AACT Herbal Dietary Supplement Section Abstracts

Jan-Mar 2026 (Q1)

Hepatotoxicity and Drug Induced Liver Injury

1. Recurrent Drug-Induced Autoimmune-like Hepatitis due to Turmeric Supplementation.

J Investig Med High Impact Case Rep. 2026 Jan-Dec;14:23247096261452814. Epub 2026 May 20.

Patel AA, Dargan KK, Formaker P, Romberg C.

Drug-induced autoimmune-like hepatitis (DI-ALH) is a rare form of drug-induced liver injury (DILI) that mimics autoimmune hepatitis (AIH). Commonly implicated agents include minocycline, nitrofurantoin, and infliximab, though a wide range of other drugs has been reported. We report a 65-year-old woman with a history of suspected turmeric-induced liver injury six years prior who presented with nausea and painless jaundice two weeks after restarting the same turmeric supplement containing black pepper extract. She denied alcohol or hepatotoxic medication use, and family and personal history of autoimmune or liver disease were unremarkable. Laboratory evaluation revealed marked transaminase elevation (AST 4310 U/L, ALT >2500 U/L), total bilirubin 18.3 mg/dL, and INR 1.1. Autoimmune testing revealed positive smooth muscle antibodies and elevated IgG, while viral, metabolic, and genetic studies were negative. Imaging demonstrated periportal edema. Despite supplement discontinuation, liver enzymes worsened, prompting a liver biopsy, which demonstrated acute hepatitis with portal and lobular inflammation, plasma cell predominance, and canalicular cholestasis without fibrosis consistent with DI-ALH. Corticosteroid therapy led to biochemical improvement over three weeks. The temporal association with exposure, autoimmune serologies, characteristic histology, and steroid responsiveness supported the diagnosis of recurrent turmeric-induced DI-ALH, with more severe injury on re-exposure suggesting immune sensitization. Piperine, included to enhance curcumin bioavailability, may potentiate hepatotoxicity. DI-ALH should be considered in patients with liver injury and recent supplement use, as immunosuppressive therapy may be beneficial when injury persists after drug withdrawal.

DOI: 10.1177/23247096261452814

PMID: 42160492

2. Drug-Induced Liver Injury with Novel Fat Burner AlbutarexV2 in an Active Duty Sailor.

Mil Med. 2026 Jan 1;191(1-2):e433-e435.

Lilley LJ, Wiseman M, Sadowski B.

Drug-induced liver injury ranges from asymptomatic to liver failure with supplements becoming an increasingly recognized cause. This case highlights the unique supplement, AlbutarexV2, and the severe cholestatic liver injury it induced with resolution occurring in six months. With steadily increasing obesity rates and supplement use, weight-loss supplements are gaining popularity with various claims of increasing energy expenditure or metabolic rate. Recognition of adverse effects from these therapies is critical to aid in identification and cessation of the agent and helping ban harmful supplements. This case demonstrates the danger of "fat-burners" and delineates the protracted and prolonged liver injury of AlbutarexV2.

DOI: 10.1093/milmed/usaf175

PMID: 40338652

3. Unveiling Drug-Induced Autoimmune-Like Hepatitis in Autoimmune Hepatitis Patients: A Multicenter Retrospective Study.

Aliment Pharmacol Ther. 2026 Feb;63(3):362-373. Epub 2025 Aug 26.

Arvaniti P, Olivas I, Pascual-Dapena A, *et al*

BACKGROUND AND AIMS: Acute or chronic exposure to drugs or herbal and dietary supplements (HDS) can cause drug-induced autoimmune-like hepatitis (DI-ALH), a self-limiting condition resembling autoimmune hepatitis (AIH). We investigated the prevalence of drug exposure among AIH patients at diagnosis to recognise cases of DI-ALH and discern features predicting AIH development. METHODS: We retrospectively included 705 patients diagnosed with AIH. DI-ALH was defined using published criteria. The clinical, biochemical, serological, and histological data of DI-ALH and AIH were analysed to identify predictors of the evolution of each phenotype. RESULTS: Most patients were female (n = 496, 70%), with a median age of 57 years and a median follow-up of 55 months. A 59% (n = 417) reported exposure to drugs or HDS, and 8% (n = 58) fulfilled the criteria for DI-ALH. Statins and HDS were the most common culprits. Patients with DI-ALH more frequently had acute severe or fulminant hepatitis (22% vs. 12%, p = 0.013) and higher transaminase levels (ALT: 966 vs. 591, p = 0.001) at diagnosis. In total, 97% of the patients received immunosuppression. DI-ALH patients had a faster biochemical response than i-AIH patients (4 vs. 5, p = 0.031), while treatment withdrawal was attempted in only 29% (n = 17). Approximately 30% (n = 17) of DI-ALH cases presented a flare during follow-up. Neither clinical, histological, nor serological findings nor RUCAM and RECAM could predict a DI-ALH flare. CONCLUSIONS: DI-ALH is often under-recognised in clinical practice, leading to

unnecessary long-term immunosuppression. A causal relationship between drugs and AIH, along with an attempt to withdraw treatment and long-term follow-up, is essential to prevent overtreatment-associated risks.

DOI: 10.1111/apt.70353

PMID: 40857202

4. A market and risk assessment of 125 turmeric supplements available in Australia, Germany, India, UK, and USA.

Naunyn Schmiedebergs Arch Pharmacol. 2026 Jan;399(1):1315-1346. Epub 2025 Aug 7.

Rahim-Mahdy H, Seifert R.

Historically prominent in Ayurvedic cultures, turmeric (Curcuma longa), or "Haldi," is renowned for its anti-inflammatory and antioxidant effects, mainly due to its active compounds, curcuminoids. Due to the increasing use of turmeric supplements, this study critically examined 125 preparations across the UK, USA, India, Australia, and Germany and evaluated their compliance with evidence-based recommendations. Results reveal significant regulatory and labeling inconsistencies across countries, with 34% of preparations failing to disclose the active curcuminoid content. This lack of dosage regulation is especially concerning when considering the ongoing research into advanced delivery systems-such as nanoparticles, liposomes, micelles, and phospholipid complexes-which significantly enhance curcumin's absorption. Curcumin, a hydrophobic compound, undergoes rapid metabolism in the liver through Phase I and II detoxification pathways, particularly via cytochrome P450 enzymes and UDP-glucuronosyltransferase enzymes. This results in limited bioavailability, as curcumin is rapidly converted to water-soluble metabolites and excreted, reducing its effectiveness at therapeutic doses. However, through modern formulation technologies, curcumin can potentially not only alter drug metabolism, but its antioxidant action via Nrf2 activation can shift to pro-oxidant effects at high doses, causing oxidative stress and the accumulation of reactive metabolites. Emerging evidence suggests chronic low-dose use may lead to gastrointestinal, hepatic, or renal toxicity, yet turmeric preparations, falling within the scope of food law, lack the stringent controls applied to pharmaceuticals and are generally assumed safe. This study highlights the need for transparent labeling, clear dosage guidelines, and an understanding of curcumin's metabolic profile to guide consumers in maximizing benefits while mitigating risks. Furthermore, it aims to assist healthcare professionals in making informed recommendations regarding curcumin supplementation. Further research must include long-term clinical trials and potential standardization of curcumin supplement formulations.

DOI: 10.1007/s00210-025-04392-5

PMID: 40773013

5. From spice to spotlight: Turmeric's safety concerns and the need for herbal education and enhanced regulation.

J Am Pharm Assoc (2003). 2026 May-Jun;66(3):103070. Epub 2026 Mar 7.

Helmer RS, Korankyi KA.

Several mass media reports have linked turmeric supplements with drug-induced liver injury bringing herbal supplement safety into the public eye. These reports raise important areas of consideration for pharmacists, including turmeric safety and efficacy, pharmacists' roles in ensuring safe supplement use, and pharmacist advocacy for improved supplement regulatory processes. Turmeric's main pharmacologically active form, curcumin, is reported to have antioxidant, antiviral, antibacterial, and anti-inflammatory properties. Turmeric supplements show generally positive, albeit weak, evidence in benefitting a variety of disease states such as arthritis, metabolic disorders, and depression. While turmeric's safety profile is largely benign, several cases of turmeric-induced liver injury have been reported with most patients having a successful dechallenge. Mechanisms of liver injury are considered idiopathic with a hepatocellular injury pattern. Few parallels exist regarding dosing, timing, or patient characteristics that may increase risk of turmeric-induced liver injury. However, pharmacists are uniquely qualified to assess medication safety and efficacy, which extends to dietary and herbal supplements. Pharmacists can use recent media headlines as a catalyst for reflection and education. Comprehensive professional development on common dietary and herbal supplements will aid pharmacists in providing public education regarding supplement safety and limitations in the supplement regulatory process. Enhanced knowledge and awareness may lead to increased advocacy for supplement regulatory reform to improve transparency, safety, and efficacy.

DOI: 10.1016/j.japh.2026.103070

PMID: 41802599

Kratom, Stimulants, and Weight-Loss/Performance Products

6. Nonswallowed Kratom-Derived Products: Unlawful Dietary Supplements That Endanger Public Health.

Public Health Rep. 2026 May-Jun;141(3):335-338. Epub 2026 Jan 26.

White CM, Sedensky A, Belcourt J, Kulkarni P.

The Dietary Supplement Health and Education Act of 1994 specified that dietary supplements must be swallowed. In this study, we investigated whether kratom-derived products are being sold to consumers in nonswallowed formulations. Kratom is the fresh or dried leaf powder of the Mitragyna speciosa tree. We identified 49 kratom-derived products being sold in the form of sublingual strips (24%), buccal pouches (8%), and vaping products (67%). Most contained 7-hydroxymitragynine (an alkaloid that the US

Food and Drug Administration seeks to make a controlled substance), but we also identified mitragynine extract and mitragynine pseudoindoxyl products. The majority had flavoring or a scent, and some had mascots, pictures of fruit or mint, or formulation colors or packaging that could appeal to children. Most products were not sold in child-resistant packaging. Several kratom vaping products additionally contained intoxicating hemp cannabinoids. With no clinical, safety, or pharmacokinetic data for kratom-derived products that bypass first-pass metabolism (ie, where a chemical absorbed through the stomach or intestines is metabolized in the liver before reaching the general bloodstream), people should be advised to avoid these products, and regulatory action is needed to prevent their sale to consumers.

DOI: 10.1177/00333549251410520

PMID: 41587771

7. In vitro inhibition of monoamine transport by amphetamine-like pre-workout supplement ingredients.

Toxicology. 2026 Jun;523:154442. Epub 2026 Mar 6.

Pinckaers NET, Sawicka PD, Wopken JP, Blankesteijn WM, van Schooten FJ, Opperhuizen A, Vrolijk M, Westerink RHS.

Phenethylamine (PEA) and alkylamine (AA) analogues are a prominent group of pre-workout food supplement ingredients. They are structurally related to the stimulant amphetamine and to the endogenous catecholamines noradrenaline and dopamine, implying potential cardiovascular and psychological effects. This study systematically investigated the inhibitory potential of 12 PEAs and 4 AAs identified in pre-workout supplements on the human dopamine transporter (hDAT), human noradrenaline transporter (hNET) and human serotonin transporter (hSERT) that are stably overexpressed in HEK 293 cells. All PEAs and AAs tested, except DMAE, inhibited substrate uptake by one or more monoamine transporters. Overall, the substances displayed the highest potency and efficacy at hNET, followed by hDAT and with considerably weaker effects on hSERT. At hNET, potency values (IC50) ranged from 0.5 μM to 123 μM, with maximal inhibition (Emax) ranging from -59.2% to -120%. Inhibition of substrate uptake by hDAT occurred with IC50 values between 4.0 and 95.8 μM and Emax values between -66.8% and -135%. For hSERT 50% inhibition was observed at concentrations ranging from 2.6 μM to 131 μM, with maximal effect between 85.3% and -64.8%. These findings indicate a potential for sympathetic activation and behavioral rewarding and reinforcing effects. Notably, the in vitro potency and efficacy of several PEAs and AAs were comparable to those of the well-known illicit stimulants amphetamine and cocaine. Together, these findings highlight the urgent need to further characterize pharmacokinetic and pharmacodynamic properties of these pre-workout supplement ingredients to support robust risk assessment and informed regulatory decision-making regarding the safety of pre-workout supplement ingredients.

DOI: 10.1016/j.tox.2026.154442

PMID: 41796714

8. Crataegus mexicana root-based supplement intoxication in a woman with weight loss persistent preoccupation: Case report.

Biomedica. 2026 Mar 2;46(1):25-29.

Abad-Cuenca S.

Body image preoccupation is increasingly common, particularly among Latin American women, influenced by societal beauty standards favoring thinness. This often drives individuals to use unregulated weight loss supplements, which can lead to serious health risks. This case reports a rare instance of acute diarrhea resulting from the unsupervised use of a Crataegus mexicana root-based supplement, a product frequently marketed for weight loss. A 41-year-old Hispanic woman presented to the emergency department with a 15-day history of daily diarrhea, epigastric pain, and malaise. She reported using the supplement for weight loss. Physical examination revealed moderate dehydration and localized tenderness in the precordial and epigastric regions. The diagnosis was acute diarrhea related to the herbal supplement, with moderate dehydration. The patient received intravenous saline and analgesics and was discharged in stable condition after 48 hours. Follow-up showed no recurrence of symptoms, but persistent body image concerns. This case highlights the dangers of unsupervised herbal supplement use for weight los and underscores the need for proper medical guidance when using supplements.

DOI: 10.7705/biomedica.7794

PMID: 41875453

Product Quality, Labeling, Contamination, and Regulatory Risk

9. Excessive manganese content in children's multivitamin supplements: Potential for neurodevelopmental harm and other adverse health outcomes.

PLoS One. 2026 Mar 18;21(3):e0343600. eCollection 2026.

Frisbie SH, Mitchell EJ, Hoeltge A, Pett LA, Hoeltge MG.

BACKGROUND: Manganese (Mn) is an essential nutrient vital for many physiological processes, but it can cause adverse health effects at high exposures, particularly during neurodevelopment. Mn is included in many children's multivitamins and mineral supplements, but it has not been documented whether the levels of Mn in such supplements are appropriate or safe. In this study, we measured Mn concentrations in children's multivitamin and mineral supplements and compared the concentrations to the Institute of Medicine's (IOM's) tolerable Upper intake Levels (ULs). METHODS: We purchased 52 multivitamin and mineral supplements in various forms, including tablets,

capsules, gummies, powders, and liquids. Of these samples, half listed supplemental Mn on their labels; half did not. We quantified their manganese concentrations using inductively coupled plasma-optical emission spectroscopy. We compared the measured Mn concentrations of the samples to the labeled concentrations and to the IOM ULs. RESULTS: Of the 26 products with supplemental Mn on their labels, 23 (88.5%) contained more Mn than shown on the label, while 3 (11.5%) contained less. The mean percent difference between labeled and measured Mn content was 42.5%. One product (4%), a liquid, would exceed the IOM's Mn ULs based on labeled concentrations alone if consumed daily, 5 products (19%) would exceed IOM ULs based on measured concentrations, and 9 (34.6%) would exceed IOM ULs based on measured concentrations if used as supplements to ordinary diets. Of the 26 products without supplemental Mn listed on their labels, 13 (50.0%) contained measurable Mn concentrations. None of the products without supplemental Mn listed on their labels would exceed IOM ULs, even if consumed as supplements to ordinary diets. CONCLUSIONS: Some children's multivitamin supplements may lead to exceedances of IOM ULs for Mn, especially when consumed as supplements to ordinary diets.

DOI: 10.1371/journal.pone.0343600

PMID: 41849337

10. Probiotic strain identification and safety assessment of unlabeled bacteria in infant products.

Int J Food Microbiol. 2026 Jan 16;445:111500. Epub 2025 Oct 21.

Wang N, Wu Y, Liu Y, Wen Q, Bai F, Tan Y, Cui Y, Liu X, Bi Y, Yang R, Luo P.

Probiotics are increasingly incorporated into infant and toddler nutritional products for their health benefits; however, concerns regarding the accuracy and safety of commercial probiotic product labeling remain unresolved. This study aimed to establish strain-level identification standards through whole-genome sequencing (WGS) and to evaluate the microbial composition and safety of 23 infant and toddler probiotic products. By integrating culturomics and WGS, analysis of probiotic strains Lacticaseibacillus rhamnosus HN001 (L. rhamnosus HN001), Bifidobacterium breve M-16V (B. breve M-16V) and Bifidobacterium animalis subsp. lactis HN019 (B. animalis subsp. lactis HN019) revealed significant diversity among isolates, with median single nucleotide polymorphism (SNP) distances ranging from 5 to 8, alongside other genomic variations such as plasmid loss. Furthermore, we identified 198 antibiotic resistance genes and 131 virulence factors in unlabeled strains. Particularly high levels of virulence factors were detected in Bacillus cereus (B. cereus) and Enterobacter hormaechei (E. hormaechei), These strains exhibited acute toxicity in mouse experiments. Live bacterial counts in some products failed to meet declared values. These findings underscore the urgency of strengthening regulatory oversight and establishing standardized genomic tools to ensure the safety and quality of probiotics.

DOI: 10.1016/j.ijfoodmicro.2025.111500

PMID: 41175552

11. Navigating the Risks Beyond the Label: Unpacking Global Nutritional Supplement Safety.

Int J Sport Nutr Exerc Metab. 2025 Dec 16;36(2):134-166. Print 2026 Mar 1.

Wardenaar FC, Burns SF, Campos M, Chan Y, Claassen-Smithers A, Dunshea-Mooij C, Haddou SE, Hoogervorst D, Jagim A, Garcia PR, Garthe I, Nugent AP, Aly MO, Saunders B, Schott KD, Sekiguchi Y, Slater G, Speers N, Stratton MT, Aussieker T.

Nutritional supplement use is common among athletes aiming to enhance performance, recovery, and health. However, variable regulatory frameworks and limited safety oversight create risks for inadvertent doping violations. This article provides a global overview of supplement use, relevant authorities, legislation, and safety measures, with a focus on third-party testing (TPT) as a risk-mitigation strategy. Data from six global regions-Africa, Asia, Australia/New Zealand, Europe, Latin America, and North America-were synthesized from peer-reviewed studies, governmental sources, and regional expert contributions. Reported supplement use ranged from 7% to 100% among athletes (variability within regions), with protein powders, vitamins/minerals, creatine, caffeine, and sports drinks being most prevalent. High-risk products (potential anti-doping rule violations), including certain herbal blends, preworkouts, and weight-management supplements, were reported across all regions. While some countries have robust regulatory systems, most lack harmonized or enforceable safety frameworks. TPT programs, which independently verify products for prohibited substances, remain concentrated in the global northwest (Europe, North America, and Australia/New Zealand); awareness and use of TPT certification vary widely, and even in regions with established systems, athlete adherence is inconsistent. Barriers to low-risk supplement use are limited TPT availability, cost, differences in labeling (including language), and cultural factors. Firsthand experiences and perceptions highlight widespread misconceptions about supplement safety and certification. The authors recommend expanded athlete and team-around-the-athlete education, improved global access to TPT low-risk supplements, and policy initiatives to harmonize safety standards. This work emphasizes the need for coordinated international efforts to protect athlete health and integrity while allowing access to evidence-based supplementation.

DOI: 10.1123/ijsnem.2025-0177

PMID: 41468235

Probiotics and Infectious Risk in Vulnerable Hosts

12. Case Series of Bacteremia Associated with Probiotic Use in Children after Cardiac Surgery, China.

Emerg Infect Dis. 2026 Jan;32(1):28-33.

Wang X, Li S, Huo D, Li C, Zhang Q, Wang X.

We examined probiotic-associated bacteremia in a cohort of postoperative pediatric cardiac surgery patients in China. Among 16,436 children who underwent cardiac surgery during 2019-2024, a total of 5,034 received probiotics; 6 developed bacteremia with probiotic strains (Bacillus subtilis, Bacillus licheniformis, Lacticaseibacillus rhamnosus). Three cases occurred in children who had not directly received probiotics, suggesting potential cross-contamination or catheter-related transmission. All 6 patients had complex congenital heart disease and central venous catheters; 5 underwent palliative surgery. Fever, elevated C-reactive protein and leukocytes, and use of respiratory support were common. Antibiotic therapy achieved blood-culture clearance in all; 1 death occurred because of underlying cardiac disease, not infection. Our findings conclude probiotic-associated bacteremia is rare and usually resolves with antibiotics; outcomes correlate more with cardiac complexity than bacteremia itself. Maintaining perioperative probiotic use and enhancing infection-control measures, specifically regarding central line care, are recommended to minimize the risk for probiotic-associated bacteremia in pediatric cardiosurgical patients.

DOI: 10.3201/eid3201.250298

PMID: 41612523

13. Current Concepts in Probiotic Safety and Efficacy.

Nutrients. 2026 Feb 21;18(4):696.

Churin AA, Sokolyanskaya LO, Lukina AP, Karnachuk OV.

Background/Objectives: Advances in molecular biology, genetics, and microbiome research have significantly expanded our understanding of probiotic microorganisms and their interactions with human health, stimulating the development of both traditional and next-generation probiotic products. Although probiotics are widely used and generally considered safe for healthy individuals, accumulating evidence indicates that their safety profile varies significantly depending on the strain, dose, host, and context, with rare but clinically significant adverse events reported in vulnerable populations. Methods: This review summarizes current knowledge on the efficacy and safety of probiotics, analyzes limitations in clinical safety reporting, and compares regulatory frameworks governing the use of probiotics as dietary supplements, medicinal products, and live biotherapeutics. Particular attention is given to new genomic and computational approaches to safety assessment. Conclusions: Overall, the review emphasizes the

need for coordinated regulation, rigorous clinical evidence, and integrated, modern safety assessment strategies to support the responsible expansion of probiotic use.

DOI: 10.3390/nu18040696

PMID: 41754214

Renal, Metabolic, and Nutritional Toxicity

14. Alpha-lipoic acid: High risk, little reward. A case of severe intoxication.

Clin Nutr ESPEN. 2026 Apr;72:102936. Epub 2026 Jan 21.

Heerfordt IM, Linnet K, Juhl CS, Huusom AJ, Horwitz H.

BACKGROUND: Alpha-lipoic acid (ALA) is a naturally occurring antioxidant and mitochondrial cofactor, widely marketed as an over-the-counter dietary supplement. In clinical studies, ALA has been safe and well-tolerated at doses around 600 mg daily. However, several case reports worldwide have documented that overdose can result in rapid and severe toxicity. CASE REPORT: We describe an elderly woman who accidently ingested 6 g of ALA, mistaking it for her usual fiber supplement. Three hours later, she was in a confused state, with nausea, vomiting, and diaphoresis. On admission, she displayed an altered mental state with a Glasgow Coma Scale score of 6-9 and mild lactic acidosis. She soon developed seizure-like activity unresponsive to midazolam and levetiracetam. She required intubation, sedation with propofol, and mechanical ventilation. She was extubated on day 2 and discharged home on day 3 without sequelae. DISCUSSION: The therapeutic benefits of ALA are limited, and compared with other vitamin supplements, it has a relatively narrow therapeutic index. This case illustrates the potential for severe and life-threatening intoxication following ingestion of amounts that may easily be present in a household supply of ALA. The clinical picture is characterized by rapid onset of gastrointestinal symptoms, seizures, and circulatory instability. As no antidote exists, management is supportive. CONCLUSION: ALA can be highly toxic in overdose. As treatment is only supportive, prevention is critical. Clear packaging and labeling, together with consumer education, may help reduce the risk of accidental ingestion.

DOI: 10.1016/j.clnesp.2026.102936

PMID: 41577082

15. L-Glutamine-Induced Acute Kidney Injury: A Clinical Observation.

Nephron. 2026;150(1):47-51. Epub 2025 Sep 29.

Bhoelan S, Kürül S, Krol CG, van Midden D, Bakker R.

INTRODUCTION: L-Glutamine is increasingly used as a dietary supplement and its use is, as is the case with other amino acids, considered safe. L-Glutamine is the most

abundant amino acid in the human body and is involved in many metabolic reactions. Within the kidney L-glutamine has an important role in the generation of ammonia and bicarbonate. CASE PRESENTATION: We report a case of acute kidney injury (AKI) as a result of tubular damage in a patient who used 18 grams of L-glutamine on a daily basis. Possible mechanisms are proposed of which increased single nephron ammonia production and toxicity seems most likely cause of AKI. CONCLUSION: We advise cautious use of L-glutamine supplements in elderly patient with an already compromised kidney function.

DOI: 10.1159/000548247

PMID: 41021436

16. Protein Isolate Supplements and Urinary Stone Risk.

Urology. 2026 Jan;207:1-7. Epub 2025 Jun 29.

Wong DG, McNeely B, Vetter J, Klim A, Black L, Knutson A, Du K, Penniston K, Asplin J, Desai A.

OBJECTIVE: To characterize the lithogenicity associated with consuming specific protein sources, we report a comparative crossover study evaluating the effects of whey, pea, soy, and rice protein isolates on urinary stone risk. METHODS: Volunteers without a history of stone disease were recruited for participation. Participants received a 5-day frozen meal plan which included three 20 g protein shakes per day. Two 24-hour urine collections were completed on the last 2 days of each phase. The exact same diet was repeated for subsequent phases, exchanging only the protein isolate in the shake. RESULTS: Nine participants-8 males, 1 female-were enrolled with mean age of 24.8 ± 1.6 years and body mass index of 22.3 ± 2.2 kg/m2. Urine calcium was significantly lower and pH was higher with pea and soy protein compared to whey protein consumption. Citrate excretion did not differ between any phases compared to whey protein. Urine oxalate was significantly higher in pea phase compared to whey. Supersaturation of calcium oxalate did not differ between any phases compared to whey. CONCLUSION: We examined the short-term urinary effect of 4 protein isolates commonly used to supplement high-protein diets and found key urinary metabolite differences. These differences were due to varying amino acid profiles but may also be related to differing constituents in each powder, such as cations and unmeasured anions.

DOI: 10.1016/j.urology.2025.06.060

PMID: 40592395

17. The Efficacy and Safety of Nutritional Supplements for Cancer Supportive Care: An Umbrella Review and Hierarchical Evidence Synthesis.

Integr Cancer Ther. 2026 Jan-Dec;25:15347354251405267. Epub 2026 Jan 3.

Benna-Doyle S, Grant S, Maunder A, Liu J, Ibrahim M, Cave A, Pandey C, Tang M, Koh ES, Delaney G, Bhuyan DJ, Choi V, Kwon K, Gonzalez M, Graham S, Malalasekera A, Ee C.

Cancer survivors experience a range of side effects during and after treatment. There is a need for a rigorous synthesis of the most recent and best available evidence on the role of nutritional supplements for supportive care in cancer, to inform shared decision-making. We searched 5 databases for umbrella reviews, meta-analyses and systematic reviews on nutritional supplements for supportive cancer care, excluding studies on pain, anxiety and depression, which are covered in recent guidelines. We found 52 reviews that reported on 250 RCTs on 18 supplements for 16 indications. Almost all reviews were of low/critically low quality (assessed using A MeaSurement Tool to Assess systematic Reviews version 2). There was moderate-certainty evidence for benefit from the following supplements: amino acids and oral proteolytic enzymes for severity of radiation-induced dermatitis, N-acetyl cysteine for prevention of chemotherapy-induced peripheral neuropathy (CIPN) in individuals with gastrointestinal cancers. There was low to very low certainty evidence that glutamine, zinc, probiotics and melatonin may be effective for oral mucositis; Vitamin E, omega-3 fatty acids, glutamine and other amino acids may be effective for preventing CIPN. Serious adverse events were reported for high-dose Vitamin A, and dose-related adverse events were reported with zinc and Vitamin E. However, the majority of nutritional supplements were associated with only minor adverse events. Due to the low to very low certainty of the majority of evidence, firm clinical recommendations cannot be made. Further research to conclusively evaluate benefit and harm, including potential impact on efficacy of standard treatments, should be conducted.

DOI: 10.1177/15347354251405267

PMID: 41482855

Vascular, Bleeding, Allergic, and Developmental Safety Signals

18. Toxic effects of herbal supplements on endothelial and vascular system among rural Thai patients: A multicenter cohort study.

J Stroke Cerebrovasc Dis. 2026 May;35(5):108610. Epub 2026 Mar 14.

Dorlohtahe S, Kedthongma W, Phakdeekul W.

BACKGROUND: The use of herbal supplements among elderly Thais has increased from 65.7% to 73.9% (2022-2024). Evidence regarding cardiovascular safety remains limited, particularly regarding interactions with potentially inappropriate medications (PIMs) in patients with multimorbidity and polypharmacy. This study investigated the association and incidences between herbal supplement use and vascular as well as endovascular diseases (VEDs) among elderly Thai patients. METHODS: A retrospective, propensity score-matched cohort study was carried out. Data were collected from electronic medical records at 12 community hospitals in Sakon Nakhon Province, Thailand (January 2022-December 2024). The cohort included 38,240 adults aged ≥60 years without baseline VEDs. Using 1:1 propensity score matching, we created matched cohorts of 11,587 pairs balanced for age, sex, comorbidities, and polypharmacy. We compared herbal supplement users (documented through prescription records, patient self-reports, and pharmacy data) to non-users. The primary outcome was incident VEDs, a composite of cerebrovascular disease, peripheral vascular disease, and acute coronary syndrome, identified via ICD-10 codes. We used Cox proportional hazards regression adjusted for baseline characteristics. RESULTS: During the follow-up with 38,240 person-years, 2,792 incident VEDs occurred. Herbal supplement use was significantly associated with increased VED risk (aHR 1.52, 95% CI 1.39-1.67). A clear dose-response relationship emerged: <6 months (aHR 1.24); 6-12 months (aHR 1.68); 1-2 years (aHR 2.12); and >2 years (aHR 2.24; P-trend <0.001). Risks were higher among patients aged ≥75 years (aHR 1.68), with polypharmacy (aHR 1.73), multimorbidity (aHR 1.71), and diabetes (aHR 1.64). Synergistic interaction occurred between herbal supplements and potentially inappropriate medications (PIMs) (combined aHR 2.94; RERI 0.53, P < 0.001). CONCLUSIONS: Herbal supplement use was associated with substantially increased cardiovascular risk among elderly Thais through dose-dependent and synergistic mechanisms. These findings necessitate the urgent integration of herbal use assessment into routine geriatric care as well as the development of evidence-based safety guidelines.

DOI: 10.1016/j.jstrokecerebrovasdis.2026.108610

PMID: 41839245

19. Potential supplement-drug interactions and bleeding in patients with cancer: A UK Biobank study.

J Integr Med. 2026 Jan;24(1):90-97. Epub 2025 Oct 13.

Lam CS, Hua R, Au-Doung LW, Wu YK, Koon HK, Zhou KR, Loong HH, Chung VC, Lee R, Chan A, Cheung YT.

OBJECTIVE: Interactions between supplements and drugs may potentially increase the risk of bleeding in patients with cancer. However, studies on drug interactions and bleeding risk in cancer patients in a real-world setting are limited. This study investigates supplement-drug interactions associated with bleeding risk using data from the UK Biobank database (https://www.ukbiobank.ac.uk). METHODS: Participants included in this study had a cancer diagnosis and had completed supplement-use assessment after their diagnosis. Potential supplement-drug interactions associated with bleeding were identified using four tertiary databases. Logistic regression was used to investigate the association between potential clinical predictors and the use of supplement-drug pairs with interactions that potentially increase the bleeding risk. Exploratory analysis utilized log-binomial regression to examine the association between potentially interacting supplement-drug pairs and the incidence rates of five major bleeding outcomes (gastrointestinal hemorrhage, intracranial hemorrhage, hematuria, hemorrhage from respiratory passages, and postmenopausal bleeding). All analyses were adjusted for relevant factors. RESULTS: This study analyzed data from 30,239 participants (mean age = 60.0 years; 61.9% female). Over half (n = 17,698, 58.5%) of the participants reported using supplements after their cancer diagnosis. Among those using both supplements and drugs, one-third (n = 4970/14,308, 34.7%) were taking potentially interacting pairs that increase bleeding risk. Younger age at cancer diagnosis, longer time since diagnosis, specific cancer types, and comorbidities were associated with the use of these interacting pairs. Exploratory analyses found no significant associations between the use of potentially interacting supplement-drug pairs and the incidence of major bleeding events (all $P > 0.05$), although the risk of minor bleeding cannot be ruled out. CONCLUSION: Approximately one-third of cancer patients who used supplements and drugs had a potential risk for bleeding due to supplement-drug interactions, suggesting the need to raise awareness about bleeding risks among patients and healthcare providers. Further pharmacovigilance monitoring and prospective cohort studies are needed to better understand the clinical impact of specific interactions. Please cite this article as: Lam CS, Hua R, Au-Doung LW, Wu YK, Koon HK, Zhou KR, Loong HHF, Chung VCH, Lee R, Chan A, Cheung AT. Potential supplement-drug interactions and bleeding in patients with cancer: A UK Biobank study. J Integr Med. 2026; 24(1):90-97.

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20. Nutritional Supplements and Cosmetic Formulations: A Review of Emerging Allergens.

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Ezzat RZ, Stirrat T, Nichols E, Ehrlich A.

Nutritional supplements and topical formulations are increasingly implicated in allergic contact dermatitis (ACD), yet their allergenic potential remains underrecognized due to inconsistent regulatory oversight, limited provider awareness, and the misconception that "natural" products are inherently safe. To identify emerging allergens in supplements and cosmetics, characterize associated ACD reactions, and highlight diagnostic and regulatory challenges. A systematic review of PubMed, Embase, MEDLINE, Web of Science, and CENTRAL databases was conducted to evaluate reports of ACD linked to dietary supplements and topical formulations. Key sensitizers include vitamin derivatives (tocopherol, phytonadione, ascorbic acid), herbal extracts (Ginkgo biloba, turmeric, St. John's Wort), and antioxidants (α-lipoic acid, resveratrol). Documented cases range from localized dermatitis to systemic reactions. Patch testing confirms sensitization, with cross-reactivity and oxidation-related allergenicity frequently observed. Patch testing may not always reveal the sensitizing agent, especially if the allergen is a contaminant, an unlisted ingredient, or undergoes chemical transformation during oxidation or formulation. The rising prevalence of supplement- and cosmetic-induced ACD underscores the need for standardized patch testing, improved ingredient labeling, and enhanced regulatory oversight, including mandated reporting of adverse reactions, premarket safety testing for allergens, and standardized labeling of known sensitizers and botanical components.

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21. The role of chrysanthemum phytochemicals in neural tube development: a narrative review of underlying mechanisms.

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Gao J, Dang Y, Chang Y, Liu Y, Sun Y, Zhao B, Sun P, Wang X, Wang J, Zhang L.

BACKGROUND: Neural tube defects (NTDs) have long been attributed to genetic and hereditary factors, but emerging evidence highlights the significant role of pharmacological and environmental agents. The global integration of traditional medicine systems, including Traditional Chinese Medicine, has introduced diverse bioactive compounds with potential to influence neurodevelopmental processes. PURPOSE: This narrative review aims to comprehensively summarize and critically evaluate the current evidence on the bioactivity of chrysanthemum (Chrysanthemum morifolium and related species) extracts and their constituents in the context of neural tube development, with a focus on elucidating underlying molecular mechanisms to inform potential therapeutic

applications and toxicological risks. STUDY DESIGN: We performed a narrative review of chrysanthemum compounds in neural development, focusing on neural tube formation. PubMed, Web of Science, and ScienceDirect were searched from January 1985 to March 2026 using terms related to chrysanthemum (e.g., Chrysanthemum, extract, phytochemicals), neurodevelopmental outcomes (neural tube defects, neurulation), and mechanisms (inflammation, oxidative stress, apoptosis). Reference lists were manually screened. No formal bias assessment or quantitative synthesis was performed; instead, findings were qualitatively synthesized to present the dual role of chrysanthemum. RESULTS: Chrysanthemum exhibits context-dependent duality in neural tube development. Beneficial effects are mediated by chlorogenic acid, Eri-7-Glc, and flavonoids via NF-κB, Nrf2/HO-1, and Wnt/β-catenin pathways, reducing oxidative stress and supporting neurulation. Conversely, natural pyrethrins induce oxidative stress and DNA damage; high-dose flavonoids act as pro-oxidants and endocrine disruptors, and readily cross the placenta, raising fetal concerns. The convergence on caspase-8 suggests a double-edged sword effect. However, direct evidence in mammalian embryos, pregnancy pharmacokinetics, and dose-response data are lacking. CONCLUSION: Chrysanthemum shows context-dependent dual effects on neurodevelopment, underscoring the need for rigorous mechanistic and toxicological studies to guide its safe use, particularly in pregnancy.

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22. Anticoagulant, antioxidant and cytotoxic potential of cinnamic acid and derivatives.

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Oliveira PEA, Silva DP, Ferreira SS, Marchi-Salvador DP, Oliveira Filho AA.

INTRODUCTION: Since antiquity, natural products have been widely used to relieve symptoms and prevent numerous diseases. Early treatments for vascular disorders, including thrombosis, relied heavily on plant-derived substances, which later served as prototypes for the development of platelet aggregation inhibitors and coagulation-modulating agents. Among these bioactive constituents, phenolic compounds-abundantly found in various botanical sources-have gained prominence due to their well-established antioxidant properties and reported anticoagulant effects. Recent studies highlight that the structural diversity of phenolic acids, particularly cinnamic acid (CA) and its derivatives, offers a valuable chemical scaffold for developing new therapeutic agents targeting thrombogenesis and oxidative imbalance. OBJECTIVE: This study aimed to evaluate, in vitro, the pharmacological (anticoagulant and antioxidant) and toxicological (oxidant and cytotoxic) activities of cinnamic acid (CA) and five synthetic derivatives-4HDCN, 4MTCN, 3,4DHCN, 3,4DMCN, and 3H4MCN. METHODS: Anticoagulant activity was assessed using a semi-automated coagulometer by measuring clotting time after exposure of human plasma to each molecule. Antioxidant,

oxidant, and cytotoxic (hemolytic) activities were determined using human erythrocytes from blood groups A, B, and O. Oxidative and antioxidant responses were quantified by spectrophotometry following exposure to phenylhydrazine as a pro-oxidant inducer. Hemolysis was evaluated at concentrations ranging from 0 to 400 mg/dL. RESULTS: In the anticoagulant assays, the derivative 3,4DHCN exhibited the strongest activity, prolonging clotting time to 176.6 s, slightly surpassing 3,4MTCN (165.6 s). All molecules demonstrated low or negligible oxidizing activity (<7.1%). Regarding antioxidant potential, 4MTCN showed the most effective protection against phenylhydrazine-induced oxidation, reducing oxidative damage to 8.7%. None of the tested compounds induced moderate or high hemolysis at concentrations up to 200 mg/dL. However, at 400 mg/dL, CA and 4HDCN produced high hemolytic rates across erythrocyte types. In type A cells, hemolysis reached 89.4% (CA) and 76.0% (4HDCN); in type B, 64.3% and 60.5%; and in type O, 90.1% and 70.7%, respectively. CONCLUSION: Dihydroxylated and dimethoxylated cinnamic acid derivatives demonstrated notable anticoagulant activity, minimal oxidative effects, low antioxidant capacity, and an absence of cytotoxicity in human erythrocytes at therapeutically relevant concentrations. These findings indicate that such molecules represent promising candidates for the development of new anticoagulant agents with favorable safety profiles.

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