AACT Herbal Dietary Supplement Section
Abstracts January 2024

1. Hepatocellular Jaundice due to Hydroxycut in Monozygotic Twins. Sigurdarson SS, KristjanssonM, Bjornsson ES.

J Clin Exp Hepatol. 2024 Mar-Apr;14(2):101294. doi: 10.1016/j.jceh.2023.10.005. Epub 2023 Oct 13.

Liver injury associated with the use of a number of different of herbal and dietary supplements are increasingly recognized. It is though often unclear which of the sometimes multiple ingredients are responsible for the liver injury. Several case reports have been published on suspected liver injury due to Hydroxycut, which is a multi-ingredient supplement often used to induce weight loss. However, the hepatotoxic potential of Hydroxycut has though been disputed, and steatotic liver disease has also been implicated in patients who are found to have elevated liver enzymes while on Hydroxycut. We report clinically apparent liver injury with jaundice associated with the use of Hydroxycut in monozygotic twins with remarkably similar type of liver injury. Both had the genotype HLA-B 35:01 allele, a risk factor for green-tea extract induced liver injury, which is included in Hydroxycut.

DOI: 10.1016/j.jceh.2023.10.005
PMCID: PMC10733688
PMID: 38144897

2. Corydalis and Drug-Induced Liver Injury: A Series of 2 Cases. Engman S, Puello F, Khoury K, Miller DM, Isidan K, Shah D.

ACG Case Rep J. 2023 Dec 21;10(12):e01230. doi: 10.14309/crj.0000000000001230. eCollection 2023 Dec.

Corydalis is an herbal plant found in Asian countries. Research has demonstrated multiple health benefits. It has also been implicated in drug-induced liver injury. Cannabis dispensaries market a sleep aid which has corydalis as an active ingredient. We present 2 cases of corydalis-induced hepatotoxicity. An asymptomatic female patient exhibited a rise and fall of her transaminases coinciding with the consumption and rechallenge of this sleep aid. A man with symptoms consistent with liver dysfunction began taking the same sleep aid. With discontinuance, his liver function returned to normal. These 2 clinical cases provide evidence for corydalis-induced liver injury.

DOI: 10.14309/crj.0000000000001230
PMCID: PMC10735149
PMID: 38130480

3. Hepatotoxicity due to dietary supplements: state-of-the-art, gaps and perspectives.
Rivero-Pino F, Casanova AG

Crit Rev Toxicol. 2023 Nov;53(10):601-610. doi: 10.1080/10408444.2023.2282415.
Epub 2023 Dec 21.

Food supplements are products intended to complement the normal diet and consist of concentrated sources of nutrients or other substances with a nutritional or physiological effect. Although they are generally considered safe if the manufacturer's recommendations are followed, many of them have shown hepatotoxic properties. This can cause many diseases (e.g. steatohepatitis and cirrhosis) characterized by progressive damage and malfunction of the liver that in the long term can lead to death. A review of the literature was carried out to elucidate which dietary supplements have been associated with cases of hepatotoxicity in recent years, with emphasis on those relevant to the consumer and the new trends (e.g. cannabidiol). It has been reported that the supplements described as hepatotoxic are mainly of botanical origin (e.g. green tea or turmeric) and those used in sports (mainly anabolic androgenic steroids). There is a great variability of compounds described as causing liver damage, although sometimes it is not possible to identify them, because they are contaminants or adulterants of the products. In addition, the prevalence of toxic effects after the administration of supplements is difficult to define due to underreporting and the lack of specific studies. Globally regarding hepatotoxicity of dietary supplements, there is a paucity of well-conducted clinical trials on the efficacy of these compounds and the frequency of related liver damage, as the use of these products is largely uncontrolled.

DOI: 10.1080/10408444.2023.2282415
PMID: 38062980 [Indexed for MEDLINE]

4. Drug induced autoimmune hepatitis: An unfortunate case of herbal toxicity from Skullcap supplement: A case report. Thakral N, Konjeti VR, Salama FW.

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

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.

DOI: 10.4254/wjh.v15.i12.1333
PMCID: PMC10784811
PMID: 38223420

5. Toxins in Botanical Drugs and Plant-derived Food and Feed - from Science to Regulation: A Workshop Review. Schrenk D, Allemang A, Fahrer J, Harms H, Li X, Lin G, Mahony C, Mulder P, Peijnenburg A, Pfuhler S, Punt A, Sievers H, Troutman J, Widjaja F.

Planta Med. 2024 Jan 10. doi: 10.1055/a-2218-5667. Online ahead of print.

In September 2022, the 3rd International Workshop on pyrrolizidine alkaloids (PAs) and related phytotoxins was held on-line, entitled 'Toxins in botanical drugs and plant-derived food and feed - from science to regulation'. The workshop focused on new findings about the occurrence, exposure, toxicity, and risk assessment of PAs. In addition, new scientific results related to the risk assessment of alkenylbenzenes, a distinct class of herbal constituents, were presented. The presence of PAs and alkenylbenzenes in plant-derived food, feed, and herbal medicines has raised health concerns with respect to their acute and chronic toxicity but mainly related to the genotoxic and carcinogenic properties of several congeners. The compounds are natural constituents of a variety of plant families and species widely used in medicinal, food, and feed products. Their individual occurrence, levels, and toxic properties, together with the broad range of congeners present in nature, represent a striking challenge to modern toxicology. This review tries to provide an overview of the current knowledge on these compounds and indicates needs and perspectives for future research.

DOI: 10.1055/a-2218-5667
PMID: 38198805

6. 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]

7. Research progress on the toxicity of toxic Traditional Herbals from Thymelaeaceae Zhao L, Zhang Y, Yin Q, Chen G, Li W, Li N.

J Ethnopharmacol. 2024 Mar 25;322:117594. doi: 10.1016/j.jep.2023.117594. Epub 2023 Dec 16.

ETHNOPHARMACOLOGICAL RELEVANCE: Plants from the Thymelaeaceae family are widely distributed in tropical and temperate regions, with approximately 113 species used as Traditional Herbals. There are numerous applications for them, such as treating leukemia, AIDS, and liver cancer. It should be noted that around 20% of these plants have shown harmful side effects when used in clinical applications,
including solid irritations to the skin and mucous membranes, carcinogenic effects, organ damage, vomiting, and diarrhea.
AIM OF THE STUDY: This paper aims to review the toxic side effects, toxic compounds, toxic mechanisms, and detoxification methods of Traditional Herbals in Thymelaeaceae, guiding their safe clinical uses.
MATERIALS AND METHODS: This review employed the keywords "Thymelaeaceae," 48 different "genus," 966 "species," and the combination of "toxicity" to identify the medicinal value and toxicity of plants from Thymelaeaceae in scientific databases (Pubmed, SciFinder Scholar, Elsevier, Web of Science, and CNKI). Information relevant to the toxicity of Traditional Herbals from Thymelaeaceae up to June 2023 has been summarized. The plant names have been checked with "World Flora Online" (www.worldfloraonline.org).
RESULTS: 28 toxic Traditional Herbals from 13 genera within the Thymelaeaceae family were categorized. Toxicities were summarized at the cellular, animal, and clinical levels. The toxic substances are primarily concentrated in the Daphne L. and Wikstroemia Endl. genera, with terpenes being the main toxic components. The toxicity mechanism is primarily associated with the mitochondrial pathways. Detoxification and enhanced efficacy can be achieved through processing methods such as vinegar-processing and sweat-soaking.
CONCLUSIONS: Medicinal plants in the Thymelaeaceae exhibit significant pharmacological activities, such as anti-HIV and anti-tumor effects, indicating a broad potential for application. However, their clinical uses are hindered by their inherent toxicity. Researching the toxic components and mechanisms of
these Traditional Herbals and exploring more effective detoxification methods can contribute to unveiling the latent value of these medicinal plants fromThymelaeaceae.

DOI: 10.1016/j.jep.2023.117594
PMID: 38110134 [Indexed for MEDLINE]

8. Overcoming the clinical challenges of traditional ayahuasca: a first-in-human trial exploring novel routes of administration of N,N-Dimethyltryptamine and harmine.

Dornbierer DA, Marten L, Mueller J, Aicher HD, Mueller MJ, Boxler M, Kometer M, Kosanic D, von Rotz R, Puchkov M, Kraemer T, Landolt HP, Seifritz E, Scheidegger M

Front Pharmacol. 2023 Nov 27;14:1246892. doi: 10.3389/fphar.2023.1246892. eCollection 2023.

Recently, the Amazonian plant medicine "ayahuasca"-containing the psychedelic compound N,N-dimethyltryptamine (DMT) and numerous β-carboline alkaloids, such as harmine-has been suggested to exhibit beneficial effects in patients with affective and other mental health disorders. Although ayahuasca ingestion is considered safe, its pharmacokinetics/pharmacodynamics and tolerability profile pose some challenges and may limit the clinical applicability in vulnerable patient populations. While overdosing and the admixture of intolerable plant constituents may explain some of the common adverse reactions, the peroral route of administration may represent another relevant source of gastro-intestinal ntolerabilities and unpredictable pharmacokinetics across users. To overcome these challenges, the present work aimed at creating ayahuasca-analogue formulations with improved pharmacokinetics and tolerability profiles. To this end, we developed peroral formulas and compared them with parenteral formulas specifically designed to circumvent the gastro-intestinal tract. In more detail, peroral administration of a capsule (containing purified DMT and harmine) was tested against a combined administration of an oromucosal harmine tablet and an intranasal DMT spray at two dose levels in an open-label within-subject study in 10 healthy male subjects. Pharmacokinetic and pharmacodynamic profiles were assessed by means of continuous blood sampling, vital sign monitoring, and psychometric assessments. Common side effects induced by traditional herbal ayahuasca such as nausea, vomiting, and diarrhea were significantly attenuated by our DMT/harmine formulations. While all preparations were well tolerated, the combined buccal/intranasal administration of harmine and DMT yielded substantially improved pharmacokinetic profiles, indicated by significantly reduced variations in systemic exposure. In conclusion, the combined buccal/intranasal administration of harmine and DMT is an innovative approach that may pave the way towards a safe, rapid-acting, and patient-oriented administration of DMT/harmine for the treatment of affective disorders. Clinical Trial Registration: clinicaltrials.gov, identifier NCT04716335.

DOI: 10.3389/fphar.2023.1246892
PMCID: PMC10711279
PMID: 38089057

9. Unmasking herbal medication-induced lead poisoning in a geriatric patient with gastrointestinal symptoms. Eldhose R, Viggeswarpu S, Jambugulam M.

BMJ Case Rep. 2023 Dec 12;16(12):e258065. doi: 10.1136/bcr-2023-258065.

Lead poisoning, often associated with occupational exposure, can also arise from intake of traditional and herbal medicines with high lead content. Geriatric patients displaying gastrointestinal symptoms from such sources are frequently misdiagnosed. An individual in his 70s reported to our geriatric clinic with vomiting, constipation and anaemia. A meticulous history unveiled his recent intake of herbal remedies. Heavy metal assay indicated elevated lead levels in his blood and urine, consistent with the high lead content we measured in the herbal medication. Following supportive treatment, nutritional supplementation and chelation therapy with calcium disodium EDTA, he improved. Follow-up tests indicated a decrease in lead levels and resolution of anaemia. This case emphasises the importance of considering lead poisoning as a potential diagnosis in patients with unexplained symptoms, particularly when there is a history of herbal or alternative medication intake. Timely recognition and appropriate management can lead to better outcome.

DOI: 10.1136/bcr-2023-258065
PMCID: PMC10728943
PMID: 38086570

10. A therapeutic potentiality and toxicity concern of nutrient plant AnnonasquamosaLinn. Manisha Chandrakar , Khomendra Kumar Sarwa , Vijendra Kumar Suryawanshi , Kumari Pramila

Traditional Medicine Research 2024;9(3):18. https://doi.org/10.53388/TMR20230729003

Abstract Annona squamosa Linn. fruit is famous for its nutritional value with a long historyof medicinal benefits due to the presence of many phytochemicals, including alkaloids, diterpenes, essential oil, phytopeptides, etc. Several studies envisaged that Annona squamosapossesses cytotoxic, diuretic, antiurolithiatic, antitumor, anti-psoriatic, antioxidant, andhepatoprotective properties. This plant is traditionally used for the treatment of woundinfection, dysentery, seizure, tumors, fever, vomiting, parasitic infections, hypertension, thyroid, toothache, acne, heart disease, inflammation, diabetes, hair loss, dandruff, hemorrhage, maggot-infected sores, abortifacient, and cough. However, some chemical constituents isolated from the plant have shown specific toxic effects in human andanimal models, such as acute oral toxic effects, genotoxic, neurotoxic, and ocular toxic. The plant has diverse pharmacological actions, the seeds of this plant possess a genotoxic effect but onthe contrary, the bark of the plant shows genoprotective activity. A large number of ethnobotanical studies reported the seed of this plant is used to induce abortion in humans, but a scientific study carried out in pregnant rats reported aqueous seed extract of the plant did not interfere with reproductive performance. The presented review summarizedthetraditional uses, pharmacological, and toxicological activities of the

isolated compoundsfrom this plant. Additionally, some patents and commercial products related to Annonasquamosa are also brought up in this article to explore its application which wouldattract the scientific community to search out its hidden side.

DOI:10.53388/TMR20230729003

11. Health Risk Assessment of Metals in Antidiabetic Herbal Preparations: A Safety Screening. Islam N., Zamir R., Faruque O.

Hindawi Evidence-Based Complementary and Alternative Medicine Volume 2024, Article ID 6507185, 12 pages https://doi.org/10.1155/2024/6507185

The present study evaluates the human health risk of metals in locally consumed herbal preparations used to treat diabetes. Atomic absorption spectroscopy (AAS) was used after microwave-assisted digestion to mineralize the samples. Toxic metal assessment was done by adopting mathematical modeling for carcinogenic and noncarcinogenic risks in the exposed population and comparing the raw results with maximum residue limits (MRLs) set by regulatory authorities. Hazard quotient (HQ) values for Fe, Hg, Cu, Pb, and Zn were recorded above 1. Noncarcinogenic health risks remain in 29% of samples for Fe, 67% of samples for Hg, 17% of samples for Cu, 33% of samples for Pb, and 4% of samples for Zn. Hazard index (HI) values in 33% of samples were above 1. Carcinogenic risks for Pb, Cr, Cd, and Ni were higher than the acceptable limit (1×10^{-6}). Carcinogenic health risks exist in 54% of samples for Pb, 58% of samples for Cr, 46% of samples for Cd, and 58% of samples for Ni. MRLs for metals were crossed in samples in varying degrees. This is a harrowing account and may put public health safety at risk. Considering these facts, there should be more investigation into toxic metals in other frequently marketed herbal drugs in the antidiabetic and other therapeutic classes. Pre- and postmarket monitoring strategies for the preparations should also be in place to ensure safe consumption.

12. Black Cohosh Interactions with Prescription Medications Associated with Serotonin Toxicity and Rhabdomyolysis: A Case Report. Dernbach M.R., Carpenter J.E., Shah N., Carter G.B.

Journal of Emergency Medicine (2024), doi: https://doi.org/10.1016/j.jemermed.2024.01.003

Background: Serotonin toxicity is a well-described phenomenon that is commonly attributed to a variety of drug-drug combinations. Some unregulated herbal supplements have been implicated in the onset of serotonin toxicity, however there is currently minimal literature available that demonstrates the potential for black cohosh to contribute to rhabdomyolysis and serotonin toxicity, despite its known serotonergic properties.
Case Report: A middle-aged female presented to the Emergency Department with serotonin toxicity and rhabdomyolysis shortly after taking black cohosh supplements, in the setting of long-term dual antidepressant use. The serotonin toxicity and rhabdomyolysis resolved with intravenous fluids, benzodiazepines, and discontinuation of the offending drugs.

Why Should an Emergency Physician be Aware of This?: Patients sometimes are not aware of how over-the-counter supplements might interact with their prescription medications. Female patients taking black cohosh to manage hot flashes and menopausal symptoms could be at risk for developing rhabdomyolysis and serotonin toxicity if they are also taking other serotonergic agents.

13. Toxicity of sibutramine hydrochloride-adulterated weight loss supplements in rats based on biochemical and organ weight parameters. Suparmi S., Yuliyanti S., Karyadini H.W., Syamusdin A.M.R., Gau E.K.

Journal of Pharmacy & Pharmacognosy Research, 12 (2), 363-370, 2024. doi: https://doi.org/10.56499/jppres23.1852_12.2.363

Abstract Context: Weight-loss supplements are typically natural or herbal supplements that promote weight loss and enhance health. However, the increase in consumption results in the fraudulent adulteration of conventional pharmaceutical drugs, such as sibutramine hydrochloride (SHCl). Aims: To determine the toxicity of weight loss supplements adulterated with SHCl in rats. Methods: Five samples (J1–J5) of weight loss supplements adulterated with SHCl were collected from an online market. The toxicity of the samples was evaluated using 42 male Wistar rats for 35 days. The rats were divided into seven groups: control, J1, J2, J3, J4, J5, and SHCl. Results: The J1 supplement resulted in the most rapid weight loss in rats compared to the other supplements tested. The kidney and liver weights of rats administered weight loss supplements adulterated with SHCl were greater than those of control rats. J1 indicated the supplement with the highest level of toxicity. The group administered J1 exhibited the highest levels of toxicity across all evaluated parameters. Conclusions: This study confirmed the toxicity of weight loss supplements adulterated with SHCl in rats, contributing to the understanding and treatment of adulterated weight loss supplements. Dietary supplements for weight

14. Hidden sodium in effervescent-tablet dietary supplements and over-the-counter drugs: a comparative cross-sectional study. Kunz M, Götzinger F, Jacobs CM, Lauder L, Ukena C, Meyer MR, Laufs U, Schulz M, Böhm M, Mahfoud F.

BMJ Open. 2023 Nov 27;13(11):e076302. doi: 10.1136/bmjopen-2023-076302.

OBJECTIVE: Dietary sodium intake represents a risk factor for cardiovascular disease and mortality. The study sought to analyse the sodium content of effervescent dietary supplements and drugs in Germany and the USA. DESIGN: Comparative cross-sectional study. SETTING AND METHODS: The sodium content of 39 dietary supplement effervescent tablets available in Germany was measured in May and June 2022 using optical emission spectrometry with inductively coupled argon plasma. The sodium content of 33 common pharmacy-only effervescent tablets (over-the-counter (OTC) drugs) in Germany was obtained from the summary of product characteristics. We compared the sodium content of the measured German dietary supplement effervescent tablets to that of 51 dietary supplement effervescent tablets available in the USA (data: National Institutes of Health's Dietary Supplement Label Database). RESULTS: The measured sodium content in the German dietary supplements was 283.9±122.6 mg

sodium/tablet, equivalent to 14±6% of the maximum recommended daily sodium intake (MRDSI). Vitamin products had the highest (378.3±112.8 mg, 19±6% of MRDSI), and calcium products had the lowest mean sodium content (170.4±113.2 mg, 9±6% of MRDSI). Vitamin products contained significantly more sodium than magnesium (378.3 mg vs 232.7 mg; p=0.004), calcium (378.3 mg vs 170.4 mg; p=0.006) and mineral products (378.3 mg vs 191.6 mg; p=0.048). The sodium content measured in products available in Germany was higher when compared with the declared sodium content on the label of the products sold in the USA (283.9 mg vs 190.0 mg; p<0.001). The median summary of product characteristics-declared sodium content of a single dose of the German OTC drugs was 157.0 mg (IQR: 98.9-417.3 mg); pain/common cold drugs contained the most sodium (median: 452.1 mg; IQR: 351.3-474.0 mg). CONCLUSION: Effervescent tablets of nutritional supplements and OTC drugs contain high amounts of sodium, which often is not disclosed.

DOI: 10.1136/bmjopen-2023-076302
PMCID: PMC10685933
PMID: 38011966 [Indexed for MEDLINE]

15. Drug-Drug Interaction Between Cannabidiol, Cyclosporine, and Mycophenolate Mofetil: A Case Report. Cuñetti L, Oricchio F, Vázquez M, Peyraube R, Manzo L, Nalerio C, Curi L, Maldonado C.

Transplant Proc. 2024 Jan 10:S0041-1345(23)00758-3. doi: 10.1016/j.transproceed.2023.11.013. Online ahead of print.

Kidney transplantation remains the optimal therapy for many patients with end-stage kidney disease (ESKD). Chronic pain is one of the most common and distressing symptoms among patients with ESKD, and its treatment is a complex and challenging task to accomplish. The benefits of cannabidiol (CBD) in chronic pain treatment have been reported recently. Cannabidiol is metabolized by cytochrome P450, mainly CYP3A4 and CYP2C19, and can also undergo direct conjugation via UDP-glucuronosyltransferase enzymes, with a growing body of evidence suggesting it is also a potent inhibitor or inducer of these pathways. Cannabidiol was also found to be a potent inhibitor of carboxylesterases in vitro. Because cytochrome P450 enzymes and carboxylesterases are also responsible for the clearance and activation of immunosuppressants, respectively, drug-drug interactions are likely to occur. Here, we report a pharmacokinetic drug interaction between CBD and cyclosporine and mycophenolate mofetil in a patient with ESKD with a kidney transplantation. It is thus crucial to take into account these interactions and monitor drug levels to avoid drug toxicity or a lack of efficacy. This study is in accordance with the guidelines of the Declaration of Helsinki and the Declaration of Istanbul.

DOI: 10.1016/j.transproceed.2023.11.013
PMID: 38212169

16. Effect of Acute and Chronic Ingestion of Exogenous Ketone Supplements on Blood Pressure: A Systematic Review and Meta-Analysis. Marcotte-Chénard A, Tremblay R, Falkenhain K, Little JP, Riesco E.

J Diet Suppl. 2023 Dec 25:1-19. doi: 10.1080/19390211.2023.2289961. Online ahead of print.

Exogenous ketone supplements have been suggested to have potential cardiovascular benefits, but their overall effect on blood pressure is unclear. Our objective was to perform a systematic review and meta-analysis on the effects of exogenous ketone supplements on blood pressure (BP) and concomitant changes in resting heart rate (HR). Five databases were searched on January 27th, 2023, for randomized and non-randomized studies. A random-effects model meta-analysis was performed including all studies jointly and separately for acute and chronic ingestion of ketone supplements. Out of 4012 studies identified in the search, 4 acute and 6 chronic studies with n = 187 participants were included. Pooled results (n = 10) showed no change in systolic (SMD [95% CI]= -0.14 [-0.40; 0.11]; I2= 30%; p = 0.17) or diastolic BP (-0.12 [-0.30; 0.05]; I2= 0%; p = 0.69), with a potential tendency observed toward increased resting heart rate (0.17 [-0.14; 0.47]; I2= 40%; p = 0.10). Similar results for systolic and diastolic BP were observed when assessing separately the effect of acute and chronic ingestion of ketone supplements ($p \geq 0.33$). Supplement dosage was found to modulate the increase in resting heart rate (0.019 ± 0.006; p = 0.013; R2=100%), suggesting that higher supplement doses lead to a higher resting heart rate. Based on currently available data, acute or prolonged ingestion of ketone supplements does not seem to modulate BP. However, a tendency for HR to increase after acute ingestion was observed, particularly with higher doses. Higher quality studies with appropriate standardized measurements are needed to confirm these results.

DOI: 10.1080/19390211.2023.2289961
PMID: 38145410