AACT Herbal Dietary Supplement Section Abstracts

March 2025

1. **Quantitative Analysis of Pyrrolizidine Alkaloids in Food Matrices and Plant-Derived Samples Using UHPLC-MS/MS.** Lin R, Peng J, Zhu Y, Dong S, Jiang X, Shen D, Li J, Zhu P, Mao J, Wang N, H(1).

   Foods. 2025 Mar 26;14(7):1147. doi: 10.3390/foods14071147.

   Pyrrolizidine alkaloids (PAs) are a class of nitrogen-containing basic organic compounds that are frequently detected in foods and herbal medicines. Owing to their potential hepatotoxic, genotoxic, and carcinogenic properties, PAs have become a significant focus for monitoring global food safety. In this study, an ultra-high-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) method was developed for the detection and analysis of three foods (tea, honey, and milk) susceptible to PA contamination. This optimized method effectively separated and detected three types of PAs, namely, three pairs of isomers and two pairs of chiral compounds. The limits of detection (LODs) and limits of quantification (LOQs) were determined to be 0.015-0.75 and 0.05-2.5 μg/kg, respectively, with the relative standard deviations (RSDs) of both the interday and intraday precisions remaining below 15%. The average PA recoveries from the honey, milk, and tea matrices fell within the ranges of 64.5-103.4, 65.2-112.2, and 67.6-107.6%, respectively. This method was also applied to 77 samples collected from 33 prefecture-level cities across 16 provinces and included 40 tea, 6 milk, 8 honey, 14 spice, and 9 herbal medicine samples. At least one PA was detected in twenty-three of the samples, with herbal medicines exhibiting the highest total PA content. The obtained results indicate that the developed method demonstrated good repeatability and stability in the detection and quantitative analyses of PAs in food- and plant-derived samples. This method is therefore expected to provide reliable technical support for food safety risk monitoring.

   DOI: 10.3390/foods14071147
   PMCID: PMC11989101
   PMID: 40238287

2. **Acute Liver Injury Following Herbal Drink Consumption With Steatosis and Immune Activation: A Case Report.** Hussaini H, Waheed A, Fadeyi O, Boostany T, Hashimoto Y, Flint AT.

   Cureus. 2025 Feb 28;17(2):e79839. doi: 10.7759/cureus.79839. eCollection 2025 Feb.

   Herbal medicines are widely used for their perceived health benefits; however, their potential for liver toxicity is well-documented. We report a case of acute liver injury (ALI) in a 32-year-old male patient following the consumption of a multi-herbal drink. The patient, with a history of cholecystectomy for gallstones and nephrolithiasis, presented with severe epigastric pain radiating to the right shoulder, nausea, high blood pressure (170/113 mmHg), and a rapid heart rate. Laboratory tests revealed significant liver damage, with aspartate aminotransferase (AST) at 1,043 U/L, alanine aminotransferase (ALT) at 1,645 U/L, and total

bilirubin at 4.8 mg/dL. Ultrasound imaging showed fatty liver disease without bile duct obstruction. Autoimmune testing was negative for antinuclear antibodies (ANA) and antimitochondrial antibodies (AMA), while elevated immunoglobulin G (IgG) levels suggested immune activation as a potential mechanism. The patient improved with supportive care. This case highlights the potential liver toxicity of polyherbal remedies and underscores the importance of early recognition and management to prevent long-term complications.

DOI: 10.7759/cureus.79839
PMCID: PMC11955213
PMID: 40161146

3. **Epigenetic modifications in drug-induced liver injury: A systematic review**. de Los Santos-Fernández RL, Segovia-Zafra A, Paz-López G, Matilla-Cabello G, Niu H, Álvarez-Álvarez I, Stephens C, González-Jiménez A, Lucena MI, Andrade RJ, Medina-Cáliz I.

Br J Clin Pharmacol. 2025 Mar 25. doi: 10.1002/bcp.70053. Online ahead of print.

Genetic susceptibility has been identified in idiosyncratic drug-induced liver injury, a potentially severe adverse reaction towards drugs, herbal products and dietary supplements. However, its occurrence cannot be fully explained by the presence of genetic variants in specific genes, suggesting that other factors are involved. Drug-induced liver injury epigenetic signatures could help explain genetic regulatory mechanisms behind this disease and might provide disease biomarkers. This systematic review aims to analyse all available information on epigenetic risk association studies in drug-induced liver injury. The main inclusion criterion was population studies on idiosyncratic drug-induced liver injury with significant risk association analysis between drug-induced liver injury and an epigenetic regulation mechanism. Out of the 7 included articles, 6 focused on DNA methylation and 1 on long noncoding RNA. All of the studies were on antituberculosis drug-induced liver injury and came from Asia. CpG site methylation in the CYP2D6 (odds ratio: 9.19, 95% confidence interval: 3.26-25.89, $P < .001$) and NAT2 (odds ratio: 8.37, 95% confidence interval: 2.39-29.32, $P = .001$) promoters conferred the highest risk. Hypomethylation of LINE-1 and Alu transposable elements has potential as antituberculosis drug-induced liver injury biomarkers, showing an area under the curve value of 0.94. To conclude, the studies mainly focused on DNA methylation modifications associated with antituberculosis drug-induced liver injury, with all of them coming from Asia, where tuberculosis is a public health burden. Despite the lack of knowledge in this area, the evidence has shown that DNA methylation alterations in antituberculosis drug-induced liver injury could have potential as a new diagnostic and therapeutic target.

DOI: 10.1002/bcp.70053
PMID: 40134104

4. **Lethal course: When plants affect the liver.** van der Lely L, Andermatt R, Lienhardt B.

   Dtsch Med Wochenschr. 2025 Mar;150(7):359-362. doi: 10.1055/a-2433-1903. Epub 2025 Mar 14.

   Article in German; Abstract available in German from the publisher

   The 55-year-old, previously healthy patient presented himself with a drop in performance and yellowing of the skin which had persisted for 3 weeks. To strengthen the immune system, he had been taking 7 different Chinese herbs for 4 months. Clinical findings included jaundice, tenderness in the right upper abdomen and grade I encephalopathy (HE).Laboratory revealed coagulopathy as well as elevated transaminases and cholestasis parameters with only slightly elevated ammonia levels. Sonographically, fibrosis or cirrhosis as well as perfusion disorder could be excluded. Due to the temporal course and the lack of previous hepatic disease, acute liver failure (ALF) was diagnosed, caused by the intake of Chinese herbs. Due to an ambivalent patient's will, referral to a transplant center and listing for transplantation were delayed. After liver transplantation graft failure developed as a result of an abdominal compartment syndrome. During the high-risk re-transplantation, a thrombus formed in the right ventricle with a fatal outcome. Timely recognition and referral of a patient with acute liver failure (HE and INR ≥ 2) is crucial.

   DOI: 10.1055/a-2433-1903
   PMID: 40086862 [Indexed for MEDLINE]

5. **Drug-Induced Liver Injury Associated with Turmeric and Piperine:** A Case and Review.

   Case Rep Gastroenterol. 2025 Feb 24;19(1):96-106. doi: 10.1159/000543679. eCollection 2025 Jan-Dec.

   Shrestha A, Elliott S, Abasszade JH, Wu K, Worland T, Simpson I, Dev A.

   INTRODUCTION: Turmeric is a common spice used in traditional Chinese and Ayurvedic medicine for a variety of purported health benefits. Recent concerns have arisen regarding turmeric-induced liver injury linked to formulations with enhanced bioavailability, often including piperine found in black pepper.CASE PRESENTATION: We explore a case of a 40-year-old female with increasing fatigue, pruritus, and dark urine following consumption of turmeric and black pepper "wellness shots" leading to a significant drug-induced liver injury.CONCLUSION: This case underscores the critical need to recognise herbal remedies, such as turmeric, as potential sources of hepatotoxicity. Despite a reputation of safety, limited regulation and testing of turmeric may mean potential adverse effects are under-recognised. Understanding the mechanisms behind turmeric and black pepper's hepatotoxicity, including the role of potential genetic predispositions, requires further investigation for its safe use.

   DOI: 10.1159/000543679
   PMCID: PMC11850025
   PMID: 39995754

6. **Turmeric supplement-associated hepatitis: a clinicopathological series of 11 cases highlighting pan-lobular and zone 3 injury**. Papke DJ Jr, Viveiros K, Zota V, Gill RM, González IA, Misdraji J, Patil D.

   Histopathology. 2025 Feb;86(3):410-422. doi: 10.1111/his.15333. Epub 2024 Oct 9.

   AIMS: Although turmeric is commonly ingested and well tolerated, there is increasing evidence that over-the-counter turmeric supplements can cause drug-induced liver injury. We sought to thoroughly characterise clinicopathological features of patients for whom liver injury was attributed clinically to turmeric supplements.
   METHODS AND RESULTS: We identified 11 patients via retrospective pathology archive review: 10 females (91%) and one male, with a median age of 58 years (range = 37-66 years). Six patients (55%) were asymptomatic with abnormal liver function tests, while five patients (45%) presented with malaise and/or jaundice. Ten patients (91%) showed predominant transaminase abnormalities, while one exhibited predominant alkaline phosphatase elevation. Histologically, biopsies showed acute hepatitis (eight cases, 73%, including five pan-lobular and three zone 3-predominant inflammation), scattered lobular aggregates of histiocytes (two; 18%) and a chronic hepatitis pattern of injury (one; 9%). Mild bile duct injury was present in five biopsies (45%). All patients stopped ingesting turmeric supplements after presenting with liver injury, and four patients additionally received steroid therapy; liver function tests normalised in all patients. Roussel Uclaf causality assessment method (RUCAM) analysis estimated the likelihood of turmeric supplement-associated liver injury to be probable (eight cases) and possible (three).
   CONCLUSIONS: Histological features in the 'possible' cases were consistent with drug-induced injury, highlighting the added benefit of histological analysis relative to RUCAM analysis isolation. This study underscores the need to obtain a full history of over-the-counter medications and supplements when investigating aetiologies for liver injury, including supplements purportedly containing innocuous compounds such as turmeric.

   DOI: 10.1111/his.15333
   PMID: 39381846 [Indexed for MEDLINE]

7. **Drug-Induced Liver Injury in Patients With Chronic Liver Disease.** habril M, Vuppalanchi R, Chalasani N.

   Liver Int. 2025 Mar;45(3):e70019. doi: 10.1111/liv.70019.

   OBJECTIVE: Drug-induced liver injury (DILI) is a global problem and can develop from exposure to prescription or over-the-counter medications as well as herbal and dietary supplements. The diagnosis of DILI is clinically challenging, and liver injury can be severe leading to liver failure, death, or liver transplantation. Patients with underlying chronic liver diseases (CLD) may be at increased risk for DILI, which is associated with factors related to drug or liver disease.
   METHODS: This review summarises current knowledge on the risk and outcomes of DILI in patients with CLD.
   RESULTS: Patients with CLD may be at an increased risk for DILI. Additionally patients with underlying CLD are at risk for more severe liver injury and worse outcomes after DILI.

DISCUSSION: The risk for and poor outcomes from DILI are accentuated in patients with CLD and potentially leading to the worst-case scenario of acute-on-chronic liver failure. We highlight the key observations on DILI with a broad range of underlying liver diseases and the high-DILI risk agents implicated in those populations.

DOI: 10.1111/liv.70019
PMCID: PMC11808633
PMID: 39927421 [Indexed for MEDLINE]

8. **Artificial Intelligence: An Emerging Tool for Studying Drug-Induced Liver Injury**. Niu H, Alvarez-Alvarez I, Chen M.

Liver Int. 2025 Mar;45(3):e70038. doi: 10.1111/liv.70038.

Drug-induced liver injury (DILI) is a complex and potentially severe adverse reaction to drugs, herbal products or dietary supplements. DILI can mimic other liver diseases clinical presentation, and currently lacks specific diagnostic biomarkers, which hinders its diagnosis. In some cases, DILI may progress to acute liver failure. Given its public health risk, novel methodologies toenhance the understanding of DILI are crucial. Recently, the increasing availability of larger datasets has highlighted artificial intelligence (AI) as a powerful tool to construct complex models. In this review, we summarise the evidence about the use of AI in DILI research, explaining fundamental AI concepts and its subfields. We present findings from AI-based approaches in DILI investigations for risk stratification, prognostic evaluation and causality assessment and discuss the adoption of natural language processing (NLP) and large language models (LLM) in the clinical setting. Finally, we explore future perspectives and challenges in utilising AI for DILI research.

DOI: 10.1111/liv.70038
PMID: 39982029 [Indexed for MEDLINE]

9. **Artificial Intelligence Models and Tools for the Assessment of Drug-Herb Interactions.** Spanakis M, Tzamali E, Tzedakis G, Koumpouzi C, Pediaditis M, Tsatsakis A, Sakkalis V.

Pharmaceuticals (Basel). 2025 Feb 20;18(3):282. doi: 10.3390/ph18030282.

Artificial intelligence (AI) has emerged as a powerful tool in medical sciences that is revolutionizing various fields of drug research. AI algorithms can analyze large-scale biological data and identify molecular targets and pathways advancing pharmacological knowledge. An especially promising area is the assessment of drug interactions. The AI analysis of large datasets, such as drugs' chemical structure, pharmacological properties, molecular pathways, and known interaction patterns, can provide mechanistic insights and identify potential associations by integrating all this complex information and returning potential risks associated with these interactions. In this context, an area where AI may prove valuable is in the assessment of the underlying mechanisms of drug interactions with natural products (i.e., herbs) that are used as dietary supplements. These products pose a challenging problem since they are complex mixtures of constituents with diverse and limited information regarding their pharmacological properties, especially their pharmacokinetic data. As the use of herbal

products and supplements continues to grow, it becomes increasingly important to understand the potential interactions between them and conventional drugs and the associated adverse drug reactions. This review will discuss AI approaches and how they can be exploited in providing valuable mechanistic insights regarding the prediction of interactions between drugs and herbs, and their potential exploitation in experimental validation or clinical tilization.

DOI: 10.3390/ph18030282
PMCID: PMC11944892
PMID: 40143062

10. **Case Report: Persistent toxic reactions in a toddler with a negative blood cantharidin toxicology test.** Duan Z, Qu Y, Tang R, Sheng M, Wang L, Li J, Zheng S, Guo L.

    Front Pediatr. 2025 Feb 27;13:1546669. doi: 10.3389/fped.2025.1546669. eCollection 2025.

    Cantharidin is a potent natural toxin and has been used in traditional Chinese medicine to treat cancers and various ailments such as rabies or psoriasis. However, improper use of cantharidin can easily lead to poisoning. Despite there is an increasing amount of literature on the toxic mechanisms of cantharidin, there is still limited knowledge about the disease progression, toxic reactions and toxic blood concentrations in children with cantharidin poisoning. Caregivers of children suffering from cantharidin poisoning might fail to provide an accurate exposure dose when the children exhibit symptoms of intoxication. Moreover, the detection results on routine blood drug screens may be negative, thus delaying the clinical diagnosis and treatment. This study describes a case of cantharidin poisoning in a 2-year-old boy who ingested a traditional Chinese herbal remedy for dog bites. The toddler exhibited severe symptoms related with digestive and urinary systems. Though cantharidin was no longer detectable in the blood 20 h after admission, the poisoning symptoms persisted for approximately 5 days, and ultrasound showed that there was still sediment in the bladder two weeks after discharge. This case highlights the need for clinicians to consider the widespread tissue distribution of cantharidin, which may lead to prolonged toxic reactions.

    DOI: 10.3389/fped.2025.1546669
    PMCID: PMC11903399
    PMID: 40083431

11. **Conundrum of Acute Liver Failure.** Vishnu BS, Teja BSS, Sri IL, Ganti E.

    Ann Afr Med. 2025 Apr 1;24(2):504-508. doi: 10.4103/aam.aam_9_25. Epub 2025 Mar 10.

    A 20-year-old male with fever, myalgia, and jaundice developed severe liver dysfunction, progressing to acute liver failure (ALF). Initial treatment for malaria and supportive care did not resolve symptoms, with persistent jaundice and elevated liver enzymes. Laboratory tests confirmed Plasmodium falciparum / Plasmodium vivax infection. Further evaluation revealed drug-induced liver injury (DILI) from prescribed medications and possible hepatotoxic effects of herbal supplements. Hepatitis A, exacerbated by malaria, DILI, and herbal toxicity, contributed to compounded hepatic dysfunction. Management included intravenous fluids, hepatoprotective agents, and antipyretics. This case underscores the importance of

considering multiple etiologies, including infections, drug toxicity, and environmental factors, in ALF.

DOI: 10.4103/aam.aam_9_25
PMID: 40064630

12. **Ayahuasca reverses ischemic stroke-induced neuroinflammation and oxidative stress**. da Silva Joaquim L, da Rosa LR, Strickert Y, Machado RS, et al.

Behav Brain Res. 2025 May 8;485:115521. doi: 10.1016/j.bbr.2025.115521. Epub 2025 Mar 3.

BACKGROUND: Ischemic stroke is a leading cause of death and disability worldwide. Survivors face disability and psychiatric sequelae resulting from ischemia-induced cell death and associated neuroinflammation, and oxidative stress. Herbal medicines have been shown to elicit neuroprotective effects following stroke due to their anti-inflammatory and antioxidant effects. Preliminary evidence suggests that Ayahuasca (AYA), a decoction made from the vine Banisteriopsis caapi containing β-carbolines and the shrub Psychotria viridis containing N, N-Dimethyltryptamine, might attenuate ischemia-induced neuroinflammation and oxidative stress. Therefore, in this study we investigated the putative protective effects of AYA in the middle cerebral artery occlusion (MCAO) model of ischemic stroke.METHODS: Wistar rats were subjected to the MCAO stroke model or sham surgery on day 0. After 24-h, rats were treated for three days with AYA (2 and 4 mL/kg, gavage) or saline. Neurological score was assessed for 72-h post-stroke. Rats were tested in the elevated plus maze, open field, and novel object recognition tests to assess locomotion, anxiety-like behavior, and recognition memory. Interleukin (IL)-6, IL-10 myeloperoxidase (MPO) activity, and the nitrite/nitrate (N/N) concentrations were determined in the prefrontal cortex (PFC), hippocampus (HPC), hypothalamus (HYP) and cortex. as markers of inflammation. Oxidative stress was quantified in the same brain areas as measured by the levels of thiobarbituric acid reactive species (TBARS), protein carbonylation, and superoxide dismutase (SOD), and catalase (CAT) activity. Mitochondrial metabolism was assessed quantifying the activity of complex 1(CI), CII, citrate synthase (CS), succinate dehydrogenase (SDH), and creatine kinase (CK).RESULTS: No differences were observed regarding neurological deficits, locomotion, anxiety-like behavior, and recognition memory. However, AYA reversed the stroke-induced increase in IL-6 levels in the PFC and the HPC, IL-10 in the PFC, HPC, and HYP, MPO activity in the PFC, and N/N concentration and CAT activity in the HYP. Moreover, AYA decreased TBARS levels in the PFC and HPC and brain-derived neurotrophic factor (BDNF) in the PFC, and increased SOD activity in the cortex. Lastly, AYA increased CI activity in the HPC and cortex and decreased SDH and CK activity in the HPC.CONCLUSION: AYA administration following ischemic stroke modulates oxidativestress and neuroinflammation in the PFC, HPC, and HYP. Despite no significant improvements in neurological or behavioral scores, these molecular changes suggest a neuroprotective role of AYA. Future studies should explore the timing of AYA treatment and putative long-term effects on functional recovery, as well as its potential in other brain regions critical for cognitive and motor functions.

DOI: 10.1016/j.bbr.2025.115521
PMID: 40043852 [Indexed for MEDLINE]

13. **Acute Kidney Failure and Hemolysis Secondary to High-Dose Teucreum polium (Lamiaceae): Case Report**. Gholami L, Ahmadi SM, Pursusan S.

    Clin Case Rep. 2025 Mar 2;13(3):e70294. doi: 10.1002/ccr3.70294. eCollection 2025 Mar.

    Traditional medicine is becoming more popular worldwide. Teucrium polium belongs to the mint family and is a medicinal plant known for reducing blood sugar, hyperlipidemia, gastrointestinal tract issues, blood pressure, and urinary tract infections. High doses of this drug may cause liver and kidney toxicity, but this toxicity has not been thoroughly investigated. In this case report, we describe hemolysis and renal failure resulting from Arbitrary and traditional consumption of a high amount of Teucreum polium by the patient. After three cups of boiled Teucreum polium (each cup is approximately 200 cc) were administered to a 45-year-old white woman with an underlying hypertension disease with the intention of abortion, she developed abdominal pain, weakness, lethargy, nausea, fever, chills, anorexia, and hematuria. Laboratory investigations revealed severe hemolysis (LDH = 3903) and a decrease in hemoglobin to 4.7 mg/dL in 12 h. There was also a significant increase in the WBC, Retic count, BUN, and creatinine. A peripheral blood smear revealed +3 schistocytes and acanthosis. Viral markers, indirect coombs, and direct coombs were all negative. The primary diagnosis was acute intravascular hemolysis with renal failure. During treatment, with blood transfusion and hydration of the patient, liver and kidney function gradually improved. Due to the toxicity of medicinal plants, the unsupervised use of medicinal plants should be avoided.

    DOI: 10.1002/ccr3.70294
    PMCID: PMC11873361
    PMID: 40034718

14. **LC-MS-MS confirmation of 11-nor-9-carboxy-tetrahydrocannabinol (Δ8, Δ9, Δ10) and hexahydrocannabinol metabolites in authentic urine specimens**. Patton AL, Muir L, Seither JZ, Walterscheid JP, Karschner EL.

    J Anal Toxicol. 2025 Feb 15;49(2):96-103. doi: 10.1093/jat/bkae091.

    Recently, tetrahydrocannabinol (THC) isomers and other semi-synthetic cannabinoids have been introduced into the consumer market as alternatives to botanical cannabis. To assess the prevalence of these potential new analytical targets, a liquid chromatography-tandem mass spectrometry confirmation method was developed for the quantitation of seven cannabinoid metabolites and the qualitative identification of four others in urine. The validated method was applied to authentic urine specimens that screened positive by immunoassay (50 ng/mL cutoff; n = 1300). The most commonly observed analytes were 11-nor-9-carboxy-Δ8-THC (Δ8- THCCOOH) and Δ9-THCCOOH, with the combination of the two being the most prominent analyte combination found. In addition to these metabolites, Δ10-THCCOOH was observed in 77 specimens. This is the first study to report Δ10-THCCOOH in authentic urine specimens, with this analyte always appearing in combination with Δ9-THCCOOH. Cross-reactivity studies were performed for (6aR,9R)-Δ10-THCCOOH using the Beckman Coulter EMIT® II Plus Cannabinoid immunoassay and demonstrated cross-reactivity equivalent to the Δ9-THCCOOH cutoff, providing added confidence in the reported prevalence and detection

patterns. Additionally, 11-nor-9(R)-carboxy-hexahydrocannabinol (9(R)-HHCCOOH) was the most abundant stereoisomer (n = 12) in specimens containing HHC metabolites alone (n = 14). This is in contrast to 9(S)-HHCCOOH, which was the predominant stereoisomer in specimens containing Δ8- and/or Δ9-THCCOOH. Although HHC and Δ10-THC metabolites are emerging toxicology findings, based on these specimens collected between April 2022 and May 2024, an analytical panel containing Δ8- and Δ9-THCCOOH appears to be sufficient for revealing cannabinoid exposure within workplace monitoring and deterrence programs.

DOI: 10.1093/jat/bkae091
PMID: 39586679 [Indexed for MEDLINE]

15. **Two Cases and a Review of the Literature Regarding Severe Interstitial Lung Disease Induced by Hangeshashinto. osugi** Y, Murakami N, Muramoto Y, et al

Intern Med. 2025 Mar 15;64(6):905-910. doi: 10.2169/internalmedicine.4067-24. Epub 2024 Aug 10.

Hangeshashinto is a traditional Japanese herbal medicine that is widely recognized for its efficacy in relieving mucositis induced by chemotherapy and radiotherapy. We herein present the cases of two patients with head and neck cancer who were clinically diagnosed with severe drug-induced interstitial lung disease (DILD) following Hangeshashinto administration for radiation-induced mucositis. Although Hangeshashinto has beneficial properties, it is also associated with a relatively low incidence of DILD, including some reports of death. To ensure patient safety, greater attention should be paid when prescribing Hangeshashinto, especially for elderly patients with factors predisposing them to develop severe DILD.

DOI: 10.2169/internalmedicine.4067-24
PMCID: PMC11986299
PMID: 39135252 [Indexed for MEDLINE]