AACT Herbal Dietary Supplement Section Abstracts January 2023

1. Utility of Therapeutic Drug Monitoring in Identifying Clinically Significant Interactions Between St. John's Wort and Prescription Drugs.
Steenkamp V, Parkar H, Dasgupta A.

Ther Drug Monit. 2023 Feb 1;45(1):35-44. doi: 10.1097/FTD.0000000000001069.

BACKGROUND: The general population widely uses herbal medicines, as they are regarded as effective and safe. St. John's wort, which is an effective herbal antidepressant, exhibits both pharmacokinetic and pharmacodynamic interactions with several drugs. The aim of this review was to highlight the clinically significant interactions of St. John's wort with drugs that require to be monitored to assess their therapeutic effect. METHODS: Published literature was searched using electronic databases, such as MEDLINE, PubMed, and Elsevier ScienceDirect using terms such as "herbal medicine," "herbal toxicity," "legislation herbal medicine," "drug-herb interactions," "St. John's wort," and "St. John's wort-drug interactions." Searches were limited to the English language, and there was no restriction on the date of publication. RESULTS: St. John's wort exhibits a number of pharmacokinetic and pharmacodynamic interactions with drugs. The most dangerous interactions occurred when used concurrently with the immunosuppressants, cyclosporine, and tacrolimus (treatment failure or organ rejection) or warfarin (treatment failure resulting in thromboembolic events) or antiretroviral agents (treatment failure and the emergence of new viral variants that are resistant to conventional drugs). CONCLUSIONS: Patients should consult their health care providers before consuming herbal supplements, especially St. John's wort, to avoid potentially dangerous drug-herb interactions.

DOI: 10.1097/FTD.0000000000001069
PMID: 36624575 [Indexed for MEDLINE]

2. A new framework for advancing in drug-induced liver injury research. The Prospective European DILI Registry. Björnsson ES, Stephens C, Atallah E, Robles-Diaz M, Alvarez-Alvarez I, Gerbes A, Weber S, Stirnimann G, Kullak-Ublick G, Cortez-Pinto H, Grove JI, Lucena MI, Andrade RJ, Aithal GP.

Liver Int. 2023 Jan;43(1):115-126. doi: 10.1111/liv.15378. Epub 2022 Aug 15.

BACKGROUND & AIMS: No multi-national prospective study of drug-induced liver injury (DILI) has originated in Europe. The design of a prospective European DILI registry, clinical features and short-term outcomes of the cases and controls is reported. METHODS: Patients with suspected DILI were prospectively enrolled in the United Kingdom, Spain, Germany, Switzerland, Portugal and Iceland, 2016-2021. DILI cases or non-DILI acute liver injury controls following causality assessment were enrolled. RESULTS: Of 446 adjudicated patients, 246 DILI patients and 100 had acute liver injury due to other aetiologies, mostly autoimmune hepatitis (n = 42) and viral hepatitis (n = 34). DILI patients (mean age 56 years), 57% women, 60% with jaundice and 3.6% had pre-existing liver disease. DILI cases and non-DILI acute liver injury controls had similar demographics, clinical features and outcomes. A single agent was implicated in 199 (81%) DILI cases. Amoxicillin-clavulanate, flucloxacillin, atorvastatin, nivolumab/ipilimumab, infliximab and nitrofurantoin were the most commonly implicated drugs. Multiple conventional medications were implicated in 37 (15%) and 18 cases were caused by herbal and dietary supplements. The most common single causative drug classes were antibacterials (40%) and antineoplastic/immunomodulating agents (27%). Overall, 13 (5.3%) had drug-induced autoimmune-like hepatitis due to nitrofurantoin, methyldopa, infliximab, methylprednisolone and minocycline. Only six (2.4%) DILI patients died (50% had liver-related death), and another six received liver transplantation. CONCLUSIONS: In this first multi-national European prospective DILI Registry study, antibacterials were the most commonly implicated medications, whereas antineoplastic and immunomodulating agents accounted for higher proportion of DILI than previously described. This European initiative provides an important opportunity to advance the study on DILI.

DOI: 10.1111/liv.15378
PMCID: PMC7614006
PMID: 35899490 [Indexed for MEDLINE]

3. Herbal therapy in opioid withdrawal syndrome: A systematic review of randomized clinical trials. Nematollahi MH, Ahmadianmoghadam MA, Mehrabani M, Moghadari M, Ghorani-Azam A, Mehrbani M.

Addict Health. 2022 Apr;14(2):152-163. doi: 10.22122/AHJ.2022.195961.1247.

BACKGROUND: Medicinal plants have revealed much attention as an alternative or complementary treatment for opioid withdrawal syndrome. The current review collects all available literature to verify the efficiency of herbal remedies in the management of symptoms associated with opioid withdrawal. METHODS: A systematic literature search was conducted from January 1990 to May 2021 on four bibliographic databases (Scopus, PubMed, Embase, and Web of Science) using the search terms "medicinal plant", "withdrawal syndrome", "opioid", and all their equivalents. All randomized controlled trials (RCTs), published in the English language were included for data synthesis. The search was performed according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA). The Cochrane risk of bias tool was used to verify the quality of the included clinical trials. FINDINGS: A total of 12 RCTs were collected and used for data synthesis. The results of these studies indicated that herbal medicines were effective in treating opioid withdrawal syndrome and could alleviate the withdrawal symptoms, such as abdominal constrictions, diarrhea, bone pain, perspiration, and insomnia, when compared to conventional medications such as buprenorphine, clonidine, and methadone. However, more than 30% of RCTs were found to be at high risk of bias in the areas of selection, performance, detection, attrition, and reporting. CONCLUSION: Although several RCTs have proven that herbal remedies are effective in reducing opioid withdrawal symptoms, the findings need to be viewed more carefully. Further RCTs with more participants, longer duration, and less risk of bias are needed in the claimed cases.

DOI: 10.22122/AHJ.2022.195961.1247
PMCID: PMC9743811
PMID: 36544511

4. Dietary supplements for obesity. Bonetti G, Herbst KL, Donato K, Dhuli K, Kiani AK, Aquilanti B, Velluti V, Matera G, Iaconelli A, Bertelli M.

J Prev Med Hyg. 2022 Oct 17;63(2 Suppl 3):E160-E168. doi: 10.15167/2421-4248/jpmh2022.63.2S3.2757. eCollection 2022 Jun.

Obesity and associated complications including diabetes, cardiometabolic dysfunction, disability, malignancy and premature mortality are considered epidemic. Research on obesity is therefore of worldwide importance. The development of obesity is a multifactorial phenomenon with contributions from biological, behavioral, genetic and environmental factors. Obesity and its associated issues require various lifestyle modifications and treatment options such medication, exercise, diet, surgery, pharmacological therapy and dietary supplements. Dietary supplements are considered an attractive alternative to traditional therapy due to their low toxicity profile and their accessibility to the general population. Dietary supplements may include one or more dietary ingredients. In this narrative review, we analyze the effects on obesity and obesity-related issues of various natural components. For example, there are a myriad of supplements that have been used as dietary supplements for weight loss such as minerals, vitamins, amino acids, metabolites, herbs, and plant extracts. This narrative review aims to present the benefits and side-effects of several ingredients of dietary supplements for weight loss and treatment of obesity. In particular, the mechanism of action, results of clinical trials, and possible side effects will be presented for the following ingredients: β-Glucans, bitter orange, calcium, vitamin D, chitosan, chromium, cocoa, coleus forskohlii, conjugate linoleic acid, ephedra sinica, fucoxanthin, garcinia cambogia, glucomannan, green coffee, green tea, guar gum, raspberry, hoodia gordonii, irvingia gabonensis, phenylpropylamine, pyruvate, white kidney bean.

DOI: 10.15167/2421-4248/jpmh2022.63.2S3.2757
PMCID: PMC9710396
PMID: 36479472 [Indexed for MEDLINE]

5. Drug-Induced Liver Injury from Herbal Liver Detoxification Tea. Niazi B, Ahmed K, Ahmed M, Ali S, Song K, Elias S.

Case Rep Gastroenterol. 2022 Nov 8;16(3):612-617. doi: 10.1159/000526311. eCollection 2022 Sep-Dec.

The increasing consumption of unregulated herbal and dietary supplements has presented clinicians with new challenges in assessing and managing acute liver injury. Patients may present in various ways ranging from asymptomatic transaminitis to acute liver failure. Several natural products have been found to mitigate drug-induced liver injury, which has led to the creation of numerous registries to outline all its aspects further. We describe the case of a 36-year-old female who developed a clinically significant acute liver injury with a cholestatic pattern due to an over-the-counter herbal liver detox tea. This is the first case reported of a hepatotoxic effect from any of these compounds or ingredients in the detox tea: burdock root, stinging nettle leaf, cleavers herb, dandelion root, lemon peel, and lemon myrtle leaf (Backhousia citriodora). Idiosyncratic drug-induced liver injury (DILI) remains poorly understood; however, recognizing potential toxins is imperative to understanding toxicogenomics and identifying those at risk.

DOI: 10.1159/000526311
PMCID: PMC9830300
PMID: 36636365

6. Case report: A rare case of death due to end-stage renal disease caused by Tripterygium wilfordii-induced myelosuppression. Zhang W, Liu X, Xia C, He L, Ma H, Wang X, Zhang P.

Front Med (Lausanne). 2022 Nov 30;9:1036422. doi: 10.3389/fmed.2022.1036422. eCollection 2022.

Tripterygium wilfordii-a traditional Chinese herbal medicine-is used to treat several diseases, including chronic kidney disease, rheumatic autoimmune disorder, and skin disorders. With the development of modern pharmacology, scientists have gradually realized that T. wilfordii has side effects on several organs and systems of the human body, including the liver, kidney, reproductive system, hematopoietic system, and immune system. Our understanding of its toxicity remains unclear. The incidence of problems in the hematopoietic system is not low but few related studies have been conducted. The serious consequences need to be of concern to clinicians and scientists. To ensure the safety of patients, it is important to elucidate the mechanism underlying the damage to the hematopoietic system caused by T. wilfordii and strategies to reduce its toxicity. Routine blood and biochemical tests should be conducted when administering T. wilfordii, and in case of any abnormality, the medication should be terminated in time along with a comprehensive symptomatic treatment. Herein, we report the case of a 50-year-old Chinese female with end-stage renal disease (ESRD) who developed severe bone marrow suppression after taking a short-term normal dose of a T. wilfordii-containing decoction. She died of sepsis and septic shock, although timely therapeutic measures (e.g., stimulating hematopoiesis, anti-infection treatment, and hemodialysis) were administered. To the best of our knowledge, this is the first report of death by T. wilfordii-induced myelosuppression from a short term, conventional dose in an adult female with ESRD. Although the underlying mechanism remains unclear, this case contradicts the notion that side effects on the hematopoietic system are non-lethal.

DOI: 10.3389/fmed.2022.1036422
PMCID: PMC9748288
PMID: 36530889

7. Sansoninto-induced Lung Injury. Komiya K, Mitsui MT, Watanabe T, Nasu M, Hiramatsu K, Kadota JI.

Intern Med. 2022 Dec 15;61(24):3709-3712. doi: 10.2169/internalmedicine.9747-22. Epub 2022 May 14.

A man in his 70s visited our department for dyspnea with pulmonary infiltrate that was unresolved by antibiotics. He had been taking Sansoninto for five years and doubled its dose a month ago. After discontinuing Sansoninto without any additional medications, his symptoms gradually disappeared, and pulmonary infiltration improved. Drug lymphocyte stimulation tests showed a positive result for Sansoninto. We diagnosed this patient with Sansoninto-induced lung injury. Sansoninto is a combination drug that consists of sansonin, bukuryo, senkyo, chimo, and kanzo. This paper reports the first case of Sansoninto-induced lung injury and discusses the mechanism considering its components.

DOI: 10.2169/internalmedicine.9747-22
PMCID: PMC9841115
PMID: 35569994 [Indexed for MEDLINE]

8. Acute myocardial necrosis caused by aconitine poisoning: A case report. Liao YP, Shen LH, Cai LH, Chen J, Shao HQ.

World J Clin Cases. 2022 Nov 26;10(33):12416-12421. doi: 10.12998/wjcc.v10.i33.12416.

BACKGROUND: Herbal medicine has a long history of use in the prevention and treatment of disease and is becoming increasingly popular globally. However, there are also widespread concerns about its safety. Among them, the cardiotoxicity of aconitine has been described. CASE SUMMARY: We report a case of a 61-year-old male with aconitine poisoning presenting with malignant arrhythmia and severe cardiogenic shock, which was successfully managed with aggressive advanced life support and heart transplantation. CONCLUSION: This is the first case wherein in vivo cardiac pathology was obtained, confirming that aconitine caused acute myocardial necrosis.

DOI: 10.12998/wjcc.v10.i33.12416
PMCID: PMC9724530
PMID: 36483800

9. Acute kidney injury in the tropics. Kusirisin P, da Silva Junior GB, Sitprija V, Srisawat N.

Nephrology (Carlton). 2023 Jan;28(1):5-20. doi: 10.1111/nep.14118. Epub 2022 Oct 17.

The tropics are a region consisting of more than 125 countries, accounting for 40% of the world's population. The region's population is expected to increase up to 60% in the coming decades. Many tropical countries continue to experience public health problems such as high rates of infectious diseases, lack of sanitation, climate change impacts, poor regulation of herbal medicines and low access to healthcare. These conditions produce the unique problem of tropical acute kidney injury (AKI), which is associated with high morbidity and mortality. Tropical infections such as

leptospirosis, dengue and malaria have varied mechanisms of AKI, including both direct kidney invasion and indirect effects, depending on the disease characteristics. Animal toxins from snakebites and arthropods along with plant toxins, such as djenkol beans, starfruit and herbal medicine, are characterized by a harmful renal effect from each toxic substance. Environmental factors such as heat stress, natural disasters and chemical compounds also lead to AKI and have a systemic effect from their own pathogenesis. The long-term kidney prognosis varies among these etiologies depending on the cause and severity of disease. However, all these conditions are potentially preventable and treatable. Prompt management and good preventive approaches are needed. This article will focus on the epidemiology, pathogenesis and management of AKI associated with tropical infections, toxins and environment impacts.

DOI: 10.1111/nep.14118
PMID: 36207807 [Indexed for MEDLINE]

10. Historical Aspects of Herbal Use and Comparison of Current Regulations of Herbal Products between Mexico, Canada and the United States of America. Rojas P, Jung-Cook H, Ruiz-Sánchez E, Rojas-Tomé IS, Rojas C, López-Ramírez AM, Reséndiz-Albor AA.

Int J Environ Res Public Health. 2022 Nov 25;19(23):15690. doi: 10.3390/ijerph192315690.

Increased life expectancy and high costs of medicines and medical care have led to the use of herbal products. However, these items may contain toxic compounds that have an impact on public health. We will focus on the regulatory aspects and differences of these products marketed in the North American region (USA-Mexico-Canada) from government websites and selected literature. Mexico has an ancestral tradition of using plants for the treatment, improvement, and maintenance of human health as compared with Canada and the USA Currently, the use of herbal products in this region has a regulatory framework. The legal framework in these three countries is related to their history, idiosyncrasies, socio-economic and cultural aspects. Therefore, there are different public policies for herbal products consumed in the region. Mexico has a more specific classification of these products. In Canada, all herbal products are classified as natural health products and the safety and efficacy must be scientifically proven. In the USA, the development of botanical drugs is very recent. In particular, both herbal products classified as food supplements in Mexico and dietary supplements in the USA may have risks in both safety and efficacy.

DOI: 10.3390/ijerph192315690
PMCID: PMC9740500
PMID: 36497761 [Indexed for MEDLINE]

11. Safety Considerations for Natural Products Commonly Used By Patients with Allergic Disease. Soffer GK, Shroff P, Horwitz R.

J Allergy Clin Immunol Pract. 2022 Dec;10(12):3131-3138. doi: 10.1016/j.jaip.2022.09.025. Epub 2022 Sep 26.

Natural products are a category of Complementary and Alternative Medicine that includes medicinal plants, vitamins, and dietary supplements. These products are often utilized by patients with allergies in conjunction with, or as an alternative to, their conventional medical therapies. Despite the wide use of these modalities, many clinicians often have limited knowledge and training in their use. It is important for health care providers to know the safety and risks of these products that their patients may use. This Clinical Commentary reviews the side effects and adverse reactions of several natural products commonly used by patients with allergies and gives an overview of the U.S. Food and Drug Administration requirements for manufacturing, advertising and distribution.

DOI: 10.1016/j.jaip.2022.09.025
PMID: 36174919 [Indexed for MEDLINE]

12. Cannabidiol exposures in the United States, National Poison Data System, July 2014-June 2021. Perez-Vilar S, Karami S, Long K, Leishear K.

Clin Toxicol (Phila). 2022 Dec 20:1-8. doi: 10.1080/15563650.2022.2156881. Online ahead of print.

INTRODUCTION: There has been an increase in the interest and availability of products asserting to contain cannabidiol (CBD). OBJECTIVE: To describe demographic and clinical patterns in cases involving CBD exposures documented by the America's Poison Centers (AAPCC). METHODS: We extracted human exposure cases involving CBD from the U.S. National Poison Data System between July 2014 and June 2021. We described monthly case counts and data on demographics, exposure reason, clinical effects, medical outcomes, and co-exposures, overall and by U.S. Food and Drug Administration (FDA) approval status. RESULTS: We identified 6,496 cases, of these, 85.2% involved exposures to non-FDA approved CBD. The monthly number of cases peaked at 336 in March 2021. Cases often occurred in children ages 2-12 years (36.2%). Although in this age group unintentional exposures represented most cases (94.1%), we identified therapeutic errors (3.9%), intentional use (3.0%), and adverse reactions (1.6%) in cases involving exposures to non-FDA approved CBD. Among the 5,248 (80.8%) cases involving exposure to a single product, we identified 44 major medical outcomes, all related to exposures to non-FDA approved

CBD. The most frequent clinical effects included neurological, cardiac, and gastrointestinal effects. Among the 1,248 (19.2%) involving exposure to more than one product, the most frequent co-exposures included stimulants and street drugs, sedatives-hypnotics, antipsychotics, and analgesics. CONCLUSIONS: This case series identified an increasing trend in CBD exposure cases managed by AAPCC. It showed serious medical outcomes in temporal association with exposure to non-FDA approved CBD products. Our findings also suggest both unintentional and intentional use of non-FDA approved CBD in children. Consumers should keep these products out of reach of children and exercise caution when purchasing and using non-FDA approved CBD products.

DOI: 10.1080/15563650.2022.2156881
PMID: 36537670

13. How Do Herbal Cigarettes Compare To Tobacco? A Comprehensive Review of Their Sensory Characters, Phytochemicals, and Functional Properties. Abdel Rahman RT, Kamal N, Mediani A, Farag MA.

ACS Omega. 2022 Dec 6;7(50):45797-45809. doi: 10.1021/acsomega.2c04708. eCollection 2022 Dec 20.

Herbal cigarettes, known as tobacco-free or nicotine-free cigarettes, are those recognized as being-tobacco free, being composed of a mixture of various herbs claimed to lessen the smoking habit hazards. However, controversial data regarding its properties occur in the literature with no comprehensive overview or analysis of its effects. Like herbal smokeless tobacco, they are often used to substitute for tobacco products (primarily cigarettes) regarded as a "nonsmoking" aid. This review capitalizes on herbal cigarettes with regard to their quality characteristics, sensory attributes, chemical composition, and health properties to rationalize their choice as a nonsmoking aid. Furthermore, the impacts of heat and/or pyrolysis that occur during smoking on its chemical composition are presented for the first time. Some herbal smokes may produce notable metabolic problems that increase the risk of several chronic metabolic diseases. In general, burning substances from plants can have a variety of negative effects on the body attributed to toxic chemicals such as carbon monoxide, polyaromatics, nicotine, and N-nitrosamines. This review compiles and discusses the phytochemical compositions detected in various herbal cigarettes alongside sensory and quality attributes and health effects.

DOI: 10.1021/acsomega.2c04708
PMCID: PMC9773184
PMID: 36570239

14. Uncovering cloves: characterization of volatile compounds present in clove cigarettes. Picanço JMA, Limberger RP, Apel MA.

Toxicol Res (Camb). 2022 Nov 10;11(6):987-1002. doi: 10.1093/toxres/tfac074. eCollection 2022 Dec.

Indonesian clove cigarettes-called "kretek" due to the crackling sound that can be heard when the product burns-are tobacco products containing clove and the "saus", a mixture of essential oils and plant extracts whose ingredients are mostly kept in secret. It is important to determine which ingredients those are to properly assess the effects that clove cigarettes can cause. An organoleptic, qualitative and quantitative analysis was made in 9 different brands of clove cigarettes obtained in Brazil. Nicotine, eugenol, menthol, and β-caryophyllene were quantified through gas chromatography coupled to mass spectrometry. The samples presented 20 different compounds, and all samples had a different combination of the compounds. Nicotine concentrations were generally higher than eugenol, and lower than nicotine concentration in a conventional cigarette. One sample had menthol even though the cigarette pack did not inform that it was a menthol product. There were traces of 2 unusual substances. Clindamycin is an antibiotic that can be used to treat bacterial infections in respiratory airways, and octodrine is an amphetaminic stimulant used in nutritional supplements, considered as a substance of doping by the World Anti-Doping Association. The presence of both substances was not tested using certified reference materials, but its possible presence raises concern about the compounds in kretek cigarettes. There should be more studies about the contents of clove cigarettes, to improve antitobacco legislations and regulations. This way it would be possible to properly inform the risks of smoking clove cigarettes and to diminish the number of tobacco users throughout the world.

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PMCID: PMC9773057
PMID: 36569486