

# AACT Herbal Dietary Supplement Section Abstracts May 2021

**1. ACG Clinical Guideline: Diagnosis and Management of Idiosyncratic Drug-Induced Liver Injury.** Chalasani NP, Maddur H, Russo MW, Wong RJ, Reddy KR; Practice Parameters Committee of the American College of Gastroenterology.

Am J Gastroenterol. 2021 May 1;116(5):878-898. doi: 10.14309/ajg.0000000000001259.

Idiosyncratic drug-induced liver injury (DILI) is common in gastroenterology and hepatology practices, and it can have multiple presentations, ranging from asymptomatic elevations in liver biochemistries to hepatocellular or cholestatic jaundice, liver failure, or chronic hepatitis. Antimicrobials, herbal and dietary supplements, and anticancer therapeutics (e.g., tyrosine kinase inhibitors or immune-checkpoint inhibitors) are the most common classes of agents to cause DILI in the Western world. DILI is a diagnosis of exclusion, and thus, careful assessment for other etiologies of liver disease should be undertaken before establishing a diagnosis of DILI. Model for end-stage liver disease score and comorbidity burden are important determinants of mortality in patients presenting with suspected DILI. DILI carries a mortality rate up to 10% when hepatocellular jaundice is present. Patients with DILI who develop progressive jaundice with or without coagulopathy should be referred to a tertiary care center for specialized care, including consideration for potential liver transplantation. The role of systemic corticosteroids is controversial, but they may be administered when a liver injury event cannot be distinguished between autoimmune hepatitis or DILI or when a DILI event presents with prominent autoimmune hepatitis features.

DOI: 10.14309/ajg.0000000000001259  
PMID: 33929376

**2. Analysis of pharmaceutical products and dietary supplements seized from the black market among bodybuilders.** Fabresse N, Gheddar L, Kintz P, Knapp A, Larabi IA, Alvarez JC.

Forensic Sci Int. 2021 May;322:110771. doi: 10.1016/j.forsciint.2021.110771. Epub 2021 Mar 30.

Substandard/counterfeit drugs are a growing global problem. According to the World Health Organisation, counterfeit medicines are medicines that are mislabelled deliberately and fraudulently regarding their identity and/or source. In high income countries, drugs seized are mainly represented by performance and image enhancing drugs (PIEDs). The aim of this study was to present the qualitative and quantitative results of toxicological analyses of pharmaceutical and dietary supplements seized from the black market among bodybuilders in France. All dietary supplements and pharmaceuticals seized from the black market and addressed to the laboratory for a qualitative and quantitative analysis between January 2016 and December 2019 were included in the study. A screening was carried out by gas chromatography-mass spectrometry and liquid chromatography-high resolution mass spectrometry. Identified compounds were quantified by liquid chromatography-tandem mass spectrometry. One hundred and ten products were seized and submitted to the laboratory for identification of active compounds and quantification: 75 pharmaceuticals and 35 dietary supplements. This included 39 oily and 3 aqueous solutions for intramuscular injection, 34 tablets, 13 capsules, 14 powders, 4 liquids and 3 lyophilizates. Among the pharmaceuticals, 25/75 (33%) were substandard (dosage not on the acceptable range defined for original products), 24/75 (32%) were counterfeit (qualitative formulation does not match the label) and 14/75 (19%) were original (qualitative formulation and levels of active ingredients fully matches the declared formulation). The analysis of the 12 remaining products revealed a correct qualitative content for 11/75 (15%), but quantitation could not be carried out because of the lack of reference standards at the time of the analysis. Fifty-four pharmaceuticals contained anabolic-androgenic steroids (AAS). Four out of 54 (7.4%) AAS were found as original, 8/54 (15%) could not be quantified (one with wrong active ingredient), corresponding to 43/54 (80%) AAS being non-original. In contrast, only 1/35 dietary supplement (3%) was adulterated, with a doping substance (1,3-dimethylbutylamine, DMBA). This work allows to show that France is not spared by the trafficking of PIEDs. The use of counterfeit drugs in mainstream population is an underestimated public health issue.

DOI: 10.1016/j.forsciint.2021.110771  
PMID: 33838562

**3. Flavonoids and hERG channels: Friends or foes?** Saponara S, Fusi F, Iovinelli D, Ahmed A, Trezza A, Spiga O, Sgaragli G, Valoti M.

Eur J Pharmacol. 2021 May 15;899:174030. doi: 10.1016/j.ejphar.2021.174030. Epub 2021 Mar 13.

The cardiac action potential is regulated by several ion channels. Drugs capable to block these channels, in particular the human ether-à-go-go-related gene (hERG) channel, also known as KV11.1 channel, may lead to a potentially lethal ventricular tachyarrhythmia called "Torsades de Pointes". Thus, evaluation of the hERG channel off-target activity of

novel chemical entities is nowadays required to safeguard patients as well as to avoid attrition in drug development. Flavonoids, a large class of natural compounds abundantly present in food, beverages, herbal medicines, and dietary food supplements, generally escape this assessment, though consumed in consistent amounts. Continuously growing evidence indicates that these compounds may interact with the hERG channel and block it. The present review, by examining numerous studies, summarizes the state-of-the-art in this field, describing the most significant examples of direct and indirect inhibition of the hERG channel current operated by flavonoids. A description of the molecular interactions between a few of these natural molecules and the *Rattus norvegicus* channel protein, achieved by an *in silico* approach, is also presented.

DOI: 10.1016/j.ejphar.2021.174030  
PMID: 33727059

**4. Profile of herbal and dietary supplements induced liver injury in Latin America: A systematic review of published reports.** Santos G, Gasca J, Parana R, Nunes V, Schinnoni M, Medina-Caliz I, Cabello MR, Lucena MI, Andrade RJ.

Phytother Res. 2021 Jan;35(1):6-19. doi: 10.1002/ptr.6746. Epub 2020 Jun 11.

Hepatotoxicity related to HDS is a growing global health issue. We have undertaken a systematic review of published case reports and case series from LA from 1976 to 2020 to describe the clinical features of HDS related hepatotoxicity in this region. We search in PubMed, Web of Science, Scopus and specific LA databases according to PRISMA guidelines. Only HILI cases published in LA that met criteria for DILI definition were included. Duplicate records or reports that lacked relevant data that precluded establishing causality were excluded. Finally, 17 records (23 cases) were included in this review. *Centella asiatica*, *Carthamus tinctorius*, and Herbalife® were the most reported HDS culprit products, the main reason for HDS consumption was weight loss. The clinical characteristics of HDS hepatotoxicity in our study were compared to those of other studies in the USA, Europe and China showing a similar signature with predominance of young females, hepatocellular damage, a high rate of ALF and mortality, more frequent inadvertent re-challenge and chronic damage. This study underscores the challenge in causality assessment when multi-ingredients HDS are taken and the need for consistent publication practice when reporting hepatotoxicity cases due to HDS, to foster HDS liver safety particularly in LA.

DOI: 10.1002/ptr.6746  
PMID: 32525269 [Indexed for MEDLINE]

**5. Autism spectrum disorder: A systematic review about nutritional interventions.** Monteiro MA, Santos AAAD, Gomes LMM, Rito RVVF.

Rev Paul Pediatr. 2020 Mar 16;38:e2018262. doi: 10.1590/1984-0462/2020/38/2018262. eCollection 2020.

**OBJECTIVE:** To identify and analyze the scientific evidence of nutritional interventions performed in children and adolescents with Autism Spectrum Disorder. **DATA SOURCES:** A systematic review was conducted in the MEDLINE, Cochrane Library, Embase, LILACS, Google Scholar, PubMed, PsycINFO and Periódicos CAPES databases, using a search strategy to identify studies published between January 2003 and March 2018, in Portuguese, English and Spanish. Were included studies that described nutritional interventions in children and adolescents with autism spectrum disorders and assessed autistic behavior and/or gastrointestinal symptoms. We excluded other review articles and studies that did not include a control group in the research design. The studies were reviewed for descriptive information, and the quality of evidence was assessed through the GRADE system. **DATA SYNTHESIS:** 18 studies were included in the review, being 16 randomized clinical trials, 1 case-control study and 1 open-label trial. As a result, the implementation of a gluten-free and casein-free diet was the most used intervention among the studies. Of the total, 10 studies showed a positive association of intervention with the evaluated results, while 8 did not find of a significant association. **CONCLUSIONS:** Although some authors report progress in the symptoms associated with autism in individuals with Autistic Spectrum Disorder undergoing nutritional interventions, there is little scientific evidence to support the use of nutritional supplements or dietary therapies in children and adolescents with autism.

DOI: 10.1590/1984-0462/2020/38/2018262  
PMCID: PMC7077797  
PMID: 32187297 [Indexed for MEDLINE]

**6. Acute feeding suppression and toxicity of raspberry ketone [4-(4-hydroxyphenyl)-2-butanone] in mice.** Hao L, Kshatriya D, Li X, Badrinath A, Szmazinski Z, Goedken MJ, Polunas M, Bello NT.

Food Chem Toxicol. 2020 Sep;143:111512. doi: 10.1016/j.fct.2020.111512. Epub 2020 Jun 19.

Raspberry ketone (RK; [4-(4-hydroxyphenyl)-2-butanone]) is used by the food and cosmetic industry as a flavoring agent. RK is also marketed as a dietary supplement for weight maintenance and appetite control. The purpose of the study was to characterize the acute feeding suppression with RK (64-640 mg/kg) by oral gavage in male and female

C57BL/6J mice. Cumulative 24 h food intake was reduced at 200 mg/kg (24% feeding suppression) in males and reliably reduced at 640 mg/kg (49-77% feeding suppression). Feeding suppression was not associated with pica behavior over the range of doses or conditioned taste aversion. In a separate experiment, a single oral gavage of RK (640 mg/kg) resulted in approximate 43% mortality rate (6 out of 14 male mice) within 2 days. Atrophy of white adipose tissue, splenic abnormalities, and thymus involution were noted after 2-4 days after oral gavage RK. Total white blood cell count, lymphocytes, monocytes, eosinophils were significantly lower, while mean red blood cells, hemoglobin, and hematocrit were significantly higher with RK treatment. Our findings indicated a dose-dependent feeding suppression with acute RK, but doses that reliably suppress food intake are associated with pathological changes.

DOI: 10.1016/j.fct.2020.111512

PMCID: PMC7483346

PMID: 32565406 [Indexed for MEDLINE]

**7. Chest Pain From Supplement Use in an Active Duty Soldier: A Case Report.** Bridwell RE, Yoo MJ, Grove JJ, Ng PC.

Mil Med. 2020 Sep 18;185(9-10):e1857-e1859. doi: 10.1093/milmed/usaa043.

Comment in Mil Med. 2020 Sep 18;185(9-10):e1381-e1382.

In the active duty population, over-the-counter performance enhancing supplements are readily available and consumed, primarily in an unsupervised manner. While some of the active ingredients, such as caffeine and creatine, have been well studied, other sympathomimetic and vasoactive components in these products have minimal data regarding their safety profile. Further potentiating the associated risks of consumption, the quantities and purities of the reported ingredients are often unverified and can vary from serving to serving. We present a case of the deleterious side effect profiles of these lesser studied components in overconsumption in an active duty soldier. Although improvements are being made regarding product safety, the paucity of ingredient regulation and quality assurance can result in warfighter morbidity and mortality, especially when these supplements are abused or combined with other products.

DOI: 10.1093/milmed/usaa043

PMID: 32175585 [Indexed for MEDLINE]

**8. Diet-induced oxalate nephropathy from excessive nut and seed consumption.** Garland V, Herlitz L, Regunathan-Shenk R.

BMJ Case Rep. 2020 Nov 30;13(11):e237212. doi: 10.1136/bcr-2020-237212.

Oxalate is a metabolite consumed in nuts, beans and leaves, and excreted in urine. Oxalosis can cause nephropathy. We describe a rare case of a high-oxalate diet intended for irritable bowel syndrome (IBS) treatment causing oxalate nephropathy. A 59-year-old woman with a history of controlled hypertension presented with creatinine 1.8 mg/dL, increased from baseline 1.3 mg/dL. She denied recent illness, urinary stones, medication adjustments, herbal supplements and non-steroidal anti-inflammatory drugs use. Diet included six tablespoons of chia seeds and five handfuls of almonds daily to manage IBS symptoms. Her electrolytes, urinalysis and renal ultrasound were unremarkable. Her 24-hour urine output revealed increased oxalate and low citrate. Renal biopsy showed glomerulosclerosis, fibrosis and calcium oxalate deposition. She switched to a low-oxalate diet, with improvement in laboratory markers. An earlier dietary history could have raised concern for oxalosis prior to renal biopsy. Providers should be trained to identify at-risk patients and provide appropriate dietary counselling.

DOI: 10.1136/bcr-2020-237212

PMCID: PMC7705561

PMID: 33257378 [Indexed for MEDLINE]

**9. The Case | Acute renal failure and a "rejuvenating powder".** Borceux P, Aydin S, Demoulin N, Devresse A.

Kidney Int. 2020 Jan;97(1):219-220. doi: 10.1016/j.kint.2019.06.008.

*(oxalate nephropathy)*

DOI: 10.1016/j.kint.2019.06.008

PMID: 31901348 [Indexed for MEDLINE]

**10. Cranberry supplementation as a cause of major intraoperative bleeding during vascular surgery due to aspirin-like platelet inhibition.** Moroi MK, Loloi J, Songdej N.

Blood Coagul Fibrinolysis. 2020 Sep;31(6):402-404. doi: 10.1097/MBC.0000000000000912.

We report severe excessive bleeding at initiation of vascular surgery in a 74-year-old woman with thoracoabdominal aortic aneurysm undergoing thoracic endovascular aortic repair. After extensive workup, bleeding cause was determined to be an aspirin-like effect from supplemental cranberry intake. After asking the patient to stop cranberry consumption, the aspirin-like effect ceased, and the patient underwent successful thoracic endovascular aortic repair. Cranberry consumption may create an aspirin-like effect that increases risk of bleeding. Providers should be aware of potential adverse effects of cranberries on platelet function and consider inquiring about supplement use in the perioperative period.

DOI: 10.1097/MBC.0000000000000912  
PMID: 32398461 [Indexed for MEDLINE]

**11. Pill-induced esophagitis caused by ingesting excessive caffeine tablets.** Miyata J, Ito Y, Ito S.

Clin J Gastroenterol. 2020 Jun;13(3):334-339. doi: 10.1007/s12328-019-01055-w. Epub 2019 Oct 23.

A 19-year-old woman with suicidal thoughts consumed 24 anhydrous caffeine tablets and was admitted to our hospital. After being discharged from the hospital, her oral intake remained impaired because of retrosternal pain and she was readmitted. An upper gastrointestinal endoscopy revealed diffuse ulcers throughout the mid-to-lower esophagus; the patient was diagnosed with caffeine-induced esophagitis. She recovered soon after conservative treatment. A follow-up endoscopy performed 1 month after the patient was discharged showed that the ulcers had healed. This case highlights the risk of esophageal injuries after ingesting excessive caffeine tablets, which were sold as dietary supplement without a prescription. Our experience indicates that endoscopic surveillance is advisable to prevent severe complications if a patient presents with esophageal symptoms suggestive of chemical esophagitis.

DOI: 10.1007/s12328-019-01055-w  
PMCID: PMC7239815  
PMID: 31646430 [Indexed for MEDLINE]

**12. Ischemic colitis induced by indigo naturalis in a patient with ulcerative colitis: a case report.** Cho B, Yoon SM, Son SM, Kim HW, Kim KB, Youn SJ.

BMC Gastroenterol. 2020 May 15;20(1):154. doi: 10.1186/s12876-020-01301-3.

**BACKGROUND:** Indigo naturalis is a Chinese herbal medicine that has currently been used to treat various inflammatory diseases, including ulcerative colitis. Recently, there are several reports concerning severe adverse events associated with indigo naturalis. **CASE PRESENTATION:** We described a case of a 44-year-old female with ulcerative colitis who presented with lower abdominal pain and hematochezia. She stopped taking her medicine for ulcerative colitis and started oral indigo naturalis 3 months before admission. Computed tomography showed segmental edematous wall thickening of the descending and sigmoid colon. Colonoscopy findings revealed erythema, edema, and submucosal hemorrhage, the surface of which presented a dark blue pigmentation. The histologic finding was consistent with ischemic colitis. We therefore considered an ischemic colitis induced by indigo naturalis, and the patient improved after supportive care and withdrawal of indigo naturalis. **CONCLUSION:** Indigo naturalis has currently been used in the patients with ulcerative colitis as an alternative therapy. However, physicians should be aware of possible severe adverse events such as ischemic colitis.

DOI: 10.1186/s12876-020-01301-3  
PMCID: PMC7229623  
PMID: 32414334 [Indexed for MEDLINE]

**13. Pemphigus foliaceus following use of herbal supplement containing Aphanizomenon flos-aquae.** Kim J, Condie D, Vasquez R.

Int J Dermatol. 2020 May;59(5):e171-e173. doi: 10.1111/ijd.14740. Epub 2019 Nov 25.

DOI: 10.1111/ijd.14740  
PMID: 31769005 [Indexed for MEDLINE]

**14. Pathophysiology, prevention, and treatment of beriberi after gastric surgery.** Wilson RB.

Nutr Rev. 2020 Dec 1;78(12):1015-1029. doi: 10.1093/nutrit/nuaa004.

Beriberi is a nutritional complication of gastric surgery, caused by deficiency of vitamin B1, or thiamine. Thiamine deficiency leads to impaired glucose metabolism, decreased delivery of oxygen by red blood cells, cardiac dysfunction, failure of neurotransmission, and neuronal death. This review describes the history and pathophysiology of beriberi as well as the relationship between beriberi and nutritional deficiencies after gastric surgery. A literature review of the history and pathophysiology of beriberi and the risk factors for thiamine deficiency, particularly after gastric resection

or bariatric surgery, was performed. Recommendations for nutritional follow-up post gastric surgery are based on current national guidelines. Patients may have subclinical thiamine deficiency after upper gastrointestinal surgery, and thus beriberi may be precipitated by acute illness such as sepsis or poor dietary intake. This may occur very soon or many years after gastrectomy or bariatric surgery, even in apparently well-nourished patients. Prompt recognition and administration of supplemental thiamine can decrease morbidity and mortality in patients with beriberi. Dietary education post surgery and long-term follow-up to determine nutritional status, including vitamin and mineral assessment, is recommended for patients who undergo gastric surgery.

DOI: 10.1093/nutrit/nuaa004

PMCID: PMC7666909

PMID: 32388553 [Indexed for MEDLINE]

**15. Thiamine-responsive acute severe pulmonary hypertension in exclusively breastfeeding infants: a prospective observational study.** Sastry UMK, M J, Kumar RK, Ghosh S, A P B, Subramanian A, Managuli A, Gangadhara M, Manjunath CN.

Arch Dis Child. 2021 Mar;106(3):241-246. doi: 10.1136/archdischild-2019-318777. Epub 2020 Sep 3.

**OBJECTIVES:** Severe pulmonary hypertension (PH) causing right heart failure can occur due to thiamine deficiency in exclusively breastfeeding infants. This study describes the clinical profile and management of thiamine-responsive acute pulmonary hypertension. **METHODS:** A prospective observational study of infants presenting with severe PH without any other significant heart or lung disease. History of symptoms, clinical examination, echocardiography and basic investigations were performed. Dietary patterns of mothers were recorded. Thiamine was administered and serial echocardiography was performed. **RESULTS:** A total of 250 infants had severe PH and 231 infants responded to thiamine. The mean age was 3.2±1.2 months. Fast breathing, poor feeding, vomiting and aphonia were the main symptoms. Tachypnoea, tachycardia and hepatomegaly were found on examination. Echocardiogram revealed grossly dilated right heart with severe PH. Intravenous thiamine was administered to all the babies based on clinical suspicion. Clinical improvement with complete resolution of PH was noticed within 24-48 hours. Babies were followed up to a maximum of 60 months with no recurrence of PH. All the mothers consumed polished rice and followed postpartum food restriction. **CONCLUSION:** Thiamine deficiency is still prevalent in selected parts of India. It can cause life-threatening PH in exclusively breastfeeding infants of mothers who are on a restricted diet predominantly consisting of polished rice. It can contribute to infant mortality. Thiamine administration based on clinical suspicion leads to remarkable recovery. High degree of awareness and thiamine supplementation in relevant geographical areas is required to tackle this fatal disease.

DOI: 10.1136/archdischild-2019-318777

PMID: 32883659 [Indexed for MEDLINE]

**16. Adverse events associated with pediatric complementary and alternative medicine in the Netherlands: a national surveillance study.** Vos B, Rake JP, Vlieger A.

Eur J Pediatr. 2021 Mar 1. doi: 10.1007/s00431-020-03899-8. Online ahead of print.

Pediatric use of complementary and alternative medicine (CAM) in the Netherlands is highly prevalent. The risks of pediatric CAM use are, however, largely unknown. Therefore, a 3-year survey was carried out at the Dutch Pediatric Surveillance Unit. Pediatricians were asked to register cases of adverse events associated with pediatric CAM usage. In 3 years, 32 unique adverse events were registered. Twenty-two of these adverse events were indirect and not related to the specific CAM therapy but due to delaying, changing, or stopping of regular treatment, a deficient or very restrictive diet or an incorrect diagnosis by a CAM therapist. These events were associated with many different CAM therapies. Nine events were deemed direct adverse events like bodily harm or toxicity and one-third of them occurred in infants. Only supplements, manual therapies, and (Chinese) herbs were involved in these nine events. In one case, there was a risk of a serious adverse event but harm had not yet occurred. **Conclusion:** Relatively few cases of adverse events associated with pediatric CAM usage were found, mostly due to delaying or stopping conventional treatment. Nevertheless, parents, pediatricians and CAM providers should be vigilant for both direct and indirect adverse events in children using CAM, especially in infants. **What's Known:** • The use of complementary and alternative medicine (CAM) in children is common. • Previous surveillance studies in other countries showed severe adverse events may occur after pediatric CAM usage. **What is New:** • In the Netherlands CAM-related adverse events are rare but can occur, with variable etiology and severity (from mild to potentially life-threatening) • Most CAM-related adverse events are not directly the result of CAM toxicities but rather are associated with withdrawal from appropriate therapies or with providers unable to recognize health-relevant states and delaying important diagnoses.

DOI: 10.1007/s00431-020-03899-8

PMID: 33649910

**17. Potential Cytochrome P450-mediated pharmacokinetic interactions between herbs, food, and dietary supplements and cancer treatments.** Gougis P, Hilmi M, Geraud A, Mir O, Funck-Brentano C.

Crit Rev Oncol Hematol. 2021 Apr 27:103342. doi: 10.1016/j.critrevonc.2021.103342. Online ahead of print.

Herbs, food and dietary supplements (HFDS), can interact significantly with anticancer drug treatments via cytochrome p450 isoforms (CYP) CYP3A4, CYP2D6, CYP1A2, and CYP2C8. The objective of this review was to assess the influence of HFDS compounds on these cytochromes. Interactions with CYP activities were searched for 189 herbs and food products, 72 dietary supplements in Web of Knowledge® databases. Analyses were made from 140 of 3,125 clinical trials and 236 of 3,374 in vitro, animal model studies or case reports. 18 trials were found to report direct interactions between 9 HFDS with 8 anticancer drugs. 21 HFDS were found to interact with CYP3A4, a major metabolic pathway for many anticancer drugs. All 261 HFDS were classified for their interaction with the main cytochromes P450 involved in the metabolism of anticancer drugs. We provided an easy-to-use colour-coded table to easily match potential interactions between 261 HFDS and 117 anticancer drugs.

DOI: 10.1016/j.critrevonc.2021.103342  
PMID: 33930533

**18. Dietary Supplement Use in US Army Personnel: A Mixed-Methods, Survey and Focus-Group Study Examining Decision Making and Factors Associated With Use.** Bukhari AS, DiChiara AJ, Merrill EP, Wright AO, Cole RE, Hatch-McChesney A, McGraw SM, Caldwell JA, Montain SJ, Thompson LA, Lieberman HR.

J Acad Nutr Diet. 2021 Feb 27:S2212-2672(21)00058-7. doi: 10.1016/j.jand.2021.01.011. Online ahead of print.

**BACKGROUND:** Dietary supplement (DS) use by Army personnel is high and is a safety and readiness issue. **OBJECTIVE:** Our aim was to examine factors motivating use of DSs among US Army personnel and preferred safety education strategies. **DESIGN:** This mixed-method study used a validated DS questionnaire and subsequent focus groups that were formed based on questionnaire-identified demographic characteristics. An embedded qualitative dominant design was used. **PARTICIPANTS/SETTING:** Data were collected from April to July 2015 from active duty soldiers at 3 military installations in the United States. **MAIN OUTCOME MEASURES:** A self-report questionnaire (n = 289) provided data on demographic characteristics, health, exercise, detailed use, and attitudes regarding DS safety and efficacy. Fourteen focus-group sessions (n = 129) examined factors motivating DS use, education strategies, and identified themes and DS-related behaviors. **STATISTICAL ANALYSIS PERFORMED:** Descriptive statistics and  $\chi^2$  analyses were conducted. **RESULTS:** Of the soldiers who completed questionnaires, 83% were male, 60% were enlisted, and 40% were officers; mean age  $\pm$  standard deviation was  $27.6 \pm 0.36$  years and 75% used at least 1 type of DS per week: 52% used protein/amino acids, 47% used multivitamins/minerals, and 35% used a combination of products. Focus groups indicated reasons for use included physical appearance, fitness, peer endorsement, ease of access, limited availability of healthy food, occupational demands, and health. Participants requested education from an expert on safe use that was not focused on dangerous products. **CONCLUSIONS:** Soldiers are high DS users, especially products marked for purported performance enhancement. Motivating factors for DS use are fitness/appearance and occupational demands, but soldiers lack knowledge of DS regulatory requirements and safety/efficacy. Soldiers wished to receive education on DSs from trusted health care professionals, such as registered dietitian nutritionists, that was not focused on dangerous products. Study findings suggest guidance and education should occur before periods of high DS use, such as deployment.

DOI: 10.1016/j.jand.2021.01.011  
PMID: 33653678

**19. High Prevalence of Supplement Intake with a Concomitant Low Information Quality among Swiss Fitness Center Users.** Mettler S, Bosshard JV, Häring D, Morgan G.

Nutrients. 2020 Aug 26;12(9):2595. doi: 10.3390/nu12092595.

**BACKGROUND:** The aim of this study was to screen the prevalence of supplement use in Swiss fitness center users and what information sources they consulted. **METHODS:** Customers of 10 fitness centers were screened with a quantitative questionnaire. **RESULTS:** Eighty two percent of the 417 fitness center users consumed at least one supplement per week. Supplement intake correlated with training frequency ( $r_s = 0.253$ ,  $p < 0.001$ ). The most prevalent products were protein supplements (used by 49% of the study population), magnesium (34%), and multi-micronutrient supplements (31%). The average number of supplement servings per week among consumers was 17.1 (SD: 16.1, median: 11.0) and the average number of different products used was 6.9 (SD: 4.4, median: 6.0). The most frequently used information sources were the coach/trainer (28%), the website of the supplement seller (26%), and training peers (24%). Thirty seven percent were informed or informed themselves about potential risks associated with the supplement used. The leading reasons for selecting the information source were the desire for scientific-based information followed by the education level of the informing person. **CONCLUSIONS:** A high prevalence of supplement intake among Swiss fitness center users was associated with a low level of information quality and a low prevalence of risk information. A discrepancy between a desire for high quality evidence-based information and a contrasting behavior was detected.

DOI: 10.3390/nu12092595

PMCID: PMC7550988  
PMID: 32859048 [Indexed for MEDLINE]

**20. Possible Adverse Effects of High-Dose Nicotinamide: Mechanisms and Safety Assessment.** Hwang ES, Song SB.

Biomolecules. 2020 Apr 29;10(5):687. doi: 10.3390/biom10050687.

Nicotinamide (NAM) at doses far above those recommended for vitamins is suggested to be effective against a wide spectrum of diseases and conditions, including neurological dysfunctions, depression and other psychological disorders, and inflammatory diseases. Recent increases in public awareness on possible pro-longevity effects of nicotinamide adenine dinucleotide (NAD<sup>+</sup>) precursors have caused further growth of NAM consumption not only for clinical treatments, but also as a dietary supplement, raising concerns on the safety of its long-term use. However, possible adverse effects and their mechanisms are poorly understood. High-level NAM administration can exert negative effects through multiple routes. For example, NAM by itself inhibits poly(ADP-ribose) polymerases (PARPs), which protect genome integrity. Elevation of the NAD<sup>+</sup> pool alters cellular energy metabolism. Meanwhile, high-level NAM alters cellular methyl metabolism and affects methylation of DNA and proteins, leading to changes in cellular transcriptome and proteome. Also, methyl metabolites of NAM, namely methyl nicotinamide, are predicted to play roles in certain diseases and conditions. In this review, a collective literature search was performed to provide a comprehensive list of possible adverse effects of NAM and to provide understanding of their underlying mechanisms and assessment of the raised safety concerns. Our review assures safety in current usage level of NAM, but also finds potential risks for epigenetic alterations associated with chronic use of NAM at high doses. It also suggests directions of the future studies to ensure safer application of NAM.

DOI: 10.3390/biom10050687  
PMCID: PMC7277745  
PMID: 32365524 [Indexed for MEDLINE]

**21. The bright and the dark sides of L-carnitine supplementation: a systematic review.** Sawicka AK, Renzi G, Olek RA.

J Int Soc Sports Nutr. 2020 Sep 21;17(1):49. doi: 10.1186/s12970-020-00377-2.

**BACKGROUND:** L-carnitine (LC) is used as a supplement by recreationally-active, competitive and highly trained athletes. This systematic review aims to evaluate the effect of prolonged LC supplementation on metabolism and metabolic modifications. **METHODS:** A literature search was conducted in the MEDLINE (via PubMed) and Web of Science databases from the inception up February 2020. Eligibility criteria included studies on healthy human subjects, treated for at least 12 weeks with LC administered orally, with no drugs or any other multi-ingredient supplements co-ingestion. **RESULTS:** The initial search retrieved 1024 articles, and a total of 11 studies were finally included after applying inclusion and exclusion criteria. All the selected studies were conducted with healthy human subjects, with supplemented dose ranging from 1 g to 4 g per day for either 12 or 24 weeks. LC supplementation, in combination with carbohydrates (CHO) effectively elevated total carnitine content in skeletal muscle. Twenty-four-weeks of LC supplementation did not affect muscle strength in healthy aged women, but significantly increased muscle mass, improved physical effort tolerance and cognitive function in centenarians. LC supplementation was also noted to induce an increase of fasting plasma trimethylamine-N-oxide (TMAO) levels, which was not associated with modification of determined inflammatory nor oxidative stress markers. **CONCLUSION:** Prolonged LC supplementation in specific conditions may affect physical performance. On the other hand, LC supplementation elevates fasting plasma TMAO, compound supposed to be pro-atherogenic. Therefore, additional studies focusing on long-term supplementation and its longitudinal effect on the cardiovascular system are needed.

DOI: 10.1186/s12970-020-00377-2  
PMCID: PMC7507632  
PMID: 32958033 [Indexed for MEDLINE]

**22. Levothyroxine Interactions with Food and Dietary Supplements—A Systematic Review.** Wiesner A, Gajewska D, Paško P.

Pharmaceuticals (Basel). 2021 Mar 2;14(3):206. doi: 10.3390/ph14030206.

Levothyroxine (l-thyroxine, l-T4) is a drug of choice for treating congenital and primary hypothyroidism. Although clinically significant interactions between l-T4 and food can alter the safety and efficacy of the treatment, they still seem to be generally underestimated by patients, physicians and pharmacists. This review aimed to investigate the effects of meals, beverages, and dietary supplements consumption on l-T4 pharmacokinetics and pharmacodynamics, to identify the most evident interactions, and to perform the recommendations for safe co-administering of l-T4 and food. A total of 121 studies were identified following a systematic literature search adhering to PRISMA guidelines. After full-text evaluation, 63 studies were included. The results proved that l-T4 ingestion in the morning and at bedtime are

equally effective, and also that the co-administration of l-T4 with food depends on the drug formulation. We found limited evidence for l-T4 interactions with coffee, soy products, fiber, calcium or iron supplements, and enteral nutrition but interestingly they all resulted in decreased l-T4 absorption. The altered l-T4 efficacy when ingested with milk, juices, papaya, aluminium-containing preparations, and chromium supplements, as well as observed enhancement effect of vitamin C on l-T4 absorption, shall be further investigated in larger, well-designed studies. Novel formulations are likely to solve the problem of coffee, calcium and iron induced malabsorption of l-T4. Maintaining a proper time interval between l-T4 and food intake, especially for coffee and calcium, or iron supplements, provides another effective method of eliminating such interactions.

DOI: 10.3390/ph14030206  
PMCID: PMC8002057  
PMID: 33801406

**23. Unknown safety profile of ingredients in hair supplements: A call to action for improved patient safety.**

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DOI: 10.1016/j.jaad.2020.05.033  
PMID: 32417421 [Indexed for MEDLINE]