conflicting reports on HDIs, much more research in this field is needed. The authors further suggest the need to standardize and better regulate herbal medicines in order to ensure their safety and efficacy when used alone or in combination with conventional drugs.

PMID: 26311243 [PubMed - as supplied by publisher]

20. [Red Yeast Rice Induced Muscular Injuries: Analysis of French Pharmacovigilance Database and Literature Review]. [Article in French] Philibert C, Bres V, Jean-Pastor MJ, Guy C, Lebrun-Vignes B, Robin P, Pinzani V, Hillaire-Buys D.

Therapie. 2015 Oct 16. [Epub ahead of print]

Abstract:

Red yeast rice (RYR) is a dietary supplement containing monacolins obtained by fermentation of *Monascus purpureus* strains. Because of its structural homology with lovastatin, monacolin K inhibits HMG-CoA reductase and shows hypocholesterolemic properties comparable to synthetic statins. We studied all cases of myopathy involving RYR reported in the French national pharmacovigilance database (6 cases) and in scientific literature (9 cases). Among these cases, 9 showed elevated creatine kinase, 3 rhabdomyolysis and 2 myalgia. Recent studies seem to show good efficacy of the RYR, however, our work reports the existence of related muscular disorders. In addition, dietary supplements currently available on the market may show considerable variability of formulation and/or the presence of contaminants. When clinico-biological disorders occur, physicians should consider the eventual use of an herbal treatment.

PMID: 26475749 [PubMed - as supplied by publisher]

21. Pyridoxine induced rosacea-like dermatitis. Rezaković S, Mokos ZB, Paštar Z.

Acta Clin Croat. 2015 Mar;54(1):99-102.

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]

22. Monkshoods: Heart-stopping Neurotoxins behind Hanaoka's Mafutsusan (Year 1804, Part 2). Bause GS.

Anesthesiology. 2015 Aug;123(2):376. doi: 10.1097/01.anes.0000466949.57529.51. (Historical)

PMID: 26196873 [PubMed - indexed for MEDLINE]

23. Clinical Aspects of Aconitum Preparations. Tai CJ, El-Shazly M, Wu TY, Lee KT, Csutor D, Hohmann J, Chang FR, Wu YC.

Planta Med. 2015 Aug;81(12-13):1017-28. doi: 10.1055/s-0035-1546183. Epub 2015 Jul 10.

Abstract:

Aconite species have played an important role in human history. Aconitum species have been used worldwide as poisons as well as remedies. Their potential in targeting several ailments such as pain, rheumatism, and lethargy has been recognized by Western, Chinese, and Indian health care practitioners. Aconite use in herbal preparations has declined, especially in Europe and the United States, in the first half of the twentieth century due to several reported toxicity cases. The situation has changed with the application of new technologies for the accurate analysis of its toxic components and the development of efficient detoxification protocols. Some Asian countries started small clinical trials to evaluate the potency and safety of different marketed aconite preparations. The current review summarizes therapeutic uses of aconite preparations in China, Taiwan, India, and Japan. It also highlights clinical trial results with special emphasis on their limitations. Modern drugs and pharmacopoeial preparations derived from aconite are also discussed.

PMID: 26166138 [PubMed - in process]

24. Aconitum Alkaloid Poisoning Because of Contamination of Herbs by Aconite Roots. Chan TY.

Phytother Res. 2015 Oct 19. doi: 10.1002/ptr.5495. [Epub ahead of print]

Abstract:

Aconitum alkaloid poisoning can occur after drinking decoction and soup made from non-toxic herbs contaminated by aconite roots. In the present review, the main objective is to describe the clinical features, investigations and possible sources of contamination. A combination of neurological, gastrointestinal and cardiovascular signs and symptoms was seen. Ventricular tachyarrhythmias could occur in 18% of subjects. Yunaconitine and crassicauline A, mainly found in certain aconite roots from Southwest China, are most commonly involved. Herbal residues and unused herbs should first be inspected for gross contamination. On-site inspection at the retailer should exclude accidental mix-up or cross-contamination when handling aconite roots. Samples of prescribed herbs are examined for gross contamination and analysed for the presence of Aconitum alkaloids. Samples of the implicated herb are also collected from the wholesaler for investigation. If post-import contamination is unlikely, the regulatory authorities of the exporting countries should be notified for follow-up actions. It is a challenging task to work out how non-toxic herbs become contaminated by aconite roots. The source control with good agricultural and collection practices and quality assurance must be enhanced.

PMID: 26481590 [PubMed - as supplied by publisher]

25. Herb-induced cardiotoxicity from accidental aconitine overdose. Sheth S, Tan EC, Tan HH, Tay L.

Singapore Med J. 2015 Jul;56(7):e116-9. doi: 10.11622/smedj.2015114.

Abstract:

Patients who overdose on aconite can present with life-threatening ventricular arrhythmia. Aconite must be prepared and used with caution to avoid cardiotoxic effects that can be fatal. We herein describe a case of a patient who had an accidental aconite overdose but survived with no lasting effects. The patient had prepared Chinese herbal medication to treat his pain, which resulted in an accidental overdose of aconite with cardiotoxic and neurotoxic effects. The patient had ventricular tachycardia, bidirectional ventricular tachycardia and ventricular fibrillation. Following treatment with anti-arrhythmic medications, defibrillation and cardiopulmonary resuscitation, he made an uneventful recovery, with no further cardiac arrhythmias reported.

PMCID: PMC4520923

PMID: 26243980 [PubMed - in process]

26. Pyrrolizidine alkaloids in medicinal plants from North America. Roeder E, Wiedenfeld H, Edgar JA.

Pharmazie. 2015 Jun;70(6):357-67.

Abstract:

Pyrrolizidine alkaloids (PAs) are mutagenic, carcinogenic, pneumotoxic, teratogenic and fetotoxic. Plants containing PAs commonly poison livestock in many countries, including the USA and Canada. In some regions of the world

PA-producing plants sometimes grow in grain crops and items of food made with PA contaminated grain, such as bread baked using contaminated flour, have been, and continue to be, responsible for large incidents of acute, often fatal human poisoning. Herbal medicines and food supplements containing PAs are also recognized as a significant cause of human poisoning and it is desirable that such medications are identified and subjected to strict regulation. In this review we consider the PAs known to be, or likely to be, present in both the traditionally used medicinal plants of North America and also medicinal plants that have been introduced from other countries and are being recommended and used as phytopharmaceuticals in the USA and Canada.

PMID: 26189295 [PubMed - indexed for MEDLINE]

27. 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 *Aristeguetia 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 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 [PubMed - in process]

28. Pyrrolizidine alkaloids in food and feed on the Belgian market. Huybrechts B, Callebaut A.

Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2015 Nov;32(11):1939-51. doi: 10.1080/19440049.2015.1086821. Epub 2015 Oct 15.

Abstract:

Pyrrolizidine alkaloids (PAs) are widely distributed plant toxins with species dependent hepatotoxic, carcinogenic, genotoxic and pneumotoxic risks. In a recent European Food Safety Authority (EFSA) opinion, only two data sets from one European country were received for honey, while one feed data set was included. No data are available for food or feed samples from the Belgian market. We developed an LC-MS/MS method, which allowed the detection and quantification of 16 PAs in a broad range of matrices in the sub ng g⁻¹ range. The method was validated in

milk, honey and hay and applied to honey, tea (*Camellia sinensis*), scented tea, herbal tea, milk and feed samples bought on the Belgian market. The results confirmed that tea, scented tea, herbal tea and honey are important food sources of pyrrolizidine alkaloid contamination in Belgium. Furthermore, we detected PAs in 4 of 63 commercial milk samples. A high incidence rate of PAs in lucerne (alfalfa)-based horse feed and in rabbit feed was detected, while bird feed samples were less contaminated. We report for the first time the presence of monocrotaline, intermedine, lycopsamine, heliotrine and echimidine in cat food.

PMID: 26373269 [PubMed - in process]

29. Śodhana: An Ayurvedic process for detoxification and modification of therapeutic activities of poisonous medicinal plants. Maurya SK, Seth A, Laloo D, Singh NK, Gautam DN, Singh AK.

Anc Sci Life. 2015 Apr-Jun;34(4):188-97. doi: 10.4103/0257-7941.160862.

Abstract:

Ayurveda involves the use of drugs obtained from plants, animals, and mineral origin. All the three sources of drugs can be divided under poisonous and nonpoisonous category. There are various crude drugs, which generally possess unwanted impurities and toxic substances, which can lead to harmful health problems. Many authors have reported that not all medicinal plants are safe to use since they can bear many toxic and harmful phytoconstituents in them. Śodhana (detoxification/purification) is the process, which involves the conversion of any poisonous drug into beneficial, nonpoisonous/nontoxic ones. Vatsanābha (*Aconitum* species), *Semecarpus anacardium*, *Strychnos nux-vomica*, *Acorus calamus*, *Abrus precatorius* etc., are some of the interesting examples of toxic plants, which are still used in the Indian system of medicine. Aconite, bhilawanols, strychnine, β -asarone, abrin are some of the toxic components present in these plants and are relatively toxic in nature. Śodhana process involves the purification as well as reduction in the levels of toxic principles which sometimes results in an enhanced therapeutic efficacy. The present review is designed to extensively discuss and understand the scientific basis of the alternative use of toxic plants as a medicine after their purification process.

PMCID: PMC4535066

PMID: 26283803 [PubMed]

30. Quantitative analysis of heavy metals in medicinal plants collected from environmentally diverse locations in India for use in a novel phytopharmaceutical product. Sadhu A, Upadhyay P, Singh PK, Agrawal A, Ilango K, Karmakar D, Singh GP, Dubey GP.

Environ Monit Assess. 2015 Aug;187(8):542. doi: 10.1007/s10661-015-4764-3. Epub 2015 Jul 30.

Abstract:

It is important to monitor the quality of the phytopharmaceutical product as its therapeutic potential depends on standardized delivery of active ingredients present in the botanical source. Minimal presence of toxic impurities like heavy metals (HMs) is warranted to ensure product safety and prevent hazardous health impacts. In the present study, conducted as part of the development of a novel phytopharmaceutical product, the chemical profile of 13 heavy metals (Fe, Cu, Mn, Zn, Ni, Co, Mo, V, Cr, As, Pb, Hg, and Cd) was studied in the whole plant, fruit, and rhizome of *Bacopa monnieri*, *Hippophae rhamnoides*, and *Dioscorea bulbifera*, respectively, from environmentally diverse regions in India. Most samples had HM profiles within permissible limits as established by regulatory authorities, with the exception of Cd and Hg in low-altitude regions. This study indicates geographical regions in India suitable for procuring raw materials to develop and manufacture phytopharmaceutical products.

PMID: 26223217 [PubMed - in process]

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

Environ Health. 2015 Aug 15;14:67. 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 [PubMed - in process]

32. Speciation and bioavailability of lead in complementary medicines. Bolan S, Naidu R, Kunhikrishnan A, Seshadri B, Ok YS, Palanisami T, Dong M, Clark I.

Sci Total Environ. 2016 Jan 1;539:304-12. doi: 10.1016/j.scitotenv.2015.08.124. Epub 2015 Sep 11.

Abstract:

Complementary medicines have associated risks which include toxic heavy metal(loid) and pesticide contamination. The objective of this study was to examine the speciation and bioavailability of lead (Pb) in selected complementary medicines. Six herbal and six ayurvedic medicines were analysed for: (i) total heavy metal(loid) contents including arsenic (As), cadmium (Cd), Pb and mercury (Hg); (ii) speciation of Pb using sequential fractionation and extended x-ray absorption fine structure (EXAFS) techniques; and (iii) bioavailability of Pb using a physiologically-based in vitro extraction test (PBET). The daily intake of Pb through the uptake of these medicines was compared with the safety guidelines for Pb. The results indicated that generally ayurvedic medicines contained higher levels of heavy metal(loid)s than herbal medicines with the amount of Pb much higher than the other metal(loid)s. Sequential fractionation indicated that while organic-bound Pb species dominated the herbal medicines, inorganic-bound Pb species dominated the ayurvedic medicines. EXAFS data indicated the presence of various Pb species in ayurvedic medicines. This implies that Pb is derived from plant uptake and inorganic mineral input in herbal and ayurvedic medicines, respectively. Bioavailability of Pb was higher in ayurvedic than herbal medicines, indicating that Pb added as a mineral therapeutic input is more bioavailable than that derived from plant uptake. There was a positive relationship between soluble Pb fraction and bioavailability indicating that solubility is an important factor controlling bioavailability. The daily intake values for Pb as estimated by total and bioavailable metal(loid) contents are likely to exceed the safe threshold level in certain ayurvedic medicines. This research demonstrated that Pb toxicity is likely to result from the regular intake of these medicines which requires further investigation.

PMID: 26363725 [PubMed - in process]

33. Nation-Based Occurrence and Endogenous Biological Reduction of Mycotoxins in Medicinal Herbs and Spices. Do KH, An TJ, Oh SK, Moon Y.

Toxins (Basel). 2015 Oct 14;7(10):4111-30. doi: 10.3390/toxins7104111.

Abstract:

Medicinal herbs have been increasingly used for therapeutic purposes against a diverse range of human diseases worldwide. Moreover, the health benefits of spices have been extensively recognized in recent studies. However, inevitable contaminants, including mycotoxins, in medicinal herbs and spices can cause serious problems for humans in spite of their health benefits. Along with the different nation-based occurrences of mycotoxins, the ultimate exposure and toxicities can be diversely influenced by the endogenous food components in different commodities of the medicinal herbs and spices. The phytochemicals in these food stuffs can influence mold growth, mycotoxin production and biological action of the mycotoxins in exposed crops, as well as in animal and human bodies. The present review focuses on the occurrence of mycotoxins in medicinal herbs and spices and the biological interaction between mold, mycotoxin and herbal components. These networks will provide insights into the methods of mycotoxin reduction and toxicological risk assessment of mycotoxin-contaminated medicinal food components in the environment and biological organisms.

PMID: 26473926 [PubMed - in process]

34. Adverse Effects of Common Drugs: Dietary Supplements. Felix TM, Karpa KD, Lewis PR.

FP Essent. 2015 Sep;436:31-40.

Abstract:

Dietary supplement-induced adverse effects often resolve quickly after discontinuation of the offending product, especially in younger patients. The potential for unwanted outcomes can be amplified in elderly patients or those taking multiple prescription drugs, especially where interactions exist with drugs metabolized by cytochrome P450 enzymes. Attributing injury or illness to a specific supplement can be challenging, especially in light of multi-ingredient products, product variability, and variability in reporting, as well as the vast underreporting of adverse drug reactions. Clinicians prescribing a new drug or evaluating a patient with a new symptom complex should inquire about use of herbal and dietary supplements as part of a comprehensive evaluation. Clinicians should report suspected supplement-related adverse effects to the local or state health department, as well as the Food and Drug Administration's MedWatch program (available at <https://www.safetyreporting.hhs.gov>). Clinicians should consider discussing suspected adverse effects involving drugs, herbal products, or dietary supplements with their community- and hospital-based pharmacists, and explore patient management options with medical or clinical toxicology subspecialists.

PMID: 26375996 [PubMed - in process]

35. Pharmacological Effects of Glycyrrhiza spp. and Its Bioactive Constituents: Update and Review.
Hosseinzadeh H, Nassiri-Asl M.

Phytother Res. 2015 Oct 13. doi: 10.1002/ptr.5487. [Epub ahead of print]

Abstract:

The roots and rhizomes of various species of the perennial herb licorice (*Glycyrrhiza*) are used in traditional medicine for the treatment of several diseases. In experimental and clinical studies, licorice has been shown to have several pharmacological properties including antiinflammatory, antiviral, antimicrobial, antioxidative, antidiabetic, antiasthma, and anticancer activities as well as immunomodulatory, gastroprotective, hepatoprotective, neuroprotective, and cardioprotective effects. In recent years, several of the biochemical, molecular, and cellular mechanisms of licorice and its active components have also been demonstrated in experimental studies. In this review, we summarized the new phytochemical, pharmacological, and toxicological data from recent experimental and clinical studies of licorice and its bioactive constituents after our previous published review.

PMID: 26462981 [PubMed - as supplied by publisher]