AACT Herbal Dietary Supplement Section Abstracts May 2022

1. Garcinia cambogia, Either Alone or in Combination With Green Tea, Causes Moderate to Severe Liver Injury. Vuppalanchi R, Bonkovsky HL, Ahmad J, Barnhart H, Durazo F, Fontana RJ, Gu J, Khan I, Kleiner DE, Koh C, Rockey DC, Phillips EJ, Li YJ, Serrano J, Stolz A, Tillmann HL, Seeff LB, Hoofnagle JH, Navarro VJ; Drug-Induced Liver Injury Network.

Clin Gastroenterol Hepatol. 2022 Jun;20(6):e1416-e1425. doi: 10.1016/j.cgh.2021.08.015. Epub 2021 Aug 14.

BACKGROUND & AIMS: Garcinia cambogia, either alone or with green tea, is commonly promoted for weight loss. Sporadic cases of liver failure from G cambogia have been reported, but its role in liver injury is controversial. METHODS: Among 1418 patients enrolled in the Drug-Induced Liver Injury Network (DILIN) from 2004 to 2018, we identified 22 cases (adjudicated with high confidence) of liver injury from G cambogia either alone (n = 5) or in combination with green tea (n = 16) or Ashwagandha (n = 1). Control groups consisted of 57 patients with liver injury from herbal and dietary supplements (HDS) containing green tea without G cambogia and 103 patients from other HDS. RESULTS: Patients who took G cambogia were between 17 and 54 years, with liver injury arising 13-223 days (median = 51) after the start. One patient died, one required liver transplantation, and 91% were hospitalized. The liver injury was hepatocellular with jaundice. Although the peak values of aminotransferases were significantly higher (2001 ± 1386 U/L) in G cambogia group ($P < .018$), the median time for improvement in total bilirubin was significantly lower compared with the control groups (10 vs 17 and 13 days; $P = .03$). The presence of HLA-B∗35:01 allele was significantly higher in the G cambogia containing HDS (55%) compared with patients because of other HDS (19%) ($P = .002$) and those with acute liver injury from conventional drugs (12%) ($P = 2.55 \times 10\text{-}6$). CONCLUSIONS: The liver injury caused by G cambogia and green tea is clinically indistinguishable. The possible association with HLA-B∗35:01 allele suggests an immune-mediated mechanism of injury. CLINICAL TRIALS: gov number: NCT00345930.

DOI: 10.1016/j.cgh.2021.08.015
PMCID: PMC9004424
PMID: 34400337 [Indexed for MEDLINE]

2. Which Features of Dietary Supplement Industry, Product Trends, and Regulation Deserve Physicians' Attention? Cadwallader AB, Council On Science And Public Health A.

AMA J Ethics. 2022 May 1;24(5):E410-418. doi: 10.1001/amajethics.2022.410.

Patients expect that dietary supplements they purchase-and physicians expect that dietary supplements they recommend-are safe, accurately labeled, quality products. Since many dietary supplements, especially vitamins and minerals, are key parts of evidence-based interventions for patients with many conditions, illegal, fraudulent, adulterated, or improperly labeled products should be regarded as sources of clinical and ethical concern. Adverse events (AEs) can occur and, when they do, relevant data should be carefully collected and analyzed. This article considers how many physicians' and patients' confusion about dietary supplement regulation can undermine quality caregiving and responses to AEs. This article also summarizes a recent American Medical Association Council on Science and Public Health report on dietary supplement supply and marketing practices and on physicians' roles in guiding patients when dietary supplement use is clinically indicated.

DOI: 10.1001/amajethics.2022.410
PMID: 35575573 [Indexed for MEDLINE]

3. Is My Patient Taking an Unsafe Dietary Supplement? Bernstein IBG, Bolte KL.

AMA J Ethics. 2022 May 1;24(5):E390-395. doi: 10.1001/amajethics.2022.390.

Dietary supplements do not require premarket approval by the US Food and Drug Administration (FDA), yet they can have side effects; interact with medications, food, or other supplements; or be unsafe, so it is important for clinicians to discuss dietary supplement use with patients. This article provides an overview of dietary supplement requirements related to safety, manufacturing, labeling, advertising, and adverse event reporting; discusses tainted supplements and the FDA's and Federal Trade Commission's enforcement actions against dietary supplements; and offers recommendations to clinicians on matters of key clinical and ethical importance during clinical encounters.

DOI: 10.1001/amajethics.2022.390
PMID: 35575570 [Indexed for MEDLINE]

4. How Should Clinicians Respond to Patient Interest in Dietary Supplements to Treat Serious Chronic Illness? Clinard V, Smith JD.

AMA J Ethics. 2022 May 1;24(5):E361-367. doi: 10.1001/amajethics.2022.361.

The Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey data reveal that consumption of over-the-counter vitamins, minerals, and herbals is widespread. Many clinicians, however, lack critical information about their patients' use of dietary supplements. Particularly clinically relevant are supplement ingredients' interactions with prescription medications, supplements' questionable effectiveness in treating serious conditions, and their potential for causing harm. This article considers how clinicians might address dietary supplements' safety, efficacy, and appropriate use with patients.

DOI: 10.1001/amajethics.2022.361
PMID: 35575566 [Indexed for MEDLINE]

5. Reimagining Roles of Dietary Supplements in Psychiatric Care. Wu K, Messamore E.

AMA J Ethics. 2022 May 1;24(5):E437-442. doi: 10.1001/amajethics.2022.437.

Despite impressive pharmaceutical advances, mental illness remains a leading cause of suffering and disability. Although some dietary supplements appear to respond to some needs not met by prescription medications, several obstacles prevent their study or use. This article proposes government-supported review and safety monitoring of supplements' use in caring for patients with mental illness.

DOI: 10.1001/amajethics.2022.437
PMID: 35575575 [Indexed for MEDLINE]

6. Age Drives the Differences in Dietary Supplement Use in Endurance Athletes: A Cross-Sectional Analysis of Cyclists, Runners, and Triathletes. Graybeal AJ, Kreutzer A, Willis JL, Moss K, Braun-Trocchio R, Shah M.

J Diet Suppl. 2022 Apr 5:1-19. doi: 10.1080/19390211.2022.2056670. Online ahead of print.

Most athletes use dietary supplements (DS) to improve health and performance beyond what can be achieved through diet. Improvements in health and exercise performance through the use of DS are especially attractive to older athletes (OA) challenged with age-related declines. However, there are few DS shown to improve endurance performance, and the prevalence of DS in OA are unknown. Two-hundred cyclists, runners, and triathletes (females = 108; age = 39.4 ± 13.5) completed a questionnaire regarding the prevalence and type of DS currently used, in addition to variables associated with using DS such as motivation and sources of information. Overall, 78.0% of athletes reported current DS use. OA used more DS (Total DS = 4.3 ± 3.0) than younger athletes (2.7 ± 1.8, $p < 0.001$), with ages 40-49 and 50-59 using more DS than ages 18-29 and 30-39 ($p < 0.05$). The majority of athletes (53.8%) used ≥ 3 DS. Age was the only significant predictor of total DS use ($p = 0.002$); OA used ≥ 3 DS more than younger ($p < 0.001$). Specifically, more athletes 40-49 (67.5%) and 50-59 (76.2%) used ≥ 3 DS compared to 18-29 (33.3%, $p = 0.003$). More OA used electrolytes ($p = 0.005$), probiotics ($p = 0.045$), melatonin ($p = 0.004$), and vitamin D ($p = 0.016$) than younger athletes. Motivations to use DS were related to age and were supplement specific.

Sources of DS information varied by sex more than age. Age is a significant determining factor for DS use in a sample of cyclists, runners, and triathletes. The prevalence and trends of DS warrant further investigation into the benefits and risks of DS to develop safe, targeted, and age-specific DS strategies on a recreative competitive level.

DOI: 10.1080/19390211.2022.2056670
PMID: 35380079

7. Relative safety and quality of various dietary supplement products U.S. Service Members ask about. Crawford C, Walter AR, Avula B, Lindsey AT, Hunter AM, Ikhlas AK, Deuster PA.

Clin Toxicol (Phila). 2022 Jun;60(6):737-744. doi: 10.1080/15563650.2022.2036751. Epub 2022 Feb 14.

CONTEXT: The purpose of this project was to determine types of dietary supplement products U.S. Service Members frequently ask about and identify risks associated with select products that consumers should be aware of when considering their use. METHODS: Forty-one dietary supplement products frequently asked about through the Operation Supplement Safety's (OPSS.org) Ask-the-Expert portal were selected. Product analysis was performed to verify whether select products were accurately labeled and to identify any risky ingredients contained in these products. Operation Supplement Safety Risk Assessment Scorecard criteria were additionally used as a screening tool to assess a product's relative safety potential. RESULTS: Among the select dietary supplements, 12 (29.3%) were marketed as pre-workout products; 14 (34.1%) for weight loss; four (9.8%) for male enhancement/testosterone boosters; and 11 (26.8%) as body building supplements. Eleven (26.8%) products had accurate labels; only eight of these had accurate labels plus no risky ingredients listed on the labels. Twenty-six (63.4%) products were misbranded; 10 (24.4%) were adulterated, and six (14.6%) were both misbranded and adulterated. Risky ingredients appeared on 23 (56%) of all product labels. Eight of these 23 products also had additional risky ingredients not listed on the labels but detected through analysis. According to the Scorecard based on label claims, 35 (85.4%) received a rating of “no-go/ risky". CONCLUSIONS: U.S. Service Members and the public at large should be aware that dietary supplements may contain risky ingredients and know how to identify ingredients on the label to evaluate potential risk.

DOI: 10.1080/15563650.2022.2036751
PMID: 35156875 [Indexed for MEDLINE]

8. The Prevalence of Dietary Supplement Usage in Military Aviators. Sammito S, Erley OM, Rose DM, Güttler N.

Int J Environ Res Public Health. 2022 Apr 20;19(9):5017. doi: 10.3390/ijerph19095017.

BACKGROUND: The prevalence of dietary supplement (DS) and energy drink (ED) usage in military personnel differs from branch to branch and is between 55% and 76% (higher values in special operations forces). Aviators with highly demanding tasks might be especially interested in using dietary supplements. To date, there are only limited data available for this special profession inside the military. METHODS: An internet-based survey was conducted on the prevalence of DS and ED usage, the reasons for their usage and the place of purchase for all wings of the German Armed Forces. RESULTS: Of the 181 pilots who participated in the survey, 34% used DSs and 16% EDs. Usage was linked to sports activities but not to the type of aircraft. DSs were purchased on the internet by 50% of the respondents; mostly protein supplements, magnesium and omega-3fatty acids. Only 42% said they would feel an effect from taking DSs. CONCLUSIONS: Although the present study showed that the prevalence of usage was comparable to that of the civilian population, the sources of supply and the range of the substances taken give cause for concern. This calls for education and information campaigns to make the pilots aware of the possible risks to their health.

DOI: 10.3390/ijerph19095017
PMCID: PMC9105340
PMID: 35564407 [Indexed for MEDLINE]

9. Possible Herb-Drug Interaction Risk of Some Nutritional and Beauty Supplements on Antiretroviral Therapy in HIV Patients. Haron MH, Avula PhD B, Gurley PhD BJ, Chittiboyina PhD AG, Khan PhD IA, Khan PhD SI.

J Diet Suppl. 2022;19(1):62-77. doi: 10.1080/19390211.2020.1846658. Epub 2020 Nov 17.

This study was carried out to assess the drug interaction potential of a variety of beauty and sports/nutritional supplements when co-administered with antiviral drug therapy, especially anti-HIV drugs. Ethanolic extracts of seven dietary supplements (two beauty products, three nutritional protein supplement products and two weight loss/body building products) were examined in human liver cells (HepG2 cells and primary hepatocytes) for their influence on the hepatic metabolism of five antiviral drugs (elvitegravir, rilpivirine, tenofovir, dolutegravir, and cobicistat), all of which are substrates for a key drug metabolizing enzyme CYP3A4. Our results showed that six of the seven supplements caused a 1.5 - 2 fold induction in PXR transcriptional activity in HepG2 cells. PXR regulates the expression of key drug metabolizing enzymes including CYP3A4. Follow up studies indicated a 1.5 - 3 fold induction in CYP3A4 enzyme activity in HepG2 cells treated with these supplements. We further investigated the effects of the supplement on the metabolism of above mentioned anti-viral drugs in HepG2 cells and primary hepatocytes. Of the five drugs, rilpivirine and dolutegravir metabolism was increased by up to 2-folds over the no supplement control by some of the supplements. Our findings indicate that concomitant consumption of these products with anti-HIV drugs may compromise the efficacy of antivirals therapy due to supplement-induced metabolism via induction of CYP3A4 activity.

DOI: 10.1080/19390211.2020.1846658
PMID: 33200619 [Indexed for MEDLINE]

10. Characterization of urinary protein profile in regular kratom (Mitragyna speciosa korth.) users in Malaysia. Jasim RK, Hassan Z, Singh D, Boyer E, Gam LH.

J Addict Dis. 2022 Apr-Jun;40(2):235-246. doi: 10.1080/10550887.2021.1981122. Epub 2021 Nov 8.

Mitragyna speciosa (Korth.) also known as kratom or ketum has been traditionally used for its diverse medicinal value in Southeast Asia. Despite of its therapeutic value, kratom's safety profile remains deficiently elucidated. Our study aims to characterize the urinary protein profile of regular kratom users to determine its toxic effects on renal functioning. A total of 171 respondents (comprising of n = 88 regular kratom users, and n = 83 healthy controls) were recruited for this study. Urine specimens were collected and analyzed using SDS-PAGE, followed by LC/MS/MS analysis. Our results show albumin is the primary, and most abundant form of protein excreted in kratom user's urine specimens (n = 60/64), indicating that kratom users are predisposed to proteinuria. Kratom users had an elevated urinary protein (with an intensity of 66.7 kDa band), and protein: creatinine ratio (PCR) concentrations relative to healthy controls. However, kratom user's urinary creatinine concentration was found to be in the normal range as the healthy control group. While, kratom users who tested positive for illicit drug use had an elevated urinary albumin concentration. Our preliminary findings indicate that regular consumption of freshly brewed kratom solution over a protracted period (for an average of eleven years) seems to induce proteinuria, suggestive of an early stage of kidney injury. Hence, further studies are urgently needed to confirm our findings, and establish kratom's renal impairing effects.

DOI: 10.1080/10550887.2021.1981122
PMID: 34747343 [Indexed for MEDLINE]

11. A Case of Hyperkalemia Induced by Kratom (Mitragyna speciosa). Torres-Ortiz A, Al Zein S, Alqudsi M.

Cureus. 2022 Apr 11;14(4):e24036. doi: 10.7759/cureus.24036. eCollection 2022 Apr.

Kratom (Mitragyna speciosa), a tree found abundantly in Southeast Asia, has been used for centuries because of its opioid-like properties. In the last 20 years, it has gained popularity in the United States of America due to its easy availability and effects on pain control. However, different types of toxicity from kratom use have been reported in the literature. Here, we present a case of kratom-induced hyperkalemia in a 61-year-old patient with no significant past medical history. His laboratory work-up excluded other etiologies, and his potassium level eventually normalized after the discontinuation of kratom. Although reasonable data exist on kratom effects on the nervous and cardiovascular systems, the magnitude of its effect on potassium homeostasis and whether it is kidney mediated or not is not well recognized.

DOI: 10.7759/cureus.24036
PMCID: PMC9093675
PMID: 35573520

12. A rare case of cade oil poisoning complicated by acute pancreatitis and acute tubular necrosis *[juniper oil].* Azizi M, El Kaouini A, Lafkih A, Bouayed MZ, Bkiyar H, Housni B.

Ann Med Surg (Lond). 2022 Apr 4;76:103562. doi: 10.1016/j.amsu.2022.103562. eCollection 2022 Apr.

INTRODUCTION: Cade oil is often used in traditional medicinal practices despite of its toxic effects, hence the occurrence of intoxication incidents often requiring intensive care. CASE PRESENTATION: We present the case of a young patient with no prior medical history who was exposed to significant doses of Cade oil both on skin and ingested, and who subsequently developed an apyretic consciousness disorder warranting an admission to our ICU department for specialized management. DISCUSSION: in this chapter we discuss the place of cade oil within Morocco's unsupervised medicinal practices. We also detail the spectrum of cade oil poisoning which is rarely reported in the literature, before discussing the therapeutic options. CONCLUSION: The phenol derivatives of Cade oil, which is still used frequently and widely, are responsible of an acute intoxication, mainly impairing the cardiovascular, respiratory and renal functions. A pancreatic involvement is rarely reported.

DOI: 10.1016/j.amsu.2022.103562
PMCID: PMC9052284
PMID: 35495391

13. Mania Associated With Rhodiola Rosea: An Adaptogen With Antidepressant Effects. Whig R, Leo RJ.

Prim Care Companion CNS Disord. 2022 Mar 17;24(2):21cr02980. doi: 10.4088/PCC.21cr02980.

DOI: 10.4088/PCC.21cr02980
PMID: 35303403 [Indexed for MEDLINE]

14. Aconitine: A review of its pharmacokinetics, pharmacology, toxicology and detoxification. Gao Y, Fan H, Nie A, Yang K, Xing H, Gao Z, Yang L, Wang Z, Zhang L.

J Ethnopharmacol. 2022 Jul 15;293:115270. doi: 10.1016/j.jep.2022.115270. Epub 2022 Apr 8.

ETHNOPHARMACOLOGICAL RELEVANCE: Aconitine, a C19-norditerpenoid alkaloid, derives from many medicinal plants such as Aconitum carmichaelii Debx. (Chinese:), Aconitum kusnezoffii Reichb (Chinese:), which were used to rheumatic fever, painful joints and some endocrinal disorders. AIMS OF THE REVIEW: The present paper reviews research progress relating to the pharmacokinetics, physiological and pathological processes of aconitine, while some promising research direction and the detoxification of aconitine are also discussed. MATERIALS AND METHODS: The accessible literature on aconitine, from 1990 to 2020, obtained from published materials of electronic databases, such as SCI finder, PubMed, Web of Science, Science Direct, Springer and Google Scholar was systematically analyzed. RESULTS: In this review, we address the pharmacokinetics of aconitine, as well as its pharmacological effects including anti-cancer, anti-inflammatory, anti-virus, immunoregulation, analgesic, insecticide and inhibition of androgen synthesis. Further, we summarize the toxicity of aconitine such as cardiotoxicity and neurotoxicity, on which we strikingly focus on the ways to reduce the toxicity of aconitine based. CONCLUSIONS: Aconitine plays an vital role in a wide range of physiological and pathological processes and we can reduce the toxicity of aconitine by compatibility and hydrolysis. Although some issues still exist, such as the correlative relationship between the dose and toxicity of aconitine not being clear, our review may provide new ideas for the application of aconitine in the treatment of related diseases.

DOI: 10.1016/j.jep.2022.115270
PMID: 35405250 [Indexed for MEDLINE]

15. A toxicological evaluation of lithium orotate. Murbach TS, Glávits R, Endres JR, Hirka G, Vértesi A, Béres E, Szakonyiné IP.

Regul Toxicol Pharmacol. 2021 Aug;124:104973. doi: 10.1016/j.yrtph.2021.104973. Epub 2021 Jun 17.

Lithium orotate, the salt of lithium and orotic acid, has been marketed for decades as a supplemental source of lithium with few recorded adverse events. Nonetheless, there have been some concerns in the scientific literature regarding orotic acid, and pharmaceutical lithium salts are known to have a narrow therapeutic window, albeit, at lithium equivalent therapeutic doses 5.5-67 times greater than typically recommended for supplemental lithium orotate. To our knowledge, the potential toxicity of lithium orotate has not been investigated in preclinical studies; thus, we conducted a battery of genetic toxicity tests and an oral repeated-dose toxicity test in order to further explore its safety. Lithium orotate was not mutagenic or clastogenic in bacterial reverse mutation and in vitro mammalian chromosomal aberration tests, respectively, and did not exhibit in vivo genotoxicity in a micronucleus test in mice. In a 28-day, repeated-dose oral toxicity study, rats were administered 0, 100, 200, or 400 mg/kg body weight/day of lithium orotate by gavage. No toxicity or target organs were identified; therefore, a no observed adverse effect level was determined as 400 mg/kg body weight/day. These results are supportive of the lack of a postmarket safety signal from several decades of human consumption.

DOI: 10.1016/j.yrtph.2021.104973
PMID: 34146638 [Indexed for MEDLINE]

16. Bioavailability, Efficacy, Safety, and Regulatory Status of Creatine and Related Compounds: A Critical Review. Kreider RB, Jäger R, Purpura M.

Nutrients. 2022 Feb 28;14(5):1035. doi: 10.3390/nu14051035.

In 2011, we published a paper providing an overview about the bioavailability, efficacy, and regulatory status of creatine monohydrate (CrM), as well as other "novel forms" of creatine that were being marketed at the time. This paper concluded that no other purported form of creatine had been shown to be a more effective source of creatine than CrM, and that CrM was recognized by international regulatory authorities as safe for use in dietary supplements. Moreover, that most purported "forms" of creatine that were being marketed at the time were either less bioavailable, less effective, more expensive, and/or not sufficiently studied in terms of safety and/or efficacy. We also provided examples of several "forms" of creatine that were being marketed that were not bioavailable sources of creatine or less effective than CrM in comparative effectiveness trials. We had hoped that this paper would encourage supplement manufacturers to use CrM in dietary supplements given the overwhelming efficacy and safety profile. Alternatively, encourage them to conduct research to show their purported "form" of creatine was a bioavailable, effective, and safe source of creatine before making unsubstantiated claims of greater efficacy and/or safety than CrM. Unfortunately, unsupported misrepresentations about the effectiveness and safety of various "forms" of creatine have continued. The purpose of this critical review is to: (1) provide an overview of the physiochemical properties, bioavailability, and safety of CrM; (2) describe the data needed to substantiate claims that a "novel form" of creatine is a bioavailable, effective, and safe source of creatine; (3) examine whether other marketed sources of creatine are more effective sources of creatine than CrM; (4) provide an update about the regulatory status of CrM and other purported sources of creatine sold as dietary supplements; and (5) provide guidance regarding the type of research needed to validate that a purported "new form" of creatine is a bioavailable, effective and safe source of creatine for dietary supplements. Based on this analysis, we categorized forms of creatine that are being sold as dietary supplements as either having strong, some, or no evidence of bioavailability and safety. As will be seen, CrM continues to be the only source of creatine that has substantial evidence to support bioavailability, efficacy, and safety. Additionally, CrM is the source of creatine recommended explicitly by professional societies and organizations and approved for use in global markets as a dietary ingredient or food additive.

DOI: 10.3390/nu14051035
PMCID: PMC8912867
PMID: 35268011 [Indexed for MEDLINE]

17. Metabolic Activation and Hepatotoxicity of Furan-Containing Compounds. Tian M, Peng Y, Zheng J.

Drug Metab Dispos. 2022 May;50(5):655-670. doi: 10.1124/dmd.121.000458. Epub 2022 Jan 25.

Furan-containing compounds are abundant in nature, and many, but not all, have been found to be hepatotoxic and carcinogenic. The furan ring present in the chemical structures may be one of the domineering factors to bring about the toxic response resulting from the generation of reactive epoxide or cis-enedial intermediates, which have the potential to react with biomacromolecules. This review sets out to explore the relationship between the metabolic activation and hepatotoxicity of furan-containing compounds on the strength of scientific reports on several typical alkylated furans, synthetic pharmaceuticals, and components extracted from herbal medicines. The pharmacological activities as well as concrete evidence of their liver injuries are described, and the potential toxic mechanisms were discussed partly based on our previous work. Efforts were made to understand the development of liver injury and seek solutions to prevent adverse effects. SIGNIFICANCE STATEMENT: This review mainly elucidates the vital role of metabolic activation in the hepatotoxicity of furan-containing compounds through several typical chemicals studied. The possible mechanisms involved in the toxicities are discussed based on collective literatures as well as our work. Additionally, the structural features responsible for toxicities are elaborated to predict toxicity potentials of furan-containing compounds. This article may assist to seek solutions for the occurring problems and prevent the toxic effects of compounds with furan(s) in clinical practice.

DOI: 10.1124/dmd.121.000458
PMID: 35078805 [Indexed for MEDLINE]

18. Identification of phosphodiesterase type-5 (PDE-5) inhibitors in herbal supplements using a tiered approach and associated consumer risk. Akuamoa F, Bovee TFH, van Dam R, Maro L, Wesseling S, Vervoort J, Rietjens IMCM, Hoogenboom RLAP.

Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2022 Mar 24:1-12.
doi: 10.1080/19440049.2022.2052972. Online ahead of print.

The use of herbal supplements for improved sexual performance is a common practice amongst the youth and some senior citizens in Ghana. These products are considered 'natural' and greatly preferred over synthetic alternatives due to the assurance of little to no adverse effects by producers. However, the high rate of adulteration often compromises their safety. Forty herbal supplements, of which 25 were previously shown to result in medium to high intake of phosphodiesterase type-5 (PDE-5) inhibitors using a PDE-Glo bioassay, were further investigated using liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis to examine the reliability of the bioassay and whether the observed higher responses could be ascribed to inherent plant constituents or adulterants. Results showed significant amounts of vardenafil, tadalafil and especially sildenafil, in 2, 1 and 10 samples, respectively, with total concentration levels resulting in estimated daily intakes (EDIs) above 25 mg sildenafil equivalents with six supplements even having EDIs above 100 mg sildenafil equivalents. Only one sample contained a natural ingredient (icariin), but its concentration (0.013 mg g-1) was too low to explain the observed potency in the bioassay. The estimated concentrations of PDE-5 inhibitors in 35 supplements, according to the bioassay, were in line with those of the LC-MS/MS analysis. However, discrepancies were observed for five supplements. Further examination of one of the latter supplements using the PDE-Glo bioassay to select the positive fraction and further examination with LC-MS/MS and 1H-NMR revealed the presence of hydroxythiohomosildenafil, a sildenafil analogue not yet included in the liquid chromatography-mass spectrometry reference library. This study demonstrates the significance of applying a tiered approach, where the use of a bioassay is followed by chemical analysis of bioactive samples in order to identify unknown bioactive compounds.

DOI: 10.1080/19440049.2022.2052972
PMID: 35323088

19. Healthcare Professionals' Knowledge and Behaviors Regarding Drug-Dietary Supplement and Drug-Herbal Product Interactions. Stanojević-Ristić Z, Mrkić I, Ćorac A, Dejanović M, Mitić R, Vitković L, Rašić J, Valjarević D, Valjarević A.

Int J Environ Res Public Health. 2022 Apr 3;19(7):4290. doi: 10.3390/ijerph19074290.

Given the widespread use of dietary supplements (DS) and herbal products (HP), healthcare professionals (HCPs) will increasingly encounter patients who use these preparations with conventional drugs and who need their services to reduce the consequences of adverse therapeutic outcomes. The aim of our survey was to assess the knowledge and behaviors of HCPs regarding the risk of potential drug-dietary supplement (DDSIs) and drug-herbal product (DHPIs) interactions. This cross-sectional survey collected data via on

paper-based questionnaire among general practitioners (GPs) (n = 105), specialty doctors (n = 87) and nurses (n = 154). The HCPs were mostly familiar with the interaction of doxycycline with magnesium (83%) and were least familiar with interaction of warfarin with glucosamine (14%). The results on DDSIs and DHPIs knowledge showed that GPs scored significantly higher than nurses (p < 0.001 and p = 0.003, respectively), while specialty doctors scored significantly higher than nurses only on DDSIs knowledge (p < 0.001). Only 28% of respondents reported that they often or always ask patients on drug therapy about the use of DS or HP, and 25% of respondents record such data in the medical documentation of patients. Our results showed that HCPs have sufficient knowledge about most major DDSIs and DHPIs, but insufficient knowledge about most moderate interactions. However, their overall knowledge and behavior regarding the risk of these interactions indicate the need for further continuing education and training.

DOI: 10.3390/ijerph19074290
PMCID: PMC8998985
PMID: 35409970 [Indexed for MEDLINE]

20. Impact of 'infodemic in pandemic' on food and nutrition related perceptions and practices of Indian internet users. Gavaravarapu SM, Seal A, Banerjee P, Reddy T, Pittla N.

PLoS One. 2022 Apr 21;17(4):e0266705. doi: 10.1371/journal.pone.0266705. eCollection 2022.

The uncontrolled spread of (mis)information, news and propaganda related to COVID 19 created an 'infodemic' leading to panic and unscientific practices among the mass. With the largest number of internet users in the world, India has witnessed a steep rise in the number of people seeking information on social media related to COVID-19, which reached a staggering 22.3 million by March, 2020. This study aimed to evaluate the trend of COVID-19 associated food and nutrition news search by Indian internet users between 27th January 2020 to 30th June 2021 (time period between the first detected COVID-19 case and the end of the second wave in India) and its impact on their perceptions and practices. The association between the change in Relative Search Volume (RSV) on Google Trends (GT) of 34 popularly searched keywords classified by the researchers under 5 different categories-"Immunity", "Eating behavior", "Food safety", "Food scares and concerns" and "Covid scare" showed a steep rise in search for immunity boosters, vitamin supplement brands "ayush kadha (ayurvedic decoction) during the first wave (April- August 2020). With a brief period of decline in the search trend, it again hiked correspondingly with the growing number of positive cases during the second wave in India. An online survey conducted on adult Indian internet users (n = 572) reported high (71.9%) consumption of Vitamin C rich fruits as well as Vitamin C (68.2%) and Zinc (61.4%) supplements to boost immunity. Traditional Indian spices like ginger and garlic were used by 62.9% and 50.9% respondents respectively. Most respondents reported to rely on social media for gathering COVID-19 associated tips for boosting immunity, however those with history of COVID-19 infection reported to rely more on doctors and health professionals for information. This study highlights the need of media and health literacy to advocate for the use of health information cautiously.

DOI: 10.1371/journal.pone.0266705
PMCID: PMC9022866
PMID: 35446865 [Indexed for MEDLINE]