AACT Herbal Dietary Supplement Section
Abstracts March 2024

1. Easy and Accessible Synthesis of Cannabinoids from CBD. Capucciati A, Casali E, Bini A, Doria F, Merli D, Porta A.

J Nat Prod. 2024 Mar 1. doi: 10.1021/acs.jnatprod.3c01117. Online ahead of print.

Cannabidiol (CBD), a prominent phytocannabinoid found in various Cannabis chemotypes, is under extensive investigation for its therapeutic potential. Moreover, because it is nonpsychoactive, it can also be utilized as a functional ingredient in foods and supplements in certain countries, depending on its legal status. From a chemical reactivity point of view, CBD can undergo conversion into different structurally related compounds both during storage and after the consumption of CBD-based products. The analytical determination of these compounds is of paramount concern due to potential toxicity and the risk of losing the active ingredient (CBD) title. Consequently, the complete stereoselective total synthesis of representative CBD-derived compounds has become a matter of great interest. The synthesis of pure CBD-derived compounds, achievable in a few synthetic steps, is essential for preparing analytical standards and facilitating biological studies. This paper details the transformation of the readily available CBD into Δ8-THC, Δ9-THC, Δ8-iso-THC, CBE, HCDN, CBDQ, Δ6-iso-CBD, and 1,8-cineol cannabinoid (CCB). The described protocols were executed without the extensive use of protecting groups, avoiding tedious purifications, and ensuring complete control over the structural features.

DOI: 10.1021/acs.jnatprod.3c01117
PMID: 38427968

2. Cannabidiol-Derived Cannabinoids: The Unregulated Designer Drug Market Following the 2018 Farm Bill. Zawatsky CN, Mills-Huffnagle S, Augusto CM, Vrana KE, Nyland JE.

Med Cannabis Cannabinoids. 2024 Feb 13;7(1):10-18. doi: 10.1159/000536339. eCollection 2024 Jan-Dec.

BACKGROUND: In this review, we summarize current scientific knowledge on psychoactive cannabinoids synthesized from cannabidiol (CBD) and sold in the semi-legal market established in response to the passage of the US Agriculture Improvement Act of 2018, commonly known as the 2018 Farm Bill. The discussion focuses on recent developments that suggest this unregulated market may be fertile ground for a potential health crisis. SUMMARY: Current research into CBD-derived cannabinoids is mainly limited to Δ8-tetrahydrocannabinol (Δ8-THC) products, with some recent publications beginning to explore O-acetyl-THC, a term describing the acetate ester of Δ8-THC or Δ9-THC, and its potential pulmonary toxicity. We advance the discussion on the CBD-derived cannabinoid market, shedding light on the introduction and associated dangers of novel cannabinoids, likely produced via fully synthetic routes using sidechain variants of CBD, with purportedly greater agonist activity at the human cannabinoid receptor 1 (as a source of euphorigenic activity) than Δ9-THC. We discuss the expanded incorporation of the acetate ester motif into other THC analogues. We also discuss the lack of regulatory oversight for the production of CBD-derived cannabinoids and the unlabeled presence of under-researched cannabinoids formed as reaction side products in the CBD-derived cannabinoid products being sold. Accordingly, we suggest approaches to monitoring the CBD-derived cannabinoid market and investigating the pharmacology of the cannabinoids being consumed. Finally, important epidemiological findings are discussed and future directions for research are suggested to call investigators to this critically understudied field. KEY MESSAGES: The CBD-derived cannabinoid market is growing internationally, and the market has diversified to include potent synthetic cannabinoids. The products sold on this

unregulated market are under-researched despite growing availability and consumer interest. Ernest investigation of the pharmacology of these novel cannabinoids and the contents of CBD-derived cannabinoid products is critical for monitoring this potential source of another vaping-related epidemic.

DOI: 10.1159/000536339
PMCID: PMC10864014
PMID: 38352661

3. Advances and Challenges in Modeling Cannabidiol Pharmacokinetics and Hepatotoxicity. Beers JL, Zhou Z, Jackson KD.

Drug Metab Dispos. 2024 Jan 29:DMD-MR-2023-001435. doi: 10.1124/dmd.123.001435.
Online ahead of print.

Cannabidiol (CBD) is a pharmacologically active metabolite of cannabis that is FDA-approved to treat seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, and tuberous sclerosis complex in children aged one year and older. During clinical trials, CBD caused dose-dependent hepatocellular toxicity at therapeutic doses. The risk for toxicity was increased in patients taking valproate (VPA), another hepatotoxic antiepileptic drug, through an unknown mechanism. With the growing popularity of CBD in the consumer market, an improved understanding of the safety risks associated with CBD is needed to ensure public health. This review details current efforts to describe CBD pharmacokinetics and mechanisms of hepatotoxicity using both pharmacokinetic models and in vitro models of the liver. In addition, current evidence and knowledge gaps related to intracellular mechanisms of CBD-induced hepatotoxicity are described. The authors propose future directions that combine systems-based models with markers of CBD-induced hepatotoxicity to understand how CBD pharmacokinetics may influence the adverse effect profile and risk of liver injury for those taking CBD. Significance Statement This review describes current pharmacokinetic modeling approaches to capture the metabolic clearance and safety profile of cannabidiol (CBD). CBD is an increasingly popular natural product and FDA-approved antiepileptic drug known to cause clinically significant enzyme-mediated drug interactions and hepatotoxicity at therapeutic doses. CBD metabolism, pharmacokinetics, and putative mechanisms of CBD-induced liver injury are summarized from available preclinical data to inform future modeling efforts for understanding CBD toxicity.

DOI: 10.1124/dmd.123.001435
PMID: 38286636

4. Gynura segetum induces hepatic sinusoidal obstruction syndrome in a child: A case report. Zheng Q, Zhang H.

Medicine (Baltimore). 2024 Mar 15;103(11):e37341. doi: 10.1097/MD.0000000000037341.

RATIONALE: Hepatic sinusoidal obstruction syndrome (HSOS), which includes hepatic stasis and portal hypertension, is a rare vascular disorder of the liver. It is often associated with hematopoietic stem cell transplantation. It is also possible to treat this disease using Chinese herbal medicines that contain pyrrolizidine alkaloids (PAs). This disease is extremely rare in children and poses a serious threat to their health. To our knowledge, this is the first case of HSOS in a child with PAs. PATIENT CONCERNS: We report a 4-year-old boy suffering from abdominal pain, hepatomegaly, massive ascites, elevated liver enzyme level, and severe portal hypertension as a result of the consumption of Gynura segetum (also known as Tusanqi in Chinese, a traditional herbal medicine containing PAs). DIAGNOSES: The child was finally diagnosed with PA-HSOS based on pathological diagnosis and imaging examination.

INTERVENTION: With active symptomatic and supportive care and sequential anticoagulation therapy, the abdominal distension and liver function improved in the patient. OUTCOMES: The patient was eventually recovered. The levels of liver enzymes, hemoglobin, and bilirubin were normal, and the international normalized ratio fluctuated between 2.0 and 3.0 during 1-year follow-up after discharge. LESSONS: This case report emphasizes the prevention of Chinese herb-induced liver injury in children and the importance of active long-term sequential anticoagulant therapy to reduce the progressive damage of PA-HSOS in the liver.

DOI: 10.1097/MD.0000000000037341
PMID: 38489699 [Indexed for MEDLINE]

5. Mechanisms of hepatocellular toxicity associated with the components of St. John's Wort extract hypericin and hyperforin in HepG2 and HepaRG cells. Abegg VF, Panajatovic MV, Mancuso RV, Allard JA, Duthaler U, Odermatt A, Krähenbühl S, Bouitbir J.

Toxicol Lett. 2024 Mar;393:1-13. doi: 10.1016/j.toxlet.2024.01.008. Epub 2024 Jan 14.

St. John's Wort preparations are used for the treatment of mild to moderate depression. They are usually well tolerated but can cause adverse reactions including liver toxicity in rare cases. To date, the mechanism(s) underlying the hepatotoxicity of St. John's Wort extracts are poorly investigated. We studied the hepatocellular toxicity of hypericin and hyperforin as the two main ingredients of St. John's Wort extracts in HepG2 and HepaRG cells and compared the effects to citalopram (a synthetic serotonin uptake inhibitor) with a special focus on mitochondrial toxicity and oxidative stress. In HepG2 cells, hypericin was membrane-toxic at 100 μM and depleted ATP at 20 μM. In HepaRG cells, ATP depletion started at 5 μM. In comparison, hyperforin and citalopram were not toxic up to 100 μM. In HepG2 cells, hypericin decreased maximal respiration starting at 2 μM and mitochondrial ATP formation starting at 10 μM but did not affect glycolytic ATP production. Hypericin inhibited the activity of complex I, II and IV of the electron transfer system and caused mitochondrial superoxide accumulation in cells. The protein expression of mitochondrial superoxide dismutase 2 (SOD2) and thioredoxin 2 (TRX2) and total and reduced glutathione decreased in cells exposed to hypericin. Finally, hypericin diminished the mitochondrial DNA copy number and caused cell necrosis but not apoptosis. In conclusion, hypericin, but not hyperforin or citalopram, is a mitochondrial toxicant at low micromolar concentrations. This mechanism may contribute to the hepatotoxicity occasionally observed in susceptible patients treated with St. John's Wort preparations.

DOI: 10.1016/j.toxlet.2024.01.008
PMID: 38219807 [Indexed for MEDLINE]

6. Insights into skullcap herb-induced liver injury. Soldera J.

World J Hepatol. 2024 Feb 27;16(2):120-122. doi: 10.4254/wjh.v16.i2.120.

This editorial addresses the growing concern of herb-induced liver injury (HILI), focusing on a unique case of Skullcap-induced HILI report. This editorial underscore the significant mortality rate linked to Skullcap-induced HILI, emphasizing the importance of vigilant monitoring and intervention. As herbal supplement usage rises, collaboration among clinicians and researchers is crucial to comprehend and address the complexities of HILI, particularly those involving Skullcap.

DOI: 10.4254/wjh.v16.i2.120
PMID: 38495279

7. (Editorial in reference to: Thakral N, Konjeti VR, Salama FW. Drug induced autoimmune hepatitis: An unfortunate case of herbal toxicity from Skullcap supplement: A case report.

World J Hepatol. 2023 Dec 27;15(12):1333-1337. doi: 10.4254/wjh.v15.i12.1333. PMID: 38223420; PMCID: PMC10784811.

BACKGROUND: The surge in traditional herbal dietary supplement (HDS) popularity has led to increased drug-induced liver injuries (DILI). Despite lacking evidence of efficacy and being prohibited from making medical claims, their acceptance has risen over sevenfold in the last two decades, with roughly 25% of United States (US) adults using these supplements monthly. An estimated 23000 emergency room visits annually in the US are linked to HDS side effects. NIH-funded research suggests HDS contribute to 7-20% of DILI cases, with similar trends in Europe—Spain reporting 2% and Iceland up to 16%. Patients with acute liver failure from HDS undergo liver transplantation more frequently than those from prescription medicines. Here we describe a case of drug-induced autoimmune hepatitis due to Skullcap supplements, this association appears to be the first documented instance in literature. CASE SUMMARY: A middle-aged Caucasian woman, previously healthy, presented with sudden jaundice. Four months earlier, her liver enzymes were normal. She mentioned recent use of Skullcap mushroom supplements. Tests for chronic liver disease were negative. The first liver biopsy indicated severe resolving drug-induced liver injury. Despite treatment, she was readmitted due to worsening jaundice. Follow-up tests raised concerns about autoimmune hepatitis. A subsequent biopsy confirmed this diagnosis. The patient responded as expected to stopping the medication with improvement in liver enzymes. CONCLUSION: This scenario highlights an uncommon instance of DILI caused by Skullcap supplements. It's crucial for hepatologists to recognize this connection due to the increasing prevalence of herbal supplements.)

8. An analysis on clinical characteristics and prognosis-related risk factors in patients with drug-induced liver injury. Wei Q, Li L, Zeng XQ, Abidan BHTYE, Yin J, Gao H, Guo JS.

Zhonghua Gan Zang Bing Za Zhi. 2024 Mar 20;32(3):214-221. doi:10.3760/cma.j.cn501113-20240201-00072.

Objective: To explore the drugs and clinical characteristics causing drug-induced liver injury (DILI) in recent years, as well as identify drug-induced liver failure, and chronic DILI risk factors, in order to better manage them timely. Methods: A retrospective investigation and analysis was conducted on 224 cases diagnosed with DILI and followed up for at least six months between January 2018 and December 2020. Univariate and multivariate logistic regression analyses were used to identify risk factors for drug-induced liver failure and chronic DILI. Results: Traditional Chinese medicine (accounting for 62.5%), herbal medicine (accounting for 84.3% of traditional Chinese medicine), and some Chinese patent medicines were the main causes of DILI found in this study. Severe and chronic DILI was associated with cholestatic type. Preexisting gallbladder disease, initial total bilirubin, initial prothrombin time, and initial antinuclear antibody titer were independent risk factors for DILI. Prolonged time interval between alkaline phosphatase (ALP) and alanine aminotransferase (ALT) falling from the peak to half of the peak (T(0.5ALP) and T(0.5ALT)) was an independent risk factor for chronic DILI [area under the receiver operating characteristic curve (AUC) = 0.787, 95%CI: 0.697~0.878, $P < 0.001$], with cutoff values of 12.5d and 9.5d, respectively. Conclusion: Traditional Chinese medicine is the main contributing cause of DILI. The occurrence risk of severe DILI is related to preexisting gallbladder disease, initial total bilirubin, prothrombin time, and antinuclear antibodies. T(0.5ALP) and T(0.5ALT) can be used as indicators to predict chronic DILI.

DOI: 10.3760/cma.j.cn501113-20240201-00072
PMID: 38584102 [Indexed for MEDLINE]

9. Supplement Use and Increased Risks of Cancer: Unveiling the Other Side of the Coin. Jabbari P, Yazdanpanah O, Benjamin DJ, Rezazadeh Kalebasty A.

Cancers (Basel). 2024 Feb 22;16(5):880. doi: 10.3390/cancers16050880.

There is a rising trend in the consumption of dietary supplements, especially among adults, with the purpose of improving health. While marketing campaigns tout the potential health benefits of using dietary supplements, it is critical to evaluate the potential harmful effects associated with these supplements as well. The majority of the scarce research on the potential harmful effects of vitamins focuses on the acute or chronic toxicities associated with the use of dietary supplements. Quality research is still required to further investigate the risks of long-term use of dietary supplements, especially the risk of developing cancers. The present review concentrates on studies that have investigated the association between the risk of developing cancers and associated mortality with the risk of dietary supplements. Such an association has been reported for several vitamins, minerals, and other dietary supplements. Even though several of these studies come with their own shortcomings and critics, they must draw attention to further investigate long-term adverse effects of dietary supplements and advise consumers and healthcare providers to ponder the extensive use of dietary supplements.

DOI: 10.3390/cancers16050880
PMCID: PMC10930792
PMID: 38473246

10. A Case Report of Acute Hepatitis Involving the Medicinal Herb Tinospora cordifolia Along with Other Variables. May K, Jeitler M, Murthy V, Stapelfeldt E, Kessler CS.

J Integr Complement Med. 2023 May;29(5):327-333. doi: 10.1089/jicm.2022.0755. Epub 2023 Mar 17.

This is a 54-year-old woman from Germany of central European origin who developed an acute hepatitis while orally taking Ayurvedic herbal remedies, among those was the medicinal herb Tinospora cordifolia. She took the plant powders from July 1, 2021, to October 1, 2021, with the intention of relieving the symptoms of her subjectively irritated gastrointestinal tract. The patient's main symptoms of acute hepatitis were progressively increasing general fatigue, nausea, and exhaustion. During an inpatient hospital admission from November 4, 2021, to November 9, 2021, she was under clinical observation, but no specific therapeutic measures were deemed necessary; however, blood chemistry showed an acute toxic hepatitis. There was no clinical or laboratory evidence of acute liver failure. Aminotransferase values decreased to normal values on December 14, 2021, by themselves. This case report contributes to the ongoing discussion about the potential risks of triggering an acute hepatitis due to the intake of herbal remedies from the Tinospora genus in rare cases, differentiating other involved risk factors. The case also shows that causality assignments are not trivial in the context of multivariate clinical scenarios. In the case of known hepatic metabolism-associated risk factors, T. cordifolia should be used with more caution based on available case reports. At the same time, no hasty and exaggerated prejudgments should be made about this medicinal herb, which has been very successfully used in traditional South Asian systems of medicine formany centuries.

DOI: 10.1089/jicm.2022.0755
PMID: 36930784 [Indexed for MEDLINE]

11. Bacillus licheniformis bloodstream infections associated with oral probiotic administration: Two case reports. Zou Q, Cai M, Hu Y, Ge C, Wang X, Duan R.

Indian J Med Microbiol. 2024 Jan-Feb;47:100485. doi: 10.1016/j.ijmmb.2023.100485. Epub 2023 Nov 1.

Bacillus licheniformis is a facultative anaerobe, gram-positive, endogenous, spore-forming bacillus. It is included in a probiotic preparation commonly used in clinical practice and is usually safe for oral administration. In this paper, we report two cases of bloodstream infection resulting from using B. licheniformis probiotic preparations for gastrointestinal bleeding. The results suggest that B. licheniformis should be used with caution in people who are immunocompromised and suffering from severe= damage to the intestinal mucosal barrier.

DOI: 10.1016/j.ijmmb.2023.100485
PMID: 37922701 [Indexed for MEDLINE]

12. Severe caffeine poisoning treated with intermittent hemodialysis under circulatory support. Mitsui D, Kamijo Y, Yoshino T, Hanazawa T, Yoshizawa T, Iwase F.

Am J Emerg Med. 2024 Feb;76:270.e5-270.e7. doi: 10.1016/j.ajem.2023.12.014. Epub 2023 Dec 12.

Caffeine poisoning can cause fatal ventricular arrhythmias. In this report, we describe a case of severe caffeine poisoning with extraordinarily high blood caffeine levels. Despite developing refractory ventricular fibrillation, the patient was successfully treated with intermittent hemodialysis (IHD) under circulatory support by venoarterial extracorporeal membrane oxygenation (VA-ECMO). A 22-year-old male was transported to our hospital approximately 2.5 h after ingesting 200 highly caffeinated tablets (200 mg/tablet) (40 g caffeine total) in a suicide attempt. On arrival, the patient vomited frequently with a Glasgow Coma Scale score E3V2M5, heart rate 185 beats/min, and a blood pressure of 97/62 mmHg. Shortly after arrival, the patient developed ventricular fibrillation which was refractory either to three electrical defibrillations or antiarrhythmic drugs, resulting in endotracheal intubation for mechanical ventilation and VA-ECMO. Starting from 2 h after arrival, intermittent hemodialysis (IHD) was performed for 11 h, which markedly improved clinical symptoms and circulatory parameters. Serum caffeine level was 454.9 mg/dL upon arrival at the hospital, but it decreased to 55.5 mg/dL by the end of IHD treatment. Renal replacement therapy (RRT) including intermittent hemodiafiltration, continuous hemodiafiltration, and IHD was continued because of rhabdomyolysis with myoglobinuria and secondary caused acute kidney injury. The patient was weaned off VA-ECMO on hospital day 7, extubated on hospital day 18, weaned from RRT on hospital day 46, and was transferred to another hospital for physical rehabilitation on hospital day 113. IHD under circulatory support by VA-ECMO should be considered in severe caffeine poisoning causing potentially fatal arrhythmias.

DOI: 10.1016/j.ajem.2023.12.014
PMID: 38129271 [Indexed for MEDLINE]

13. Traditional herbal medicine use doubled the risk of multi-organ dysfunction syndrome in children: A prospective cohort study. Teshager NW, Amare AT, Tamirat KS, Zeleke ME, Taddese AA.

PLoS One. 2024 Feb 23;19(2):e0286233. doi: 10.1371/journal.pone.0286233.eCollection 2024.

BACKGROUND: Traditional herbal medicine (THM) is frequently used in pediatric populations in many low-income countries as a form of healthcare and has been associated with a range of adverse events, including liver toxicity, renal failure, and allergic reactions. Despite these concerns, its impact on multi-organ dysfunction syndrome (MODS) risk has not been thoroughly investigated.
OBJECTIVE: This study aimed to investigate the incidence and predictors of MODS in a pediatric intensive care unit (PICU) in Ethiopia, with a focus on the association between THM use and the risk of MODS.
METHODS: This was a single-center prospective cohort study conducted at a PICU in the university of Gondar Comprehensive Specialized hospital, Northwest Ethiopia. The study enrolled eligible patients aged one month to 18 years admitted to the PICU during the study period. Data on demographic characteristics, medical history, clinical and laboratory data, and outcome measures using standard case record forms, physical examination, and patient document reviews. The predictors of MODS were assessed using Cox proportional hazards models, with a focus on the association between traditional herbal medicine use and the risk of MODS.
RESULTS: A total of 310 patients were included in the final analysis, with median age of 48 months and a male-to-female ratio of 1.5:1. The proportion and incidence of MODS were 30.96% (95% CI:25.8, 36.6) and 7.71(95% CI: 6.10, 9.40)per 100-person-day observation respectively. Renal failure (17.74%), neurologic failure (15.16%), and heart failure (14.52%) were the leading organ failures identified. Nearly one-third of patients (32.9%) died in the PICU, of which59.8% had MODS. The rate of mortality was higher in patients with MODS than in those without. The Cox proportional hazards model identified renal disease (AHR= 6.32 (95%CI: 3.17,12.61)), intake of traditional herbal medication (AHR =2.45, 95% CI:1.29,4.65), modified Pediatric Index of Mortality 2 (mPIM 2) score(AHR = 1.54 (95% CI: 1.38,1.71), and critical illness diagnoses (AHR = 2.68 (95%CI: 1.77,4.07)) as predictors of MODS.
CONCLUSION: The incidence of MODS was high. Renal disease, THM use, mPIM 2scores, and critical illness diagnoses were independent predictors of MODS. Amore than twofold increase in the risk of MODS was seen in patients who usedTMH. Healthcare providers should be aware of risks associated with THM, and educate caregivers about the potential harms of these products. Future studies with larger sample sizes and more comprehensive outcome measures are needed.

DOI: 10.1371/journal.pone.0286233
PMCID: PMC10889611
PMID: 38394174 [Indexed for MEDLINE]

14. Growing attention on the toxicity of Chinese herbal medicine: a bibliometric analysis from 2013 to 2022. Zhu KX, Wu M, Bian ZL, Han SL, Fang LM, GeF, Wang XZ, Xie SF.

Front Pharmacol. 2024 Feb 1;15:1293468. doi: 10.3389/fphar.2024.1293468.eCollection 2024.

Introduction: Despite the clinical value of Chinese herbal medicine (CHM), restricted comprehension of its toxicity limits the secure and efficacious application. Previous studies primarily focused on exploring specific toxicities within CHM, without providing an overview of CHM's toxicity. The absence of a quantitative assessment of focal points renders the future research trajectory
ambiguous. Therefore, this study aimed to reveal research trends and areas of concern for the past decade.
Methods: A cross-sectional study was conducted on publications related to CHM and toxicity over the past decade from Web of Science Core Collection database. The characteristics of the publication included

publication year, journal, institution, funding, keywords, and citation counts were recorded. Co-occurrence analysis and trend topic analysis based on bibliometric analysis were conducted on keywords and citations. Results: A total of 3,225 publications were analyzed. Number of annal publications increased over the years, with the highest number observed in 2022 (n = 475). The Journal of Ethnopharmacology published the most publications (n = 425). The most frequently used toxicity classifications in keywords were hepatotoxicity (n = 119) or drug-induced liver injury (n = 48), and nephrotoxicity (n = 40). Co-occurrence analysis revealed relatively loose connections between CHM and toxicity, and their derivatives. Keywords emerging from trend topic analysis for the past 3 years (2019-2022) included ferroptosis, NLRP3 inflammasome, machine learning, network pharmacology, traditional uses, and pharmacology. Conclusion: Concerns about the toxicity of CHM have increased in the past decade. However, there remains insufficient studies that directly explore the intersection of CHM and toxicity. Hepatotoxicity and nephrotoxicity, as the most concerned toxicity classifications associated with CHM, warrant more in-depth investigations. Apoptosis was the most concerned toxicological mechanism. As a recent increase in attention, exploring the mechanisms of ferroptosis in nephrotoxicity and NLRP3 inflammasome in hepatotoxicity could provide valuable insights. Machine learning and network pharmacology are potential methods for future studies.

DOI: 10.3389/fphar.2024.1293468
PMCID: PMC10867220
PMID: 38362153

15. Comparison of Essential and Toxic Metals Levels in some Herbal Teas: a Systematic Review. Salmani MH, Gholami M, Ranjbar MJ, Mokhberi F.

Biol Trace Elem Res. 2024 Feb;202(2):615-623. doi: 10.1007/s12011-023-03698-w.
Epub 2023 May 17.

In the present study, we reviewed the literature as a systematic review to investigate the concentration of some metals (essential, nonessential, and toxic metals) in herbal teas and their health risks. The search extended the literature from the database, including Google Scholar, PubMed, and Scopus, using the terms "herbal teas" combined with "heavy metals, essential metals, thyme, rosemary, chamomile, and tea" also with "iron, zinc, aluminum, chromium, cobalt, nickel, manganese, arsenic, cadmium, and lead" in titles and abstracts. The search was limited to articles published from 2012 to 2023 years. Initially, 212 articles were found; by detailed consideration, only 49 papers fit the inclusion criteria and were selected for further study. The mean of metal concentration, standard deviation, data distribution, and sample size were applied to generate data from the articles. The results indicated that all commonly consumed herbal teas included metals. None of them meet the requirements of the WHO requirements. However, more than 70% of their health risks are acceptable. The risks of arsenic and lead in tea and cadmium in black tea were considerably higher than in others. According to the review results, it is important to prevent heavy metal contamination of herbal teas by modifying cultivation patterns and also to prevent to onsumption of low-quality herbal
teas.
DOI: 10.1007/s12011-023-03698-w
PMID: 37198356 [Indexed for MEDLINE]

16. Effects of Wuzhi Capsule on Whole-Blood Tacrolimus Concentration Levels: A Systematic Review and Meta-Analysis. Zhang C, Ren X, Liu Y, Huang L, Feng Y, Zhang X.

Ther Drug Monit. 2024 Feb 1;46(1):33-41. doi: 10.1097/FTD.0000000000001155. Epub 2023 Nov 27.

BACKGROUND: Wuzhi Capsule (WZC) is a traditional Chinese medicinal herb widely used to treat drug-induced hepatitis or liver dysfunction and is usually prescribed in China to increase tacrolimus concentration. Several studies with small sample sizes have shown that WZC can increase tacrolimus concentration levels in clinical practice. This study aimed to evaluate the effect of WZC on whole-blood tacrolimus concentration levels and safety. METHODS: We searched 7 databases for randomized clinical trials (RCTs) and observational studies (OSs) comparing whole-blood tacrolimus concentration levels between WZC and non-WZC treatments. Data analysis was performed using Review Manager version 5.3. This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses reporting guidelines. RESULTS: Eleven studies involving 6 RCTs and 5 OSs were included. The meta-analysis indicated that whole-blood tacrolimus concentration levels in the WZC group was significantly higher than that of the non-WZC group [weighted mean difference = 1.38, 95% CI (confidence interval), 1.21-1.56, $P < 0.001$], and similar results were shown in all the subgroups of follow-up time, different primary disease, and different WZC doses. In the self-control OSs, the whole-blood tacrolimus concentration levels in the WZC group was significantly higher than the non-WZC group (weighted mean difference = 1.17, 95% CI, 0.71-1.64, $P < 0.001$). WZC was generally well tolerated and there was no significant difference in the incidence of adverse reactions between the 2 groups. CONCLUSIONS: WZC can increase whole-blood tacrolimus concentration levels. This may be an economical and practical treatment choice for patients, especially those with poor oral tacrolimus absorption capabilities. Nevertheless, RCTs and OSs with large sample sizes and high quality are needed in the future to confirm these positive results.

DOI: 10.1097/FTD.0000000000001155
PMCID: PMC10769163
PMID: 38150711 [Indexed for MEDLINE]