

AMERICAN ACADEMY OF CLINICAL TOXICOLOGY
Herbs & Dietary Supplements Special Interest Group

ABSTRACTING SERVICE

July 12, 2009

1. Gunduz A, Merice ES, Baydin A, Topbas M, Uzun H, Turedi S, Kalkan A. Does mad honey poisoning require hospital admission? *Am J Emerg Med.* 2009;27(4):424-7.
BACKGROUND: The aim of this study was to describe current patterns of monitoring and treatment of mad honey intoxication to make recommendations for a more standardized approach to care of patients with mad honey poisoning. METHODS: Patients presenting to emergency departments because of honey poisoning between January and October 2007. Age, length of stay in the emergency department, pulse rate, and systolic and diastolic blood pressure are cited as mean +/- SD. RESULTS: Forty-seven cases presenting to the 3 health institutions during 2007 were investigated. It was determined that patients had ingested "mad" honey between 0.5 and 9 hours (mean +/- SD, 2.8 +/- 1.8 hours) before presentation. Patients' pulse rates were 30 to 77/min (mean +/- SD, 46.6 +/- 12.1/min), and systolic blood pressure ranged from 50 to 140 mm Hg (mean +/- SD, 46.6 +/- 12.1 mm Hg). Patient rhythms on arrival were determined as 37 (7.7%) sinus bradycardia, 6 (12.8%) nodal rhythm, 3 (6.4%) normal sinus rhythm, and 1 (2.1%) complete atrioventricular block. Lengths of stay in hospital were 3.6 +/- 2.2 hours in the first university hospital, 22.2 +/- 3.8 hours in the second university hospital, and 3.4 +/- 1.7 hours in the state hospital. A 0.5 to 2 mg of atropine was given to all patients. CONCLUSIONS: Our study did not reveal any difference in complications or mortality between patients cared for with brief emergency department observation when compared with patients cared for with 1 day inpatient observation.
2. Truong D, Hindmarsh W, O'Brien PJ. The molecular mechanisms of diallyl disulfide and diallyl sulfide induced hepatocyte cytotoxicity. *Chem Biol Interact.* 2009;180(1):79-88.
Diallyl disulfide (DADS) and diallyl sulfide (DAS) are the major metabolites found in garlic oil and have been reported to lower cholesterol and prevent cancer. The molecular cytotoxic mechanisms of DADS and DAS have not been determined. The cytotoxic effectiveness of hydrogen versus allyl sulfides towards hepatocytes was found to be as follows: NaHS>DADS>DAS. Hepatocyte mitochondrial membrane potential was decreased and reactive oxygen species (ROS) and TBARS formation was increased by all three allyl sulfides. (1) DADS induced cytotoxicity was prevented by the H(2)S scavenger hydroxocobalamin, which also prevented cytochrome oxidase dependent mitochondrial respiration suggesting that H(2)S inhibition of cytochrome oxidase contributed to DADS hepatocyte cytotoxicity. (2) DAS cytotoxicity on the other hand was prevented by hydralazine, an acrolein trap. Hydralazine also prevented DAS induced GSH depletion, decreased mitochondrial membrane potential and increased ROS and TBARS formation. Chloral hydrate, the aldehyde dehydrogenase 2 inhibitor, however had the opposite effects, which could suggest that acrolein contributed to DAS hepatocyte cytotoxicity.
3. Garrouste C, Hemery M, Boudat AM, Kamar N. Amanita phalloides poisoning-induced end-stage renal failure. *Clin Nephrol.* 2009;71(5):571-4.
Fungi poisoning is quite frequent: in particular, Amanita phalloides has life-threatening toxicity. It is responsible for fulminant hepatitis, and also has renal toxicity. Herein, we report on a patient who developed acute renal failure after ingesting A. phalloides, which required definitive renal replacement therapy, despite rapid liver injury recovery. A kidney biopsy showed massive acute tubular necrosis, mainly in the proximal convoluted tubule, and mild interstitial infiltration by mononuclear cells.
4. Chan TY. Aconite poisoning. *Clin Toxicol (Phila).* 2009;47(4):279-85.

INTRODUCTION: Aconitine and related alkaloids found in the *Aconitum* species are highly toxic cardiotoxins and neurotoxins. The wild plant (especially the roots and root tubers) is extremely toxic. Severe aconite poisoning can occur after accidental ingestion of the wild plant or consumption of an herbal decoction made from aconite roots. In traditional Chinese medicine, aconite roots are used only after processing to reduce the toxic alkaloid content. Soaking and boiling during processing or decoction preparation will hydrolyze aconite alkaloids into less toxic and non-toxic derivatives. However, the use of a larger than recommended dose and inadequate processing increases the risk of poisoning. **METHODS:** A Medline search (1963-February 2009) was conducted. Key articles with information on the use of aconite roots in traditional medicine, active (toxic) ingredients, mechanisms of toxicity, toxicokinetics of *Aconitum* alkaloids, and clinical features and management of aconite poisoning were reviewed. **MECHANISMS OF TOXICITY:** The cardiotoxicity and neurotoxicity of aconitine and related alkaloids are due to their actions on the voltage-sensitive sodium channels of the cell membranes of excitable tissues, including the myocardium, nerves, and muscles. Aconitine and mesaconitine bind with high affinity to the open state of the voltage-sensitive sodium channels at site 2, thereby causing a persistent activation of the sodium channels, which become refractory to excitation. The electrophysiological mechanism of arrhythmia induction is triggered activity due to delayed after-depolarization and early after-depolarization. The arrhythmogenic properties of aconitine are in part due to its cholinolytic (anticholinergic) effects mediated by the vagus nerve. Aconitine has a positive inotropic effect by prolonging sodium influx during the action potential. It has hypotensive and bradycardic actions due to activation of the ventromedial nucleus of the hypothalamus. Through its action on voltage-sensitive sodium channels in the axons, aconitine blocks neuromuscular transmission by decreasing the evoked quantal release of acetylcholine. Aconitine, mesaconitine, and hypaconitine can induce strong contractions of the ileum through acetylcholine release from the postganglionic cholinergic nerves. **CLINICAL FEATURES:** Patients present predominantly with a combination of neurological, cardiovascular, and gastrointestinal features. The neurological features can be sensory (paresthesia and numbness of face, perioral area, and the four limbs), motor (muscle weakness in the four limbs), or both. The cardiovascular features include hypotension, chest pain, palpitations, bradycardia, sinus tachycardia, ventricular ectopics, ventricular tachycardia, and ventricular fibrillation. The gastrointestinal features include nausea, vomiting, abdominal pain, and diarrhea. The main causes of death are refractory ventricular arrhythmias and asystole and the overall in-hospital mortality is 5.5%. **MANAGEMENT:** Management of aconite poisoning is supportive, including immediate attention to the vital functions and close monitoring of blood pressure and cardiac rhythm. Inotropic therapy is required if hypotension persists and atropine should be used to treat bradycardia. Aconite-induced ventricular arrhythmias are often refractory to direct current cardioversion and antiarrhythmic drugs. Available clinical evidence suggests that amiodarone and flecainide are reasonable first-line treatment. In refractory cases of ventricular arrhythmias and cardiogenic shock, it is most important to maintain systemic blood flow, blood pressure, and tissue oxygenation by the early use of cardiopulmonary bypass. The role of charcoal hemoperfusion to remove circulating aconitine alkaloids is not established. **CONCLUSIONS:** Aconite roots contain aconitine, mesaconitine, hypaconitine, and other *Aconitum* alkaloids, which are known cardiotoxins and neurotoxins. Patients present predominantly with neurological, cardiovascular, and gastrointestinal features. Management is supportive; the early use of cardiopulmonary bypass is recommended if ventricular arrhythmias and cardiogenic shock are refractory to first-line treatment.

5. Lurie Y, Wasser SP, Taha M, Shehade H, Nijim J, Hoffmann Y, Basis F, Vardi M, Lavon O, et al. Mushroom poisoning from species of genus *Inocybe* (fiber head mushroom): a case series with exact species identification. *Clin Toxicol (Phila)*. 2009;47(6):562-5.
BACKGROUND: Many species of the genus *Inocybe* (family Cortinariaceae, higher Basidiomycetes) are muscarine-containing mycorrhizal mushrooms, ubiquitous around the world. The few published reports on the poisonous *Inocybe* mushrooms are often limited

by the inadequate identification of the species. The clinical course of patients with typical muscarinic manifestations, in whom *Inocybe* spp. was unequivocally identified, is reported. CASE SERIES: Between November 2006 and January 2008 14 consecutive patients with typical muscarinic syndrome after mushroom ingestion were recorded. The clinical manifestations included combinations of nausea, vomiting, diarrhea, abdominal pain, hypersalivation, diaphoresis, tachycardia, bradycardia, hypotension, lacrimation, blurred vision, miosis, tremor, restlessness, flushing, and syncope. Time to onset of toxicity ranged between 15 min and 2 h after consumption, 5 h in one patient. Treatment was supportive, including intravenous fluids, antiemetics, and 1 mg atropine intravenously. Full recovery ensued within 12 h. In all the cases, an expert mycologist unequivocally identified the leftovers of the consumed mushrooms as *Inocybe fastigiata*, *Inocybe geophylla*, and *Inocybe patouillardii*. CONCLUSION: In this case series of patients who ingested identified muscarine-containing mushrooms supportive treatment and atropine resulted in recovery in all cases.

6. Nayak B, Roy MM, Das B, Pal A, Sengupta MK, De SP, Chakraborti D. Health effects of groundwater fluoride contamination. *Clin Toxicol (Phila)*. 2009;47(4):292-5.
INTRODUCTION: The people in Berhait block, Sahibganj district, Jharkhand state, India, have been exposed chronically to fluoride-contaminated groundwater. Hereby, we report the clinical effects of chronic exposure to fluoride. METHODS: The study population was a convenience sample of 342 adults and 258 children living in the affected area. All volunteers filled out questionnaires and were examined. Well water from the six affected villages and urine samples were analyzed for fluoride using an ion-sensitive electrode. RESULTS: Twenty nine percent of 89 well water samples had fluoride concentrations above the Indian permissible limit of fluoride in drinking water. Eighty-five children and 72 adults had clinical fluorosis. Urine fluoride concentrations in children were 0.758-2.88 mg/L whereas in adults they were 0.331-10.36 mg/L. DISCUSSION: Clinical effects of fluoride included abnormal tooth enamel in children; adults had joint pain and deformity of the limbs and spine, along with ligamentous calcifications and exostosis formations in seven patients. Elevated urine fluoride concentrations supported the clinical diagnosis of fluorosis. Owing to insufficient fluoride-safe wells and lack of awareness of the danger of fluoride toxicity, villagers often drink fluoride-contaminated water. CONCLUSION: Villagers of Berhait block, including children, are at risk from chronic fluoride toxicity. To combat the situation, villagers need fluoride-safe water, education, and awareness of the danger about fluoride toxicity.
7. Schep LJ, Slaughter RJ, Becket G, Beasley DM. Poisoning due to water hemlock. *Clin Toxicol (Phila)*. 2009;47(4):270-8.
INTRODUCTION: Water hemlock, which encompasses a range of species divided across two genera (*Cicuta* and *Oenanthe*), are regarded as being among the most poisonous plants both in North America and in the United Kingdom. Despite their toxicity, the literature consists almost entirely of case reports. AIM: The aim of this review is to summarize this literature by covering all aspects of taxonomy and botanical characterization, principal toxins, basic pharmacology including mechanisms of toxicity, and the clinical features, diagnosis, and management of poisoning. MECHANISMS OF TOXICITY: The principal toxins, cicutoxin and oenanthotoxin, belong to a group of C17 conjugated polyacetylenes. They act as (noncompetitive) gamma-aminobutyric acid antagonists in the central nervous system (CNS), resulting in unabated neuronal depolarization that can lead to seizures. Ingestion of even a small amount of plant matter may result in severe intoxication. FEATURES: After ingestion, the patient is most likely to experience CNS stimulatory effects including seizures that, in the absence of aggressive supportive care, can result in death. Other features include nausea, vomiting, diarrhea, tachycardia, mydriasis, rhabdomyolysis, renal failure, coma, respiratory impairment, and cardiac dysrhythmias. MANAGEMENT: Treatment consists mainly of prompt airway management and seizure control, plus decontamination if achieved early and after stabilization. In the event of renal failure, the

use of hemodialysis has been employed successfully. CONCLUSIONS: The ingestion of water hemlock can lead to serious complications that may be fatal. Prognosis is good, however, if prompt supportive care is provided.

8. Krishnan S, Cairns R, Howard R. Cannabinoids for the treatment of dementia. *Cochrane Database Syst Rev.* 2009(2):CD007204.
BACKGROUND: Following the discovery of an endogenous cannabinoid system and the identification of specific cannabinoid receptors in the central nervous system, much work has been done to investigate the main effects of these compounds. There is increasing evidence that the cannabinoid system may regulate neurodegenerative processes such as excessive glutamate production, oxidative stress and neuroinflammation. Neurodegeneration is a feature common to the various types of dementia and this has led to interest in whether cannabinoids may be clinically useful in the treatment of people with dementia. Recent studies have also shown that cannabinoids may have more specific effects in interrupting the pathological process in Alzheimer's disease. OBJECTIVES: To determine from available research whether cannabinoids are clinically effective in the treatment of dementia. SEARCH STRATEGY: The Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG), The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS were searched on 11 April 2008 using the terms: cannabis or cannabinoid* or endocannabinoid* or cannabidiol or THC or CBD or dronabinol or delta-9-tetrahydrocannabinol or marijuana or marihuana or hashish. The CDCIG Specialized Register contains records from all major health care databases (The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS) as well as from many clinical trials registries and grey literature sources. SELECTION CRITERIA: All double-blind and single (rater)-blind randomized placebo controlled trials assessing the efficacy of cannabinoids at any dose in the treatment of people with dementia. DATA COLLECTION AND ANALYSIS: Two reviewers independently examined the retrieved studies for inclusion according to the selection criteria. They then independently assessed the methodological quality of selected trials and extracted data where possible. MAIN RESULTS: Only one study met the inclusion criteria. The data in the study report were presented in such a way that they could not be extracted for further analysis and there was insufficient quantitative data to validate the results. AUTHORS' CONCLUSIONS: This review finds no evidence that cannabinoids are effective in the improvement of disturbed behaviour in dementia or in the treatment of other symptoms of dementia. More randomized double-blind placebo controlled trials are needed to determine whether cannabinoids are clinically effective in the treatment of dementia.
9. Motoo Y, Arai I, Hyodo I, Tsutani K. Current status of Kampo (Japanese herbal) medicines in Japanese clinical practice guidelines. *Complement Ther Med.* 2009;17(3):147-54.
BACKGROUND AND AIMS: Kampo (Japanese herbal) medicines are often used in clinical practice in Japan. However, it is unclear how Kampo medicines are quoted and evaluated in current clinical practice guidelines (CPGs). Here, we systematically reviewed Japanese CPGs, and aimed to reveal how Kampo medicines are described in the CPGs. MATERIALS AND METHODS: We reviewed the quasi-comprehensive list of Japanese CPGs available from the Toho University Medical Media Center (TUMMC) having the largest data base on Japanese CPGs, and also used a hand search. CPGs containing Kampo products were classified into three types based on how Kampo was handled. CPGs that provided recommendations based on evidence were classified as "type A". Those which cited references but did not provide any recommendations were classified as "type B". Those which described the Kampo practice or Kampo-related terms without providing any relevant references were classified as "type C". RESULTS: By the end of March of 2007, 35 (10.1%) of 346 CPGs listed by TUMMC contained descriptions of Kampo products. We discovered one Kampo-related CPGs in a hand search process. Of these 36 CPGs, 6 were "type A", 13 were "type B", and 17 were "type C". Although results from pertinent randomized controlled trials (RCTs) were available, we noticed that some well-known RCTs

- studying Kampo medicines are missing in corresponding CPGs. CONCLUSIONS: We revealed that the citation rate of Kampo medicines in CPGs was approximately 10% and that some pivotal trials for Kampo medicines were not quoted in CPGs. Kampo medicines in CPGs should be assessed more comprehensively and scientifically.
10. Sarris J, Adams J, Wardle JL. Time for a reassessment of the use of Kava in anxiety? *Complement Ther Med.* 2009;17(3):121-2.
 11. Nardelli A, Morren MA, Goossens A. Contact allergy to fragrances and parabens in an atopic baby. *Contact Dermatitis.* 2009;60(2):107-9.
 12. Waters AJ, Sandhu DR, Lowe G, Ferguson J. Photocontact allergy to PABA in sunscreens: the need for continued vigilance. *Contact Dermatitis.* 2009;60(3):172-3.
 13. Mazzanti G, Menniti-Ippolito F, Moro PA, Cassetti F, Raschetti R, Santuccio C, Mastrangelo S. Hepatotoxicity from green tea: a review of the literature and two unpublished cases. *Eur J Clin Pharmacol.* 2009;65(4):331-41.
PURPOSE: To review the current literature on suspected green tea-related hepatic reactions and to describe two new cases reported within the framework of the Italian surveillance system of natural health products. RESULTS: A literature search of publication between 1999 and October 2008 retrieved 34 cases of hepatitis. Histological examination of the liver revealed inflammatory reactions, cholestasis, occasional steatosis, and necrosis. A positive dechallenge was reported in 29 cases. There was one reported death. A positive rechallenge occurred in seven cases (20%). In the two new cases, the causality assessment was judged as "possible" according to the RUCAM score. CONCLUSIONS: Our analysis of the published case reports suggests a causal association between green tea and liver damage. The hepatotoxicity is probably due to (-)-epigallocatechin gallate or its metabolites which, under particular conditions related to the patient's metabolism, can induce oxidative stress in the liver. In a few cases, toxicity related to concomitant medications could also be involved.
 14. Triunfante P, Soares ME, Santos A, Tavares S, Carmo H, Bastos Mde L. Mercury fatal intoxication: two case reports. *Forensic Sci Int.* 2009;184(1-3):e1-6.
We report two cases of fatal intoxications with mercury, one intentional and the other allegedly resulting from a drug formulation mistake. Both cases occurred in the year of 2004. The first case refers to a man who ingested a great portion of a mercuric chloride solution. He attended a hospital emergency, submitted to treatment, but died after 49 days. In the second case, a woman applied on the chest skin an ointment containing a great quantity of mercury bromide. After 7 days of treatment in the hospital, she died. In both cases, samples of tissues and organs were collected at autopsy for mercury analysis. Because methylation of mercury in humans after exposure to metallic or inorganic mercury is almost unknown, both total mercury and methylmercury were quantified in the post-mortem samples. The quantifications were carried out by Cold Vapour Generation Atomic Absorption Spectrometry for total mercury and by HPLC-UV for methylmercury. The total mercury contents found in the post-mortem fluid and tissue samples were consentaneous with mercury poisoning. For the first case, the concentrations found, expressed in microg/g wet weight, were in the liver 49.9, lung 3.27 and brain 0.33, and for blood 11.7 microg/mL. For the second case, the concentrations expressed in microg/g wet weight were in the liver 46.6, lung 14.6, brain 0.21, kidney 77.7, stomach 7.12, spleen 6.4 and heart 2.34, and for blood and urine 2.95 and 1.40 microg/mL, respectively. Only in the first case was methylmercury found and quantified in liver (1.70 microg/g wet weight) and in blood (0.15 microg/mL) samples.
 15. Doumouchsis KK, Doumouchsis SK, Doumouchsis EK, Perrea DN. The effect of lead

intoxication on endocrine functions. *J Endocrinol Invest.* 2009;32(2):175-83.

Studies on the effects of lead on the endocrine system are mainly based on occupationally lead-exposed workers and experimental animal models. Although evidence is conflicting, it has been reported that accumulation of lead affects the majority of the endocrine glands. In particular, it appears to have an effect on the hypothalamic-pituitary axis causing blunted TSH, GH, and FSH/LH responses to TRH, GHRH, and GnRH stimulation, respectively. Suppressed GH release has been reported, probably caused by reduced synthesis of GHRH, inhibition of GHRH release or reduced somatotrope responsiveness. Higher levels of PRL in lead intoxication have been reported. In short-term lead-exposed individuals, high LH and FSH levels are usually associated to normal testosterone concentrations, whereas in long-term exposed individuals' low testosterone levels do not induce high LH and FSH concentrations. These findings suggest that lead initially causes some subclinical testicular damage, followed by hypothalamic or pituitary disturbance when longer periods of exposure take place. Similarly, lead accumulates in granulosa cells of the ovary, causing delays in growth and pubertal development and reduced fertility in females. In the parenchyma of adrenals histological and cytological changes are demonstrated, causing changes in plasma basal and stress-mediated corticosterone concentrations and reduced cytosolic and nuclear glucocorticoid receptor binding. Thyroid hormone kinetics are also affected. Central defect of the thyroid axis or an alteration in T4 metabolism or binding to proteins may be involved in derangements in thyroid hormone action. Lead toxicity involves alterations on calcitropic hormones' homeostasis, which increase the risk of skeletal disorders.

16. Fu PP, Chiang HM, Xia Q, Chen T, Chen BH, Yin JJ, Wen KC, Lin G, Yu H. Quality assurance and safety of herbal dietary supplements. *J Environ Sci Health C Environ Carcinog Ecotoxicol Rev.* 2009;27(2):91-119.

Since the U.S. Congress passed the Dietary Supplement Health and Education Act (DSHEA) in 1994, use of herbal products has been growing rapidly worldwide. To ensure consumer health protection, the quality and safety of herbal plants, particularly those used for dietary supplement preparations, must be determined. To date, toxicological data on the identification of genotoxic and tumorigenic ingredients in many raw herbs and their mechanisms of action are lacking. Thus, identification of carcinogenic components in herbal plants is timely and important. In this review, the issues of quality control and safety evaluation of raw herbs and herbal dietary supplements are discussed. Two examples of tumorigenicity and mechanism of tumor induction are discussed: aristolochic acid and riddelliine, both of which have been detected in Chinese herbal plants. It is proposed that an organized effort with international participation on cancer risk assessment should be actively pursued so that the safety of commercial herbal plants and herbal dietary supplements can be ensured.

17. Cohen PJ. Medical marijuana: the conflict between scientific evidence and political ideology. Part one of two. *J Pain Palliat Care Pharmacother.* 2009;23(1):4-25.
- Whether "medical marijuana" (*Cannabis sativa* used to treat a wide variety of pathologic states) should be accorded the status of a legitimate pharmaceutical agent has long been a contentious issue. Is it a truly effective drug that is arbitrarily stigmatized by many and criminalized by the federal government? Or is it without any medical utility, its advocates hiding behind a screen of misplaced (or deliberately misleading) compassion for the ill? Should Congress repeal its declaration that smoked marijuana is without "current medical benefit"? Should cannabis be approved for medical use by a vote of the people as already has been done in 13 states? Or should medical marijuana be scientifically evaluated for safety and efficacy as any other new investigational drug? How do the competing--and sometimes antagonistic--roles of science, politics and prejudice affect society's attempts to answer this question? This article examines the legal, political, policy, and ethical problems raised by the recognition of medical marijuana by over one-fourth of our states although its use remains illegal under federal law. Although draconian punishment can be imposed for

the "recreational" use of marijuana, I will not address the contentious question of whether to legalize or decriminalize the use of marijuana solely for its psychotropic effects, a fascinating and important area of law and policy that is outside the scope of this paper. Instead, the specific focus of this article will be on the conflict between the development of policies based on evidence obtained through the use of scientific methods and those grounded on ideological and political considerations that have repeatedly entered the longstanding debate regarding the legal status of medical marijuana. I will address a basic question: Should the approval of medical marijuana be governed by the same statute that applies to all other drugs or pharmaceutical agents, the Food, Drug, and Cosmetic Act (FD&C Act), after the appropriate regulatory agency, the Food and Drug Administration (FDA), has evaluated its safety and efficacy? If not, should medical marijuana be exempted from scientific review and, instead, be evaluated by the Congress, state legislatures, or popular vote? I will argue that advocacy is a poor substitute for dispassionate analysis, and that popular votes should not be allowed to trump scientific evidence in deciding whether or not marijuana is an appropriate pharmaceutical agent to use in modern medical practice.

18. Christl SU, Seifert A, Seeler D. Toxic hepatitis after consumption of traditional kava preparation. *J Travel Med.* 2009;16(1):55-6.
Liver toxicity from the use of kava dietary supplements has been reported, but little is known about the side effects of traditional kava preparations. We present a case study of a tourist who developed serious toxic liver disease after consumption of kava beverages in traditional Samoan kava ceremonies.
19. Lai MN, Lai JN, Chen PC, Tseng WL, Chen YY, Hwang JS, Wang JD. Increased risks of chronic kidney disease associated with prescribed Chinese herbal products suspected to contain aristolochic acid. *Nephrology (Carlton).* 2009;14(2):227-34.
AIM: Nephropathy associated with aristolochic acid (AA) has been documented by human and animal studies. Ancient Chinese herbology claimed to reduce toxicity in their mixtures. It was the objective of this study to determine the risk of chronic kidney disease (CKD) associated with AA-related Chinese herbal products (CHP) or mixtures of herbs in a national cohort. METHODS: A retrospective follow-up study was conducted, using a systematic random sample (200 000 people) in the National Health Insurance reimbursement database during 1997-2002. The incidence rates of CKD and end-stage renal disease (ESRD) were calculated for the whole sample and those that had used CHP suspected to contain AA. Cox regression models were constructed to control potential confounders, including age, sex, hypertension, diabetes mellitus, and use of non-steroidal anti-inflammatory drugs and acetaminophen. RESULTS: A total of 199 843 persons were included in the final analysis, 102 464 (51.3%) men and 97 379 (48.7%) women, with an average incidence rate of 1964/10(6) person-years for CKD and 279/10(6) person-years for ESRD. After controlling other risk factors, the hazard ratios for development of CKD seemed to increase for patients that had consumed more than 30 g Mu-Tong, and more than 60 g Fangchi. CONCLUSION: Prescription of more than 30 g Mu-Tong or more than 60 g Fangchi CHP was associated with an increased risk of developing CKD. In addition to prohibiting the use of Guan-Mu-Tong and Guang-Fangchi, patients who have used these CHP should continue to be followed up.
20. Chen Y, Zhu B, Zhang L, Yan S, Li J. Experimental study of the bone marrow protective effect of a traditional Chinese compound preparation. *Phytother Res.* 2009;23(6):823-6.
This study investigated the effect of Wei Gan Li on bone marrow haemopoiesis in myelosuppressed anaemic mice induced by (60)Cogamma, cyclophosphamide and chloramphenicol. After treatment with Wei Gan Li, colony forming units of granulocyte macrophages, erythroid cells, burst forming unit-erythroid cells, megakaryocytes and the proliferation of bone marrow stromal cells were measured by in vitro cell culture techniques. Bone marrow haemopoietic stem cells were measured by flow cytometry. The peripheral blood cell count was found to have significantly recovered after Wei Gan Li

administration and the proliferation of bone marrow haemopoietic stem/progenitor cells and BMSC were also significantly increased. Wei Gan Li was therefore found to promote the recovery of bone marrow haemopoietic function in myelosuppressed anaemic mice.

21. Franco JL, Posser T, Mattos JJ, Trevisan R, Brocardo PS, Rodrigues AL, Leal RB, Farina M, Marques MR, et al. Zinc reverses malathion-induced impairment in antioxidant defenses. *Toxicol Lett.* 2009;187(3):137-43.
Malathion toxicity has been related to the inhibition of acetylcholinesterase and induction of oxidative stress, while zinc has been shown to possess neuroprotective effects in experimental and clinical studies. In the present study the effect of zinc chloride (zinc) was addressed in adult male Wistar rats following a long-term treatment (30 days, 300mg/L in tap water ad libitum) against an acute insult caused by a single malathion exposure (250mg/kg, i.p.). Malathion produced a significant decrease in hippocampal acetylcholinesterase, as well as a decrease in the activity of several hippocampal antioxidant enzymes: glutathione reductase, glutathione S-transferase, catalase and superoxide dismutase. The pretreatment with zinc did not completely prevent acetylcholinesterase activity impairment; however, antioxidant activity was completely restored. Zinc administration significantly increased HSP60, but not HSP70, expression. The HSP60 increase suggests a novel zinc-dependent pathway, which may be related to a counteracting mechanism against malathion effects. Based on these results the following hypothesis can be presented: the published "pro-oxidative" effect of malathion may be related, among others, to compromised antioxidant defenses, while the zinc "antioxidant" action may be related to the preservation of antioxidant defenses. In conclusion, our data points to the inhibition of antioxidant enzymes as an important non-cholinergic effect of malathion, which can be rescued by oral zinc treatment.
22. Dara L, Hewett J, Lim JK. Hydroxycut hepatotoxicity: a case series and review of liver toxicity from herbal weight loss supplements. *World J Gastroenterol.* 2008;14(45):6999-7004.
Dietary supplements represent an increasingly common source of drug-induced liver injury. Hydroxycut is a popular weight loss supplement which has previously been linked to hepatotoxicity, although the individual chemical components underlying liver injury remain poorly understood. We report two cases of acute hepatitis in the setting of Hydroxycut exposure and describe possible mechanisms of liver injury. We also comprehensively review and summarize the existing literature on commonly used weight loss supplements, and their individual components which have demonstrated potential for liver toxicity. An increased effort to screen for and educate patients and physicians about supplement-associated hepatotoxicity is warranted.
23. Sontineni SP, Chaudhary S, Sontineni V, Lanspa SJ. Cannabinoid hyperemesis syndrome: clinical diagnosis of an underrecognised manifestation of chronic cannabis abuse. *World J Gastroenterol.* 2009;15(10):1264-6.
Cannabis is a common drug of abuse that is associated with various long-term and short-term adverse effects. The nature of its association with vomiting after chronic abuse is obscure and is underrecognised by clinicians. In some patients this vomiting can take on a pattern similar to cyclic vomiting syndrome with a peculiar compulsive hot bathing pattern, which relieves intense feelings of nausea and accompanying symptoms. In this case report, we describe a twenty-two year-old-male with a history of chronic cannabis abuse presenting with recurrent vomiting, intense nausea and abdominal pain. In addition, the patient reported that the hot baths improved his symptoms during these episodes. Abstinence from cannabis led to resolution of the vomiting symptoms and abdominal pain. We conclude that in the setting of chronic cannabis abuse, patients presenting with chronic severe nausea and vomiting that can sometimes be accompanied by abdominal pain and compulsive hot bathing behaviour, in the absence of other obvious causes, a diagnosis of

cannabinoid hyperemesis syndrome should be considered.