AACT Herbal Dietary Supplement Section Abstracts July 2023

1. An Indonesian slimming drug with undeclared ingredients causing harm. van de Koppel S, Ekhart C**,** Roelen C, Ohana D, Kooijman M, van Hunsel F.

Drug Test Anal. 2023 Jun;15(6):695-700. doi: 10.1002/dta.3460. Epub 2023 Mar 14.

This paper reports the presence of undeclared drugs in the herbal slimming supplement Sulami®. The four cases of the adverse drug reactions related to Sulami® were reported to the Dutch Pharmacovigilance Centre (Lareb) or the Dutch Poisons Information Centre (DPIC). The analysis of all four collected samples revealed adulteration with sibutramine and canrenone. Both drugs can cause serious adverse drug reactions. From a legal point of view, it is clear that Sulami® does not meet the legal requirement for safety. As defined in the European General Food Law Regulation, food business operators are responsible for food safety. This also applies to online store owners who sell herbal preparations. Thus, it is clear that it is forbidden to sell Sulami® on the European and Dutch market. Collaboration between involved national authorities makes it possible to identify risky products. This allows the nationally responsible regulators to take targeted action. They can call on users to report sell points what makes it possible to arrest the sellers and confiscate the dangerous products. Beyond the national, also, the European enforcement organizations should take legal measures where possible, to protect public health. The Heads of Food Safety Agencies Working Group on Food Supplements "an Initiative on European level" is a good example of efforts to improve consumer safety.

DOI: 10.1002/dta.3460
PMID: 36808870 [Indexed for MEDLINE]

2. Presence and Quantity of Botanical Ingredients With Purported Performance-Enhancing Properties in Sports Supplements. Cohen PA, Avula B, Katragunta K, Travis JC, Khan I.

JAMA Netw Open. 2023 Jul 3;6(7):e2323879. doi: 10.1001/jamanetworkopen.2023.23879.

Comment in JAMA Netw Open. 2023 Jul 3;6(7):e2323832.

Plain Language Summary: This case series study examines the accuracy of labels of dietary sports supplements containing botanical ingredients.

DOI: 10.1001/jamanetworkopen.2023.23879
PMCID: PMC10352857
PMID: 37459101 [Indexed for MEDLINE]

3. The Evolving Profile of Idiosyncratic Drug-Induced Liver Injury. Fontana RJ, Bjornsson ES, Reddy R, Andrade RJ.

Clin Gastroenterol Hepatol. 2023 Jul;21(8):2088-2099. doi: 10.1016/j.cgh.2022.12.040. Epub 2023 Mar 1.

Idiosyncratic drug-induced liver injury (DILI) is an infrequent but important cause of liver disease. Newly identified causes of DILI include the COVID vaccines, turmeric, green tea extract, and immune checkpoint inhibitors. DILI is largely a clinical diagnosis of exclusion that requires evaluation for more common causes of liver injury and a compatible temporal association with the suspect drug. Recent progress in DILI causality assessment includes the development of the semi-automated revised electronic causality assessment method (RECAM) instrument. In addition, several drug-specific HLA associations have been identified that can help with the confirmation or exclusion of DILI in individual patients. Various prognostic models can help identify the 5%-10% of patients at highest risk of death. Following suspect drug cessation, 80% of patients with DILI fully recover, whereas 10%-15% have persistently abnormal laboratory studies at 6 months of follow-up. Hospitalized patients with DILI with an elevated international normalized ratio or mental status changes should be considered for N-acetylcysteine therapy and urgent liver transplant

evaluation. Selected patients with moderate to severe drug reaction with eosinophilia and systemic symptoms or autoimmune features on liver biopsy may benefit from short-term corticosteroids. However, prospective studies are needed to determine the optimal patients and dose and duration of steroids to use. LiverTox is a comprehensive, freely accessible Web site with important information regarding the hepatotoxicity profile of more than 1000 approved medications and 60 herbal and dietary supplement products. It is hoped that ongoing "omics" studies will lead to additional insight into DILI pathogenesis, improved diagnostic and prognostic biomarkers, and mechanism-based treatments.

DOI: 10.1016/j.cgh.2022.12.040
PMID: 36868489 [Indexed for MEDLINE]

4. Drug-Induced Acute-on-Chronic Liver Failure: Challenges and Future Directions. Ma J, Ghabril M, Chalasani N.

Clin Liver Dis. 2023 Aug;27(3):631-648. doi: 10.1016/j.cld.2023.03.007. Epub 2023 Apr 23.

Drug-induced liver injury (DILI) is a global problem related to prescription and over-the-counter medications as well as herbal and dietary supplements. It can lead to liver failure with the risk of death and need for liver transplantation. Acute-on-chronic liver failure (ACLF) may be precipitated by DILI and is associated with a high risk of mortality. This review addresses the challenges in defining the diagnostic criteria of drug-induced ACLF (DI-ACLF). The studies characterizing DI-ACLF and its outcomes are summarized, highlighting geographic differences in underlying liver disease and implicated agents, as are future directions in the field.

DOI: 10.1016/j.cld.2023.03.007
PMID: 37380287 [Indexed for MEDLINE]

5. Is Baikiain in Tara Flour a Causative Agent for the Adverse Events Associated with the Recalled Frozen French Lentil & Leek Crumbles Food Product? - A Working Hypothesis. Chittiboyina AG, Ali Z, Avula B, Khan SI, Mir TM, Zhang J, Aydoğan F, Zulfiqar F, Techen N, Parveen I, Pandey P, Adams SJ, Wang YH, Zhao J, Marshall GD, Pugh ND, Khan IA.

Chem Res Toxicol. 2023 Jun 19;36(6):818-821. doi: 10.1021/acs.chemrestox.3c00100. Epub 2023 May 31.

The French Lentil & Leek Crumbles frozen food product was recently recalled due to reports of gastrointestinal issues. So far, 393 adverse illness complaints and 133 hospitalizations have been reported from consumption of this food, and the tara (Tara spinosa) protein flour ingredient is hypothesized to be responsible. A multipronged approach resulted in identification of (S)-(-)-baikiain in tara as a compound of interest due to its abundance, possible metabolic fate, and close resemblance to irreversible inhibitors of L-pipecolate oxidase. Oral administration of baikiain in ND4 mice showed a statistically significant increase in blood ALT levels and a reduction in liver GSH.

DOI: 10.1021/acs.chemrestox.3c00100
PMCID: PMC10283043
PMID: 37255213 [Indexed for MEDLINE]

6. Tinospora cordifolia (Guduchi/Giloy)-Induced Liver Injury: A Case Review. Nnamani I, Tolu-Akinnawo O, Dufera RR, Akintunde A, Maliakkal B.

Cureus. 2023 May 31;15(5):e39793. doi: 10.7759/cureus.39793. eCollection 2023 May.

Tinospora cordifolia (Guduchi/Giloy) is a relatively common herbal supplement whose use has recently become prominent in Southeast Asia. It was promoted to the public in India as an immunity booster, especially against the novel COVID-19. There have been reports, mostly from India, of an association between Guduchi/Giloy and liver injury. We present a 50-year-old female with a history of Hashimoto thyroiditis, who presented with abdominal discomfort and nausea of two weeks duration, which coincided with starting HistaEzeTM supplement containing Tinospora cordifolia. The vital signs upon presentation showed no significant abnormalities. Labs were significant for severely elevated transaminases; however, viral panels, autoimmune serologies, and imaging studies were unremarkable. Roussel Uclaf causality assessment method (RUCAM) score was at 6, which was indicative of probable drug/herb-induced liver

injury. HistaEzeTM was discontinued, and the patient took a three-day course of oral steroids with significant interval improvement in clinical status, as evidenced by progressive normalization of the transaminases level. The transaminases decreased by greater than 50% within two weeks of discontinuation and trended back to baseline within three months. This case highlights the worldwide availability and use of Tinospora cordifolia, which can cause liver injury that appears to be idiosyncratic and possibly immune-mediated. Further research on the precise mechanism of its hepatotoxicity is warranted.

DOI: 10.7759/cureus.39793
PMCID: PMC10238282
PMID: 37273324

7. Hematuria and dietary supplements - A case report on pronounced bleeding following a minimally invasive urological intervention in a patient on long term garlic supplements. Nair A, Abdelqader B, Sureshkumar S, Katmawai-Sabbagh S.

Urol Case Rep. 2023 Jul 4;50:102493. doi: 10.1016/j.eucr.2023.102493. eCollection 2023 Sep.

This report focuses on a patient encounter with suspected significant hematuria post operation occurring primarily due to garlic supplementation. A 65-year-old male underwent day case PVP. He had significant hematuria post operation requiring added use of bipolar coagulation. He was fit and well with no other past medical or drug history apart from dietary supplementation of garlic extracts. There are various mechanisms that components of garlic like allicin can produce antiplatelet effect on blood. This represents a novel case of unexpected bleeding in patient strongly attributed to dietary supplements for a less invasive technique with better hemostatic profile like PVP.

DOI: 10.1016/j.eucr.2023.102493
PMCID: PMC10362071
PMID: 37484191

8. A Case of Abnormal Liver Function Tests in a Patient Receiving Total Parenteral Nutrition. Tran T, Rim DS, Nolen-Doerr E, Lopez M, Nah Y, Sharma K, Shin JH, Kim DW.

J Investig Med High Impact Case Rep. 2023 Jan-Dec;11:23247096231181969. doi: 10.1177/23247096231181969.

Hepatic dysfunction is prevalent in patients receiving total parenteral nutrition (TPN), resulting from steatosis, cholestasis, and cholecystitis. Regular assessments and monitoring of TPN patients are essential, even for clinically stable patients on long-term TPN. Furthermore, it is crucial to establish a differential diagnosis for hepatic dysfunction and investigate for other possible causes of elevated liver enzymes and underlying liver conditions. We present the case of a 56-year-old female patient with severe protein-calorie malnutrition on TPN, who exhibited significantly elevated liver enzymes during the routine periodic assessment. Subsequent investigation revealed that the patient had been taking traditional Chinese herbal medications concurrently with TPN. After discontinuing the herbal medications, the patient's liver enzymes returned to normal levels within 3 weeks.

DOI: 10.1177/23247096231181969
PMCID: PMC10331775
PMID: 37357868 [Indexed for MEDLINE]

9. Drug-induced liver injury associated to red yeast rice. García-García MD, Bellido Muñoz F, Cordero Ruiz P, Caunedo Álvarez Á.

Rev Esp Enferm Dig. 2023 Jul 14. doi: 10.17235/reed.2023.9797/2023. Online ahead of print.

Hepatotoxicity is defined as a liver injury induced by a drug or a non-pharmacological agent like herbal medications or dietary supplements. Red yeast rice is rich in monacolin K, which has the same chemical structure as lovastatin, reason why it has been used for the management of hiperlipidemia. A 62 years old woman presented to the emergency service with 38.5ºC fever, coluricorine and loss of weight in the previous 3 weeks. The patient was taking RYR since the week before to the initial symptoms. Mixed hepatocellular and cholestatic acute hepatitis was diagnosed. Autoimmune liver serology resulted positive. Total DILI

RECAM Score was 8 (highly probable DILI). Conservative treatment with exclusion of RYR was decided and during follow-up bilirubin and transaminases gradually dropped off. It has been reported a few cases of hepatitis associated to the use of RYR, promoted by a toxic or immunogenic metabolite. Cross-reactions may justify positive autoantibodies so hepatotoxicity should not be discard as a diagnose.

DOI: 10.17235/reed.2023.9797/2023
PMID: 37449514

10. Drug Interactions Causing Warfarin Overdose in a Patient with Pancreatic Cancer: A Case Report. Moussouni M, Graff V, Couturier F, Herrscher H.

Chemotherapy. 2023;68(2):111-114. doi: 10.1159/000528063. Epub 2022 Nov 29.

Mistletoe, Viscum album, is a medicinal plant used in complementary medicine in oncology. Patients do not necessarily mention to their oncologist this phytotherapeutic treatment which may be responsible for unsuspected drug interactions. Some patients are adept at taking medicinal plants, a practice often unknown to health professionals who take care of them. This case reports drug interactions leading to bleeding secondary to warfarin overdose. A patient over 75 years of age was treated with nab-paclitaxel and gemcitabine as a first course for metastatic pancreatic adenocarcinoma (day 0). He was also treated with warfarin for atrial fibrillation. At day 3, he reported faintness and melena. At day 5, the biological assessment revealed anemia with hemoglobinemia of 5.1 g/dL and an international normalized ratio of 7.3, indicating vitamin K antagonist (VKA) overdose. Warfarin was discontinued and the patient received vitamin K supplementation and transfusions. The final diagnosis was an anemic syndrome due to gastrointestinal bleeding secondary to VKA overdose. Based on the chronology, a drug interaction between chemotherapy and warfarin was first suspected. Then, the patient interview found out that he self-medicated with subcutaneous injections of mistletoe extracts: 10 mg on day 0 and on day 2. Nab-paclitaxel can displace warfarin from its albumin binding sites and increase the free and active concentration of warfarin. Mistletoe extracts (V. album) are used as complementary medicine in oncology. Warfarin is predominantly metabolized in the liver by 1A2, 2C9, and 3A4 cytochrome P450 (CYP) isoforms. An inhibitor of these cytochromes prevents the degradation of warfarin into inactive metabolites, leading to accumulation or even overdose of this narrow therapeutic index VKA. Nab-paclitaxel and gemcitabine do not act on these cytochromes. V. album is a cytochrome P450 3A4 inhibitor which therefore probably led to an increase in exposure to warfarin. Thus, there are two pharmacokinetic hypotheses that may explain warfarin overdose: the displacement of warfarin from its albumin binding sites or the inhibition of CYP3A4 by mistletoe. This adverse drug event was reported to the Regional Pharmacovigilance Center of Strasbourg on June 30, 2021, and registered under the number ST20212767.

DOI: 10.1159/000528063
PMID: 36446317 [Indexed for MEDLINE]

11. Silymarin, an antioxidant flavonoid, protects the liver from the toxicity of the anticancer drug paclitaxel. Gür FM, Bilgiç S.

Tissue Cell. 2023 Aug;83:102158. doi: 10.1016/j.tice.2023.102158. Epub 2023 Jul 7.

One of the biggest factors that negatively affect the cancer treatment plan is the toxic effects of chemotherapeutics on non-target cells and tissues. This information prompted us to investigate the protective effects of silymarin (SL), a hepatoprotective agent, against the hepatotoxic effects of the anticancer drug paclitaxel (PAC). Four groups were formed from 28 rats as control, PAC (2 mg/kg), SL (100 mg/kg) and PAC + SL (combination of PAC with SL). After completing the experimental procedures, the tissues collected after anesthesia were analyzed by Western blot, qRT-PCR, biochemical, stereological, immunohistochemical, and histopathological techniques. Administration of PAC significantly increased the expression of tumor necrosis factor-alpha (TNF-α), Bax, cytochrome-c (cyt-c), and active caspase-3, as well as malondialdehyde (MDA) levels in liver tissue and decreased glutathione (GSH) levels compared with the control group. PAC also resulted in a significant increase in serum triglyceride (TG), cholesterol (CH), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels compared with the control group. Pathological changes such as microvesicular steatosis, the formation of Councilman bodies, an increase in total sinusoidal volume, and a decrease in the total number of hepatocytes were observed in the liver tissue of the PAC group. Almost all analysis results in the PAC + SL group were similar to those in the control group, and no significant pathological alterations were observed in this group. The data obtained

show that SL protects the liver from the harmful effects of PAC, especially thanks to its TNF-α suppressor, anti-inflammatory, anti-apoptotic and antioxidant effects. Based on this result, in cases where PAC is used in cancer treatment, it can be recommended to be used together with SL to prevent harmful effects on healthy liver tissue and to continue treatment uninterruptedly and effectively.

DOI: 10.1016/j.tice.2023.102158
PMID: 37459721 [Indexed for MEDLINE]

12. Potency trends of cannabis in Jamaica during the period of 2014 to 2020. Lindsay CM, Bernard KK, Hammond AM, Beckford S, Abel WD, Brown PD, Young LE.

Drug Test Anal. 2023 Jun 12. doi: 10.1002/dta.3527. Online ahead of print.

Reports suggest that cannabis potency has dramatically increased over the last decade in the USA and Europe. Cannabinoids are the terpeno-phenolic compounds found in the cannabis plant and are responsible for its pharmacological activity. The two most prominent cannabinoids are delta-9-tetrahydrocannabinol (Δ9 THC) and cannabidiol (CBD). Cannabis potency is measured not only by the Δ9 THC levels but also by the ratio of Δ9 THC to other non-psychoactive cannabinoids, namely, CBD. Cannabis use was decriminalized in Jamaica in 2015, which opened the gates for the creation of a regulated medical cannabis industry in the country. To date, there is no information available on the potency of cannabis in Jamaica. In this study, the cannabinoid content of Jamaican-grown cannabis was examined over the period 2014-2020. Two hundred ninety-nine herbal cannabis samples were received from 12 parishes across the island, and the levels of the major cannabinoids were determined using gas chromatography-mass spectrometry. There was a significant increase ($p < 0.05$) in the median total THC levels of cannabis samples tested between 2014 (1.1%) and 2020 (10.2%). The highest median THC was detected in the central parish of Manchester (21.1%). During the period, THC/CBD ratios increased from 2.1 (2014) to 194.1 (2020), and there was a corresponding increase in the percent freshness of samples (CBN/THC ratios <0.013). The data show that a significant increase in the potency of locally grown cannabis has occurred in Jamaica during the last decade.

DOI: 10.1002/dta.3527
PMID: 37309060

13. An evaluation of adverse drug reactions and outcomes attributed to kratom in the US Food and Drug Administration Adverse Event Reporting System from January 2004 through September 2021. Li X, Ndungu P, Taneja SB, Chapin MR, Egbert SB, Akenapalli K, Paine MF, Kane-Gill SL, Boyce RD.

Clin Transl Sci. 2023 Jun;16(6):1002-1011. doi: 10.1111/cts.13505. Epub 2023 Mar 20.

Kratom is a widely used Asian botanical that has gained popularity in the United States due to a perception that it can treat pain, anxiety, and opioid withdrawal symptoms. The American Kratom Association estimates 10-16 million people use kratom. Kratom-associated adverse drug reactions (ADRs) continue to be reported and raise concerns about the safety profile of kratom. However, studies are lacking that describe the overall pattern of kratom-associated adverse events and quantify the association between kratom and adverse events. ADRs reported to the US Food and Drug Administration Adverse Event Reporting System from January 2004 through September 2021 were used to address these knowledge gaps. Descriptive analysis was conducted to analyze kratom-related adverse reactions. Conservative pharmacovigilance signals based on observed-to-expected ratios with shrinkage were estimated by comparing kratom to all other natural products and drugs. Based on 489 deduplicated kratom-related ADR reports, users were young (mean age 35.5 years), and more often male (67.5%) than female patients (23.5%). Cases were predominantly reported since 2018 (94.2%). Fifty-two disproportionate reporting signals in 17 system-organ-class categories were generated. The observed/reported number of kratom-related accidental death reports was 63-fold greater than expected. There were eight strong signals related to addiction or drug withdrawal. An excess proportion of ADR reports were about kratom-related drug complaints, toxicity to various agents, and seizures. Although further research is needed to assess the safety of kratom, clinicians and consumers should be aware that real-world evidence points to potential safety threats.

DOI: 10.1111/cts.13505
PMCID: PMC10264943
PMID: 36861661 [Indexed for MEDLINE]

14. Description of Kratom Exposure Events in Wisconsin as Reported to the Wisconsin Poison Center, January 1, 2010 to September 1, 2022. DeJonge P, Gummin D, Titelbaum N, Meiman J.

WMJ. 2023 Jul;122(3):187-190.

BACKGROUND: Consumption of kratom (Mitragyna speciosa), an herbal substance, can result in adverse health effects. We characterized kratom-associated adverse events in Wisconsin to provide pertinent recommendations for clinicians and public health practitioners. METHODS: Using Wisconsin Poison Center data, we searched for and summarized all records associated with exposure to "kratom," "electronic delivery device containing kratom," or "mitragyna" from January 1, 2010, to September 1, 2022. RESULTS: Kratom-associated exposure calls to the Wisconsin Poison Center increased 3.75 times during 2016 - 2020. Among all 59 calls, 26 (44.1%) reported concomitant use of another substance, agitation was the most common symptom reported (n = 23, 39%), and 7 persons required critical care. Three unintentional ingestions were reported in children aged less than 2 years old. DISCUSSION: Kratom-associated exposure calls to the Wisconsin Poison Center generally have been increasing in frequency since 2011. Wisconsinites who choose to use kratom might benefit from education regarding health risks and safe storage practices to avoid unintentional pediatric exposure.

PMID: 37494649 [Indexed for MEDLINE]

15. Translating Kratom-Drug Interactions: From Bedside to Bench and Back. Tanna RS, Cech NB, Oberlies NH, Rettie AE, Thummel KE, Paine MF.

Drug Metab Dispos. 2023 Aug;51(8):923-935. doi: 10.1124/dmd.122.001005. Epub 2023 Jun 7.

Kratom is a botanical natural product belonging to the coffee family, with stimulant effects at low doses and opioid-like effects at higher doses. During the last two decades, kratom has been purported as a safer alternative to pharmaceutical and illicit drugs to self-manage pain and opioid withdrawal symptoms. Kratom alkaloids, typically mitragynine, have been detected in biologic samples from overdose deaths. These deaths are often observed in combination with other drugs and are suspected to result from polyintoxications. This review focuses on the potential for kratom to precipitate pharmacokinetic interactions with object drugs involved in these reported polyintoxications. The legal status, chemistry, pharmacology, and toxicology are also summarized. The aggregate in vitro and clinical data identified kratom and select kratom alkaloids as modulators of cytochrome P450 (P450) enzyme activity, notably as inhibitors of CYP2D6 and CYP3A, as well as P-glycoprotein-mediated efflux activity. These inhibitory effects could increase the systemic exposure to co-consumed object drugs, which may lead to adverse effects. Collectively, the evidence to date warrants further evaluation of potential kratom-drug interactions using an iterative approach involving additional mechanistic in vitro studies, well designed clinical studies, and physiologically based pharmacokinetic modeling and simulation. This critical information is needed to fill knowledge gaps regarding the safe and effective use of kratom, thereby addressing ongoing public health concerns. SIGNIFICANCE STATEMENT: The botanical kratom is increasingly used to self-manage pain and opioid withdrawal symptoms due to having opioid-like effects. The legal status, chemistry, pharmacology, toxicology, and drug interaction potential of kratom are reviewed. Kratom-associated polyintoxications and in vitro-in vivo extrapolations suggest that kratom can precipitate pharmacokinetic drug interactions by inhibiting CYP2D6, CYP3A, and P-glycoprotein. An iterative approach that includes clinical studies and physiologically based pharmacokinetic modeling and simulation is recommended for further evaluation of potential unwanted kratom-drug interactions.

DOI: 10.1124/dmd.122.001005
PMCID: PMC10353077
PMID: 37286363 [Indexed for MEDLINE]

16. Lead and arsenic contamination in henna samples marketed in Iran. Rezaeian M, Mohamadi M, Ahmadinia H, Mohammadi H, Ghaffarian-Bahraman A.

Environ Monit Assess. 2023 Jul 3;195(8):913. doi: 10.1007/s10661-023-11532-y.

Since ancient times, people around the world have used natural cosmetics to improve or change the appearance of their nails, skin, and hair. Henna is a plant-based dye that has been used over the centuries for medical and cosmetic purposes. The present work was aimed to investigate the presence of lead (Pb) and

arsenic (As) in various types of commonly consumed henna samples in Iran. A total of thirty-nine henna samples from both local and imported products (3 colors in 13 brands) were randomly collected from popular and herbal medicine markets. The atomic absorption spectrometry (AAS) technique was used for the analysis of the samples. The amount of Pb and As in 100% samples was higher than the calculated limit of quantitation (LOQ). The concentrations of Pb and As in the samples were at the ranges of 9.56-16.94 μg/g and 0.25-1.12 μg/g, respectively. The mean level of Pb was higher in black and red products, compared with the green henna. The levels of Pb and As in 53.85% and 7.7% of the henna samples exceeded the permissible limits recommended by the World Health Organization (WHO), respectively. In addition, the mean levels of Pb and As contamination in the imported samples were significantly higher, in comparison to the local henna samples. To our knowledge, this is the first study assessing Pb and As contamination in the henna samples consumed in Iran. Our study demonstrated that there is a potential risk of exposure to Pb through henna in the Iranian consumers.

DOI: 10.1007/s10661-023-11532-y
PMID: 37395865 [Indexed for MEDLINE]

17. Plant Toxic Proteins: Their Biological Activities, Mechanism of Action and Removal Strategies. Kocyigit E, Kocaadam-Bozkurt B, Bozkurt O, Ağagündüz D, Capasso R.

Toxins (Basel). 2023 May 24;15(6):356. doi: 10.3390/toxins15060356.

Plants evolve to synthesize various natural metabolites to protect themselves against threats, such as insects, predators, microorganisms, and environmental conditions (such as temperature, pH, humidity, salt, and drought). Plant-derived toxic proteins are often secondary metabolites generated by plants. These proteins, including ribosome-inactivating proteins, lectins, protease inhibitors, α-amylase inhibitors, canatoxin-like proteins and ureases, arcelins, antimicrobial peptides, and pore-forming toxins, are found in different plant parts, such as the roots, tubers, stems, fruits, buds, and foliage. Several investigations have been conducted to explore the potential applications of these plant proteins by analyzing their toxic effects and modes of action. In biomedical applications, such as crop protection, drug development, cancer therapy, and genetic engineering, toxic plant proteins have been utilized as potentially useful instruments due to their biological activities. However, these noxious metabolites can be detrimental to human health and cause problems when consumed in high amounts. This review focuses on different plant toxic proteins, their biological activities, and their mechanisms of action. Furthermore, possible usage and removal strategies for these proteins are discussed.

DOI: 10.3390/toxins15060356
PMCID: PMC10303728
PMID: 37368657 [Indexed for MEDLINE]

18. Overview of aristolochic acid nephropathy: an update. Zhou Q, Jiang L, Su T, Liu G, Yang L.

Kidney Res Clin Pract. 2023 Jun 15. doi: 10.23876/j.krcp.22.211. Online ahead of print.

Aristolochic acid nephropathy (AAN) is a rapidly progressive renal interstitial fibrosis caused by medical or environmental exposure to aristolochic acid (AA). Since the outbreak of AAN in Belgium was reported nearly 30 years ago, the safety of herbal remedies has drawn considerable attention, and AAN has become a global public health problem. Breakthroughs have been made to better understand the disease, including the toxicity of AAs, the possible mechanisms of AAN, the disease patterns, and the pathological features; however, some critical problems remain unresolved. Because of the insidious onset of the disease, the incidence of AAN and the prevalence of exposure to AAs are unknown and might be largely underestimated. During the past decades, AA-containing herbs have been strictly administrated in many regions and the occurrence of AAN has declined sharply, yet cases of AAN are still sporadically reported. Despite the progress in the understanding of the disease's pathogenesis, there is no effective treatment for delaying or reversing the renal deterioration caused by AAN. Therefore, the risk of exposure to AAs should be taken seriously by public health workers and clinicians. In this review, we updated the latest data on AAN, summarized the advances throughout these years, and put forward some challenges for future research.

DOI: 10.23876/j.krcp.22.211
PMID: 37448287

19. 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. 2023;20(4):602-620. doi: 10.1080/19390211.2022.2056670. Epub 2022 Apr 5.

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 [Indexed for MEDLINE]

20. Toxicity, formation, contamination, determination and mitigation of acrylamide in thermally processed plant-based foods and herbal medicines: A review. Fan M, Xu X, Lang W, Wang W, Wang X, Xin A, Zhou F, Ding Z, Ye X, Zhu B.

Ecotoxicol Environ Saf. 2023 Jul 15;260:115059. doi: 10.1016/j.ecoenv.2023.115059. Epub 2023 May 29.

Thermal processing is one of the important techniques for most of the plant-based food and herb medicines before consumption and application in order to meet the specific requirement. The plant and herbs are rich in amino acids and reducing sugars, and thermal processing may lead to Maillard reaction, resulting as a high risk of acrylamide pollution. Acrylamide, an organic pollutant that can be absorbed by the body through the respiratory tract, digestive tract, skin and mucous membranes, has potential carcinogenicity, neurological, genetic, reproductive and developmental toxicity. Therefore, it is significant to conduct pollution determination and risk assessment for quality assurance and security of medication. This review demonstrates state-of-the-art research of acrylamide focusing on the toxicity, formation, contamination, determination, and mitigation in taking food and herb medicine, to provide reference for scientific processing and ensure the security of consumers.

DOI: 10.1016/j.ecoenv.2023.115059
PMID: 37257344 [Indexed for MEDLINE]