

**AMERICAN ACADEMY OF CLINICAL TOXICOLOGY**  
**Herbs & Dietary Supplement Special Interest Group**  
**Abstracting Service**

August 30, 2009

1. Hsu HR, Mei YY, Wu CY, Chiu PH, Chen HH. Behavioural and toxic interaction profile of ketamine in combination with caffeine. *Basic Clin Pharmacol Toxicol.* 2009;104(5):379-83.  
Ketamine street tablets often contain several other compounds in addition to ketamine, among them is caffeine. The purpose of this study was to examine whether caffeine interacts with ketamine-induced behavioural and toxic effects. Male ICR mice were treated with ketamine alone or ketamine combined with various doses of caffeine, then the locomotor activity, rotarod test, prepulse inhibition of acoustic startle, loss of righting reflex, and mortality rate were examined. Caffeine enhanced the locomotor hyperactivity, caused disruption of the rotarod performance, and mortality rates due to ketamine, whereas prepulse inhibition deficits and anaesthesia remained unaffected. These findings demonstrate that use of ketamine in combination with caffeine enhances its stimulant responses and lethal risk, suggesting that a potentially toxic interaction exists between ketamine and caffeine.
2. Cao ZY, Chen XZ, Chang ET, Du J. Effective components of Chinese herbal compound decoction and Maillard reaction. *Chin J Integr Med.* 2009;15(3):224-8.  
This paper intends to explore the color changes considered to be Maillard reaction during the process of Chinese herbal medicine. The Maillard reaction products (MRPs) are often in substantial proportions of Chinese herbal compound decoctions but their effects are often neglected. By considering the effects of MRPs in studies of effective components on Chinese herbal compounds, a new perspective is established in future researches of Chinese herbal compound decoctions.
3. Dumont GJ, Kramers C, Sweep FC, Touw DJ, van Hasselt JG, de Kam M, van Gerven JM, Buitelaar JK, Verkes RJ. Cannabis coadministration potentiates the effects of "ecstasy" on heart rate and temperature in humans. *Clin Pharmacol Ther.* 2009;86(2):160-6.  
This study assessed the acute physiologic effects over time of (co)administration of Delta9-tetrahydrocannabinol (Delta9-THC) (the main psychoactive compound of cannabis) and 3,4-methylenedioxymethamphetamine (MDMA or "ecstasy") in 16 healthy volunteers. Pharmacokinetics and cardiovascular, temperature, and catecholamine responses were assessed over time. Both single-drug conditions robustly increased heart rate, and coadministration showed additive effects. MDMA increased epinephrine and norepinephrine concentrations, whereas THC did not affect the catecholamine response. Coadministration of MDMA and THC attenuated the increase of norepinephrine concentrations relative to administration of MDMA alone. These results show that THC mediates heart rate increase independent of sympathetic (catecholaminergic) activity, probably through direct cannabinoid receptor type 1 (CB(1)) agonism in cardiac tissue. Furthermore, THC coadministration did not prevent MDMA-induced temperature increase, but it delayed the onset and prolonged the duration of temperature elevation. These effects may be of particular relevance for the cardiovascular safety of ecstasy users who participate in energetic dancing in nightclubs with high ambient temperature.

4. Bjornstad K, Hulten P, Beck O, Helander A. Bioanalytical and clinical evaluation of 103 suspected cases of intoxications with psychoactive plant materials. *Clin Toxicol (Phila)*. 2009;47(6):566-72.  
INTRODUCTION: Problems associated with the increasing abuse of plant-derived psychoactive substances have recently attracted attention. This study involved bioanalytical and clinical examinations of intoxication cases suspected to be linked to such plant materials. METHODS: Urine samples were collected at emergency wards in Sweden from patients who either admitted or were suspected of ingestion of psychoactive plant materials. The bioanalytical investigation employed a liquid chromatography-tandem mass spectrometry multicomponent method covering 10 plant-derived substances (atropine, dimethyltryptamine, ephedrine, harmaline, harmine, ibogaine, lysergic acid amide, psilocin, scopolamine, and yohimbine) and a gas chromatography-mass spectrometry method for asarone. Routine testing for illicit drugs was also performed. RESULTS: Over a 4-year period, 103 urine samples collected from mainly young people (age range 13-52 years, median 19) were studied. Among 53 cases where ingestion of any of the 11 plant-derived substances covered in this study was admitted or suspected, 41 (77%) could be confirmed bioanalytically. Nine of the 11 substances tested for were detected, the exceptions being ibogaine and yohimbine. Psilocin, originating from ingestion of hallucinogenic mushrooms, was the most frequent drug accounting for 54% of the cases. The most common means of drug acquisition (56%) was purchase over the Internet. CONCLUSION: The patients using psychoactive plant materials were mainly young and commonly used the Internet for drug acquisition. Having access to bioanalytical methods for detection of plant-derived psychoactives is therefore considered important, when providing clinical toxicology service.
5. Cheung WI, Tse ML, Ngan T, Lin J, Lee WK, Poon WT, Mak TW, Leung VK, Chau TN. Liver injury associated with the use of Fructus Psoraleae (Bol-gol-zhee or Bu-gu-zhi) and its related proprietary medicine. *Clin Toxicol (Phila)*. 2009;47(7):683-5.  
Fructus Psoraleae (FP) is used by herbalists for the treatment of postmenopausal osteoporosis, vitiligo, and psoriasis. It is used alone, or in combination with other herbs, in some countries in the form of proprietary medicine. It is recognized as one of the emerging hepatotoxins and here we report three cases of acute hepatitis after exposed to FP and its related proprietary medicine. It seems possible that psoralen and its related chemicals may be responsible for the hepatotoxicity. Decoction with other herbs may result in higher concentration of toxic constituents and in more severe liver injury. In summary, FP is associated with hepatotoxicity in some individuals. Pharmacovigilance for the potential side effects of herbal products is necessary.
6. Flower A, Liu JP, Chen S, Lewith G, Little P. Chinese herbal medicine for endometriosis. *Cochrane Database Syst Rev*. 2009(3):CD006568.  
BACKGROUND: Endometriosis is characterized by the presence of tissue that is morphologically and biologically similar to normal endometrium in locations outside the uterus. Surgical and hormonal treatment of endometriosis have unpleasant side effects and high rates of relapse. In China, treatment of endometriosis using Chinese herbal medicine (CHM) is routine and considerable research into the role of CHM in alleviating pain, promoting fertility, and preventing relapse has taken place. OBJECTIVES: To review the effectiveness and safety of

CHM in alleviating endometriosis-related pain and infertility. SEARCH STRATEGY: We searched the Menstrual Disorders and Subfertility Group Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library) and the following English language electronic databases (from their inception to the present): MEDLINE, EMBASE, AMED, CINAHL, NLH on the 30/04/09. We also searched Chinese language electronic databases: Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Chinese Sci & Tech Journals (VIP), Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), and Chinese Medical Current Contents (CMCC). SELECTION CRITERIA: Randomised controlled trials (RCTs) involving CHM versus placebo, biomedical treatment, another CHM intervention, or CHM plus biomedical treatment versus biomedical treatment were selected. Only trials with confirmed randomisation procedures and laparoscopic diagnosis of endometriosis were included. DATA COLLECTION AND ANALYSIS: Risk of bias assessment, and data extraction and analysis were performed independently by three review authors. Data were combined for meta-analysis using relative risk (RR) for dichotomous data. A fixed-effect statistical model was used, where appropriate. Data not suitable for meta-analysis are presented as descriptive data. MAIN RESULTS: Two Chinese RCTs involving 158 women were included in this review. Both these trials described adequate methodology. Neither trial compared CHM with placebo treatment. There was no evidence of a significant difference in rates of symptomatic relief between CHM and gestrinone administered subsequent to laparoscopic surgery (95.65% versus 93.87%; risk ratio (RR) 1.02, 95% confidence interval (CI) 0.93 to 1.12, one RCT). The intention-to-treat analysis also showed no significant difference between the groups (RR 1.04, 95% CI 0.91 to 1.18). There was no significant difference between the CHM and gestrinone groups with regard to the total pregnancy rate (69.6% versus 59.1%; RR 1.18, 95% CI 0.87 to 1.59, one RCT). CHM administered orally and then in conjunction with a herbal enema resulted in a greater proportion of women obtaining symptomatic relief than with danazol (RR 5.06, 95% CI 1.28 to 20.05; RR 5.63, 95% CI 1.47 to 21.54, respectively). Overall, 100% of women in all the groups showed some improvement in their symptoms. Oral plus enema administration of CHM showed a greater reduction in average dysmenorrhoea pain scores than did danazol (mean difference (MD) -2.90, 95% CI -4.55 to -1.25;  $P < 0.01$ ). Combined oral and enema administration of CHM showed a greater improvement, measured as the disappearance or shrinkage of adnexal masses, than with danazol (RR 1.70, 95% CI 1.04 to 2.78). For lumbosacral pain, rectal discomfort, or vaginal nodules tenderness, there was no significant difference either between CHM and danazol. AUTHORS' CONCLUSIONS: Post-surgical administration of CHM may have comparable benefits to gestrinone but with fewer side effects. Oral CHM may have a better overall treatment effect than danazol; it may be more effective in relieving dysmenorrhea and shrinking adnexal masses when used in conjunction with a CHM enema. However, more rigorous research is required to accurately assess the potential role of CHM in treating endometriosis.

7. Li Q, Chen X, He L, Zhou D. Traditional Chinese medicine for epilepsy. *Cochrane Database Syst Rev.* 2009(3):CD006454.

BACKGROUND: Seizures are poorly controlled in many people with epilepsy, despite current antiepileptic treatments. Some turn to alternative or complementary therapy to treat their condition and the use of traditional Chinese medicinal herbs (TCMH) is increasingly popular. However, it remains unclear whether the existing

evidence is rigorous enough to support its use. OBJECTIVES: To determine the effectiveness and safety of traditional Chinese medicine in people with epilepsy. SEARCH STRATEGY: Our search included the Cochrane Epilepsy Group's Specialised Register and the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2007, Issue 1), MEDLINE (1950 to 2007) and EMBASE (1974 to 2007). SELECTION CRITERIA: Randomised controlled trials evaluating traditional Chinese medicine in people of any age with any type of epilepsy, and comparing one formula of TCM with no intervention, placebo or single Western medicine (monotherapy). DATA COLLECTION AND ANALYSIS: Two review authors independently extracted trial data and assessed quality. We assessed the following outcomes: (a) seizure freedom for at least one year; (b) 50% or greater reduction in seizure frequency; (c) percentage reduction in seizure frequency and duration; and (d) adverse events. MAIN RESULTS: Five short-term studies involving 1125 participants met the inclusion criteria. All the studies were of poor methodological quality and had a high probability of selection, detection and performance bias. Two studies assessed seizure freedom for one year. One found no difference between Xiaxingci granule and phenytoin for primary generalized tonic-clonic seizures (RR 1.00; 95% CI 0.07 to 14.90). The other study found no difference between Dianxianning pill and valproate (RR 13.00; 95% CI 0.74 to 227.72) for different types of epilepsy. Three studies assessed a 50% or greater reduction in seizure frequency. One found an advantage for Tianmadingxian capsule when compared to phenytoin (RR 1.37; 95% CI 1.23 to 1.53) in different types of epilepsy, the second an advantage for Zhixian I pill when compared to phenytoin (RR 1.31; 95% CI 1.16 to 1.48) in primary generalized tonic-clonic seizure, and the third an advantage for an 'Antiepilepsy capsule' when compared to phenobarbital (RR 1.21; 95% CI 1.02 to 1.43) for primary and secondary generalized tonic-clonic seizure. One study reported the incidence of adverse effects and the Peto odds ratio was 0.04 (99% CI 0.01 to 0.12,  $P < 0.00001$ ) favouring TCMH compared to phenobarbital. AUTHORS' CONCLUSIONS: The current evidence is insufficient to support the use of traditional Chinese medicine as a treatment for epilepsy. Much larger, high quality randomised clinical trials are needed to evaluate the effectiveness and safety of traditional Chinese medicinal herbs for treating epilepsy.

8. Marques RC, Dorea JG, Bernardi JV, Bastos WR, Malm O. Prenatal and postnatal mercury exposure, breastfeeding and neurodevelopment during the first 5 years. *Cogn Behav Neurol.* 2009;22(2):134-41.

OBJECTIVE: We evaluated the association between infant hair-Hg and Gesell schedules (GS). BACKGROUND: Longitudinal assessment of prenatal and postnatal Hg exposure during the first 60 months. METHODS: We used hair-Hg as a marker of postnatal Hg exposure (inorganic and methyl-Hg from breast milk, and ethyl-Hg from thimerosal) and GS measured at 6, 36, and 60 months. RESULTS: Hair-Hg at 6 months responded to events related to Hg exposure and breastfeeding. However, most neurodevelopment delays observed at 6 months were overcome with infant growth; at 60 months 87% of children showed adequate GS (>85). Length of lactation and hair-Hg were each significantly correlated with GS, but in opposite ways: length of lactation was positive and significantly correlated with all GS at 60 months; hair-Hg concentrations were negative and significantly correlated with GS at 6 months ( $r=-0.333$ ;  $P=0.002$ ) and 60 months ( $r=-0.803$ ;  $P=0.010$ ), but not at 36 months. Multiple regression models showed that the GS outcome at 60 months

depended on GS at 36 months that in turn was influenced by infants' developmental and Hg exposure variables. GS at 6 months was significantly influenced by prenatal (maternal and infant hair-Hg at birth) and postnatal Hg exposure at 6 months. CONCLUSIONS: Until there is more refined approach to recognize children sensitive to Hg exposure, and in situations of uncertainty (EtHg exposure), the neurodevelopment benefit of breastfeeding should be recommended.

9. Shankland WE, 2nd. Four common herbs seen in dental practice: properties and potential adverse effects. *Cranio*. 2009;27(2):118-24.  
The use of herbal supplements in North America is steadily growing and raises concerns about safety, efficacy, and how they affect safe patient care. The most notable and direct health risks associated with herbal supplements include hypertension, prolonged bleeding, and the potential for drug-herb interactions, which is of particular concern for patients undergoing anesthesia, both general and local anesthesia. In this article, four of the most commonly used herbs today in North America will be discussed: garlic, ginkgo, ginseng, and ginger. The pharmacology, benefits, and possible side effects of these herbs will be presented. Awareness of the rising use of herbs is important to prevent, recognize, and treat potential problems that can arise from herbal preparations taken alone or in conjunction with prescription medications.
10. Jager G, Ramsey NF. Long-term consequences of adolescent cannabis exposure on the development of cognition, brain structure and function: an overview of animal and human research. *Curr Drug Abuse Rev*. 2008;1(2):114-23.  
Over the last decade there has been a steady increase in the prevalence of frequent cannabis use among teenagers, accompanied by a decrease in age of first use. Evidence from both animal and human studies suggests that the severity of the effects of cannabis use on cognitive development is dependent on the age when cannabis use begins. One possible explanation is that those who begin cannabis use early in adolescence are more likely to become heavily dependent. It is plausible that chronic cannabis abuse will then interfere with educational and vocational training. From a more biological perspective, however, use of cannabis during critical developmental periods in the still maturing brain may induce persistent alterations in brain structure and brain function. Therefore, the effects of frequent cannabis use during adolescence could be different from and more serious than during adulthood, an issue increasingly recognized in the field of cannabis research. In this paper we review the relevant animal and human literature on long-term effects of frequent exposure to cannabis during adolescence on the development of cognition, brain structure and function, and discuss implications, methodological and conceptual issues, and future prospects.
11. Panagis G, Vlachou S, Nomikos GG. Behavioral pharmacology of cannabinoids with a focus on preclinical models for studying reinforcing and dependence-producing properties. *Curr Drug Abuse Rev*. 2008;1(3):350-74.  
Cannabis preparations as recreational drugs are the most widely used illicit drugs in the world. Although cannabis derivatives produce clear subjective motivational responses in humans leading to drug-seeking behavior and in a specific proportion in repeated drug use, the reinforcing/rewarding attributes of these subjective effects are difficult to define in experimental animals. This led to the notion of

cannabinoids being considered as "atypical" or "anomalous" drugs of abuse. To this end, our knowledge and understanding of the way cannabis and its main psychoactive constituent, Delta(9)-tetrahydrocannabinol (Delta(9)-THC), act in the central nervous system to exert their reinforcing/rewarding effects is far from complete. The aim of the present article is to review from a preclinical perspective the current status of what is known about the behavioral pharmacology of cannabinoids including the recently identified cannabinoid neurotransmission modifiers with a particular emphasis on their motivational/reinforcing and dependence-producing properties. We conclude that cannabinoids exhibit reinforcing/rewarding properties in experimental animals mostly under particular experimental conditions, which is not the case for other drugs of abuse, such as opiates, psychostimulants, alcohol and nicotine. The paper will discuss these findings critically and also point to open questions that should be addressed in the future in order to improve our understanding of these specific actions of cannabinoids that will also impact drug discovery and development efforts of related compounds as therapeutics in the clinic.

12. Tweddell P, Boyle C. Potential interactions with herbal medications and midazolam. *Dent Update*. 2009;36(3):175-8.  
In the management of patients who require intravenous sedation with midazolam care must be taken if the patient is taking herbal drugs. There is a potential for harmful drug interactions between herbal drugs and midazolam. Assessment of which herbal drugs a patient is taking should be part of the treatment planning stage so interactions can be avoided or anticipated. Clinical Relevance: Growing numbers of patients are taking herbal or Chinese medication and may not disclose this to the sedation team. Such drugs have the potential for interactions and can affect induction and recovery from sedation.
13. Siems W, Salerno C, Crifo C, Sommerburg O, Wiswedel I. Beta-carotene degradation products - formation, toxicity and prevention of toxicity. *Forum Nutr*. 2009;61(75-86).  
Carotenoids are widely used as important micronutrients in food. Furthermore, carotenoid supplementation has been used in the treatment of diseases associated with oxidative stress such as various types of cancer, inflammatory diseases or cystic fibrosis. However, in some clinical studies harmful effects have been observed, e.g. a higher incidence of lung cancer in individuals exposed to extraordinary oxidative stress. The causal mechanisms of harmful effects are still unclear. Carotenoid breakdown products (CBPs) including highly reactive aldehydes and epoxides are formed during oxidative attacks in the course of antioxidative action. We investigated the formation of CBPs by stimulated neutrophils (and at further conditions), tested the hypothesis that CBPs may exert mitochondriotoxicity and tried to prevent toxicity in the presence of members of the antioxidative network. Stimulated neutrophils are able to degrade beta-carotene and to generate a number of CBPs. Concerning mitochondriotoxicity, we found that CBPs strongly inhibit state 3 respiration of rat liver mitochondria at concentrations between 0.5 and 20 microM. This was true for retinal, beta-ionone, and for mixtures of cleavage/breakdown products. The inhibition of mitochondrial respiration was accompanied by a reduction in protein sulfhydryl content, decreasing GSH levels and redox state, and elevated accumulation of malondialdehyde. Changes in mitochondrial membrane potential favor functional deterioration in the adenine nucleotide translocator as a sensitive target. The presence of additional antioxidants

such as alpha-tocopherol, ascorbic acid, N-acetyl-cysteine or others could mitigate mitochondriotoxicity. The findings reflect a basic mechanism of increasing the risk of cancer induced by carotenoid degradation products.

14. Wu T, Yang X, Zeng X, Eslick GD. Traditional Chinese medicinal herbs in the treatment of patients with esophageal cancer: a systematic review. *Gastroenterol Clin North Am.* 2009;38(1):153-67, x.  
Traditional Chinese medicines are sometimes used as an adjunct to radiotherapy or chemotherapy for esophageal cancer. These medicines may have a benefit on the survival and quality of life of patients who have advanced esophageal cancer. Evidence from current studies appears weak due to methodological limitations. Due to conflicting reports, it is difficult to argue for or against the use of traditional Chinese medicines as a treatment for esophageal cancer.
15. Cooper ZD, Haney M. Actions of delta-9-tetrahydrocannabinol in cannabis: relation to use, abuse, dependence. *Int Rev Psychiatry.* 2009;21(2):104-12.  
Cannabis use disorders have been recently identified as a relevant clinical issue: a subset of cannabis smokers seeks treatment for their cannabis use, yet few succeed in maintaining long-term abstinence. The rewarding and positive reinforcing effects of the primary psychoactive component of smoked cannabis, delta-9-tetrahydrocannabinol (THC) are mediated by the cannabinoid CB1 receptor. The CB1 receptor has also been shown to mediate cannabinoid dependence and expression of withdrawal upon cessation of drug administration, a phenomenon verified across species. This paper will review findings implicating the CB1 receptor in the behavioural effects of exogenous cannabinoids with a focus on cannabinoid dependence and reinforcement, factors that contribute to the maintenance of chronic cannabis smoking despite negative consequences. Opioidergic modulation of these effects is also discussed.
16. Sewell RA, Ranganathan M, D'Souza DC. Cannabinoids and psychosis. *Int Rev Psychiatry.* 2009;21(2):152-62.  
Recent advances in knowledge about cannabinoid receptor function have renewed interest in the association between cannabis and psychosis. Case series, autobiographical accounts, and surveys of cannabis users in the general population suggest an association between cannabis and psychosis. Cross-sectional studies document an association between cannabis use and psychotic symptoms, and longitudinal studies suggest that early exposure to cannabis confers a close to two-fold increase in the risk of developing schizophrenia. Pharmacological studies show that cannabinoids can induce a full range of transient positive, negative, and cognitive symptoms in healthy individuals that are similar to those seen in schizophrenia. There is considerable evidence that in individuals with an established psychotic disorder such as schizophrenia, exposure to cannabis can exacerbate symptoms, trigger relapse, and worsen the course of the illness. Only a very small proportion of the general population exposed to cannabis develop a psychotic illness. It is likely that cannabis exposure is a 'component cause' that interacts with other factors to 'cause' schizophrenia or other psychotic disorder, but is neither necessary nor sufficient to do so alone. Further work is necessary to identify the factors that underlie individual vulnerability to cannabinoid-related psychosis and to elucidate the biological mechanisms underlying this risk.

17. Barbee G, Berry-Caban C, Barry J, Borys D, Ward J, Salyer S. Analysis of mushroom exposures in Texas requiring hospitalization, 2005-2006. *J Med Toxicol.* 2009;5(2):59-62.

INTRODUCTION: Texas has approximately 200 species of wild mushrooms, including toxic and hallucinogenic varieties. Mushroom ingestions in Texas were studied for 2005-2006. METHODS: Data was obtained via Texas Poison Control Centers and retrospectively reviewed. Case notes were reviewed individually regarding initial reporting, age, signs and symptoms, toxic effect, management, and patient outcomes. RESULTS: A total of 742 exposures occurred during the study period. All exposures were acute and intentional. Of these exposures, 59 (7.9%) were admitted to the hospital, with 17 (28.8% of admissions) requiring admission to a critical care unit. Four cases required inpatient psychiatric admission. The average age of admitted exposures was 20.5 years, with a male-to-female predominance of 3.3:1. Eleven (22.9%) of the admitted exposures were identified, with Psilocybin being the most common agent (n = 10, 91%). Among the admissions, co-ingestions were identified with the mushroom ingestion in eleven patients (40.7%). The most common symptoms in admitted patients were vomiting (n = 34, 57.6%), nausea (n = 19, 32.2%), altered mental status (n = 17, 28.8%), abdominal pain (n = 13, 22%), and diarrhea (n = 10, 16.9%). CONCLUSIONS: All mushroom exposures examined were acute and intentional. Major toxic reactions were uncommon, and no deaths were reported. Serious poisoning from mushroom ingestion is rare in Texas; however, there is greater need for information dissemination on morbidity.

18. Pierog J, Kane B, Kane K, Donovan JW. Management of isolated yew berry toxicity with sodium bicarbonate: a case report in treatment efficacy. *J Med Toxicol.* 2009;5(2):84-9.

INTRODUCTION: Taxus species are known to be toxic and may result in significant dysrhythmias. Treatment of taxus induced cardiac dysrhythmias is based largely on case reports. We describe a case of a 24-year-old male with Taxus cuspidate (yew berry) toxicity initially treated with amiodarone bolus and infusion and subsequently managed with sodium bicarbonate boluses and continuous infusion. CASE REPORT: The patient was found at home by his parents with witnessed "seizure-like" activity 2 hours after reportedly chewing and swallowing 168 yew seeds. The initial prehospital rhythm strip demonstrated ventricular tachycardia (VT); the patient was hypotensive with fluctuating levels of alertness. Prehospital cardioversion was attempted without success. Staff at the local presenting emergency department (ED) consulted toxicology for management of the presumed yew berry ingestion, complicated by cardiac dysrhythmias and mental status change with seizure. Amiodarone 300-mg IV and diazepam 5-mg IV were given. Cardioversion was attempted 4 times without change in the wide complex tachycardia, presumed to be VT, at a rate of 166. An amiodarone drip at 1 mg/min was initiated. The patient was transferred to an intensive care unit (ICU) at a regional toxicology center. On arrival to the toxicology center the patient was alert and verbally appropriate without complaints. Initial heart rate was 76 and regular with premature ventricular contractions (PVCs). A wide complex tachycardia associated with hypotension recurred; however, normal mental status was maintained. A bolus of 100 mEq of sodium bicarbonate (NaHCO<sub>3</sub>) was given intravenously followed by sodium bicarbonate infusion at 37.5 mEq/hr. The amiodarone drip was discontinued. Subsequent electrocardiograms (EKG's) revealed a prolonged, but steadily narrowing QRS complex. Ultimately, the QRS complex closed to 92 ms, with a rate

of 94, PR 154 and a QT/QTc of 390/487. CONCLUSION: This case describes successful treatment of an isolated *Taxus cuspidate* (yew berry) ingestion with significant toxicity initially with amiodarone bolus and infusion. Due to lack of significant change in telemetry recordings with amiodarone, treatment with sodium bicarbonate bolus and infusion was initiated. While the QRS narrowed significantly temporally related to the bicarbonate, it is difficult to determine if correction of the cardiac dysrhythmias was solely due to the sodium bicarbonate, or the synergism of sodium bicarbonate and amiodarone, or possibly spontaneous improvement due to taxine clearance. One should use caution while drawing conclusions from a single case; however, based on the clinical improvement of this patient, both with EKG recordings and vital signs, this report would suggest that isolated *Taxus cuspidate* ingestion from yew berry plants can be treated with sodium bicarbonate.

19. Stellpflug S, Harris C. What signs and symptoms would be expected after ingestion of this plant? *J Med Toxicol.* 2009;5(2):62, 90-1.

20. Su-Yin A, Wong J, Wiegand T, Olson K. Tretinoin overdose: a first case report. *J Med Toxicol.* 2009;5(2):73-5.

INTRODUCTION: Tretinoin (Vesanoid) is an all-trans-retinoic acid, and is related to retinol (Vitamin A). To date, there have been several case reports on overdose with its isomer isotretinoin, but none involving overdose of tretinoin. We report the first known case of a patient who ingested a massive overdose of tretinoin. CASE REPORT: A 31-year-old man ingested 1000 mg of tretinoin (100 pills of Vesanoid 10 mg) in a suicide attempt. He developed nonbloody diarrhea, but otherwise had no complaints. Clinical examination was normal. The patient was treated with activated charcoal and was hydrated. The patient's blood results did not show any deterioration on the third consecutive day. He was discharged well on the third day, but was subsequently lost to follow-up. DISCUSSION: Although there has been no reported experience with acute tretinoin overdose in humans, our patient took a dose approximately 3 times the recommended maximum tolerated daily dose in patients with myelodysplastic syndrome or solid tumors (195 mg/m<sup>2</sup> per day). Overdose with other retinoids such as isotretinoin have been associated with only minor symptoms that resolved quickly. Our patient had diarrhea, which also resolved quickly with symptomatic treatment and hydration. CONCLUSION: We believe this to be the first case report of an acute oral overdose of tretinoin. The patient developed diarrhea, but was otherwise asymptomatic.

21. Altaweel MM, Hanzlik RP, Ver Hoeve JN, Eells J, Zhang B. Ocular and systemic safety evaluation of calcium formate as a dietary supplement. *J Ocul Pharmacol Ther.* 2009;25(3):223-30.

PURPOSE: The objective of this study was to perform a preliminary evaluation of the ocular and systemic safety of calcium formate, a dietary calcium supplement for prevention and management of osteoporosis. Although formate is an endogenous product of metabolism, high concentrations are associated with toxicity during methanol overdose. METHODS: In this prospective clinical trial, 12 healthy women ingested calcium formate (1,300 mg) three times a day for 14 days. Study evaluations included physical and ocular examination, extensive laboratory testing, serum calcium and formate levels, Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity, color vision, visual fields, visual evoked potential (VEP), and full-field, pattern, and multifocal electroretinograms (MERG). RESULTS: The mean

baseline serum level of formate was 0.572 +/- 0.06 mM. Peak serum levels and final serum formate did not differ significantly from baseline. The final concentration was 0.582 +/- 0.091 mM. Accumulation of serum formate did not occur. There was also no evidence of toxicity with calcium formate ingestion. All examinations and tests remained normal, including optic nerve and retinal function. Three subjects had mild transient symptoms attributable to any calcium formulation. CONCLUSIONS: Calcium formate is highly bioavailable and well-tolerated. Serum formate remained at basal levels and did not accumulate with repeated dosing. Systemic and ocular safety was demonstrated by objective testing. Given its high oral bioavailability, calcium formate may be a good choice for calcium supplementation in the prevention and management of osteoporosis. Further study will be needed to evaluate its long-term safety in a larger group of subjects representing more varied age, health, dietary, and nutritional status.

22. Centers for Disease C, Prevention. Hepatitis temporally associated with an herbal supplement containing artemisinin - Washington, 2008. *MMWR Morb Mortal Wkly Rep.* 2009;58(31):854-6.

Artemisinins are a class of compounds that include artesunate, artemether, and artemisinin and have potent antimalarial activity. In combination with other drugs (artemisinin combination therapy), these compounds are the first-line treatment recommended by the World Health Organization for Plasmodium falciparum infections. Artemisinins have been available in the United States without a prescription as herbal supplements for at least 10 years; these supplements are marketed for general health maintenance and for treatment of parasitic infections and cancers. On August 27, 2008, CDC was notified of a patient who developed hepatitis after a 1-week course of an herbal supplement containing artemisinin. The patient had abdominal pain, dark urine, and laboratory results consistent with hepatitis (e.g., serum alanine aminotransferase of 898 IU/L [normal: 10-55 IU/L]). Samples of the supplement were sent to CDC and the Georgia Institute of Technology for analysis to determine the amount of artemisinin and to identify any contaminants. Analysis indicated that the supplement contained 94%-97% of the 100 mg of artemisinin stated on the packaging and the supplement contained no other common pharmaceutical active ingredients. Given the patient's clinical course and laboratory evaluation, CDC investigators concluded that the hepatitis might have been associated with ingestion of the herbal supplement containing artemisinin. More data are needed to establish any causal connection between artemisinin and hepatitis. Health-care providers should be aware of the possibility of hepatic toxicity in patients taking herbal supplements containing artemisinin.
23. Prakash S, Hernandez GT, Dujaili I, Bhalla V. Lead poisoning from an Ayurvedic herbal medicine in a patient with chronic kidney disease. *Nat Rev Nephrol.* 2009;5(5):297-300.

BACKGROUND: A 60-year-old man with a history of diabetes and hypertension was referred to a nephrology clinic for investigation of his elevated serum creatinine level. INVESTIGATIONS: Physical examination; laboratory investigations, including measurement of whole-blood lead level, body lead burden and urine albumin:creatinine ratio; history of lead exposure and use of herbal medical products; and renal ultrasonography. DIAGNOSIS: Stage 3 chronic kidney disease that was probably worsened by consumption of lead in the form of an Ayurvedic herbal remedy. MANAGEMENT: Cessation of the herbal product, followed by lead-

chelation therapy with calcium disodium ethylenediaminetetraacetic acid. The patient's whole-body lead burden and blood lead level decreased to acceptable levels and his serum creatinine value was within the normal range at final follow-up.

24. Myers GJ, Thurston SW, Pearson AT, Davidson PW, Cox C, Shamlaye CF, Cernichiari E, Clarkson TW. Postnatal exposure to methyl mercury from fish consumption: a review and new data from the Seychelles Child Development Study. *Neurotoxicology*. 2009;30(3):338-49.  
BACKGROUND: Fish is an important source of nutrition worldwide. Fish contain both the neurotoxin methyl mercury (MeHg) and nutrients important for brain development. The developing brain appears to be most sensitive to MeHg toxicity and mothers who consume fish during pregnancy expose their fetus prenatally. Although brain development is most dramatic during fetal life, it continues for years postnatally and additional exposure can occur when a mother breast feeds or the child consumes fish. This raises the possibility that MeHg might influence brain development after birth and thus adversely affect children's developmental outcomes. We reviewed postnatal MeHg exposure and the associations that have been published to determine the issues associated with it and then carried out a series of analyses involving alternative metrics of postnatal MeHg exposure in the Seychelles Child Development Study (SCDS) Main Cohort. METHODS: The SCDS is a prospective longitudinal evaluation of prenatal MeHg exposure from fish consumption. The Main Cohort includes 779 subjects on whom recent postnatal exposure data were collected at the 6-, 19-, 29-, 66-, and 107-month evaluations. We examined the association of recent postnatal MeHg exposure with multiple 66- and 107-month outcomes and then used three types of alternative postnatal exposure metrics to examine their association with the children's intelligence quotient (IQ) at 107 months of age. RESULTS: Recent postnatal exposure at 107 months of age was adversely associated with four endpoints, three in females only. One alternative postnatal metric was beneficially associated with 9-year IQ in males only. CONCLUSIONS: We found several associations between postnatal MeHg biomarkers and children's developmental endpoints. However, as has been the case with prenatal MeHg exposure in the SCDS Main Cohort study, no consistent pattern of associations emerged to support a causal relationship.
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BACKGROUND: The public and some health care providers regard complementary and alternative medications as safe. There is no scientific basis for that belief, but there is evidence of poor quality control and toxicity of some remedies. CASE: A white pregnant woman presented with diffuse, acute abdominal pain ultimately diagnosed as lead poisoning due to the use of traditional Asian Indian health supplements. CONCLUSION: Use of traditional medicines may extend beyond the ethnic group in which the traditional medicine originated. When symptoms warrant, poisoning with lead or other heavy metals should be considered in the differential diagnosis.

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PURPOSES: (1) Measure the prevalence of herbal product (HP) use, alone, and concomitantly with prescribed medications during pregnancy, (2) identify the most frequently consumed HP during gestation and (3) determine predictors of HP use at the beginning of pregnancy, and during the third trimester. METHODS: A questionnaire was mailed to 8505 women selected from the Quebec Pregnancy Registry which was created by the linkage of three administrative databases: RAMQ, Med-Echo and ISQ. Women were eligible if they were continuously insured by the RAMQ drug plan for at least 12 months before the first day of gestation and during pregnancy, and if they gave birth to a live born between January 1998 and December 2003 in one of the Quebec's hospitals. Women with diabetes and psychoses, and women who delivered a baby with birth defects were selected first. Descriptive statistics and multivariate logistic regression models were used to analyse data. RESULTS: Of the 3354 women (39%) who answered the questionnaire, and were included in the study, nine per cent used HP during pregnancy. 69% of users took at least one prescribed medication concomitantly. Chamomile, green tea, peppermint and flax were the most frequently HP used. Multivariate analyses showed that body mass index (BMI), multivitamin use and one to three prescribed medications used before pregnancy were predictors of HP use at the beginning of pregnancy; adherent women, smokers and users of HP prior to pregnancy were predictors of HP use during the third trimester. CONCLUSION: HP use alone and concomitantly with prescribed medications during pregnancy is common, and needs to be addressed by health professionals.
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Chinese medicine plays an important role in providing medical care for people in countries with large Chinese communities, including Hong Kong. The aconite herb is one of the commonly-prescribed ingredients for various clinical problems. However, due to its narrow therapeutic index, toxicities are not uncommonly encountered, including life-threatening cardiac arrhythmias like ventricular arrhythmias. We report a 57-year-old woman with reversible intraventricular conduction defect attributed to the use of processed Fuzi.