



# The American Academy of Clinical Toxicology

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Herbs & Dietary Supplements Special Interest Group  
Abstracting Service  
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1. Chu Y, Liu H. Advances of research on anti-HIV agents from traditional Chinese herbs. *Adv Dent Res.* 2011;23(1):67-75. PMID: 21441484

The current approach for dealing with the global pandemic of AIDS focuses on pharmaceuticals. The classic treatment of AIDS is highly active antiretroviral therapy, but most people living with HIV/AIDS-especially those in developing countries-have little or no access to the treatment because of the high cost of the therapy. Such treatment is associated with toxic side effects and drug resistance. As such, the search for better anti-HIV agents continues, with much attention focused on natural sources-particularly, plant species. Thousands of herbs have been screened for anti-HIV activity, and new compounds have been discovered from the extracts, many of which demonstrate inhibitory activity against HIV. Their mechanisms of action include inhibiting the activities of reverse transcriptase, protease, and integrase; weakening infection at the level of viral entry; and downregulating related gene expression. This provides researchers with new clues to synthesize drugs for the anti-HIV battle. Some synthetic derivatives of the anti-HIV natural products have stronger inhibitory effects in vitro than do their natural counterparts. Various mixed preparations of these anti-HIV herbs are in clinical trials or are applied in the treatment of people living with HIV/AIDS-some of which yield lower plasma viral load, enhance immune function, relieve related symptoms and signs, improve the quality of life, or, in combination with highly active antiretroviral therapy, alleviate the side effects of biomedical drugs. This article reviews current laboratory findings and clinical trials of anti-HIV agents from traditional herbs-particularly, herbs in traditional Chinese medicine. Drug interactions with highly active antiretroviral therapy and criteria for clinical evaluation of traditional Chinese medicine treatment are also discussed.

2. Liu X, Han Y, Peng K, Liu Y, Li J, Liu H. Effect of traditional Chinese medicinal herbs on *Candida* spp. from patients with HIV/AIDS. *Adv Dent Res.* 2011;23(1):56-60. PMID: 21441482

As an opportunistic infection, candidiasis is common among individuals infected with HIV. About 90% of patients develop oral and/or oropharyngeal candidiasis in various stages of AIDS. Triazole antifungal agents, such as fluconazole and

itraconazole, are considered to be first-choice agents for treatment and prevention because of their relatively low side effects and high effectiveness on mucosal infections. However, with prolonged exposure to azoles, drug resistance becomes a challenge for clinicians and patients alike. In traditional Chinese medicine, more than 300 herbs have been discovered to have "pesticidal" activities, and some of these have been used as antifungal agents in clinical practice for many years. Crude extracts from a number of medicinal herbs have been shown to exhibit antifungal activities in vitro. These include cortex moutan, cortex pseudolaricis, rhizoma alpiniae officinarum, rhizoma coptidis, clove and cinnamon, anemarrhena cortex phellodendri, ramulus cinnamomi, and Chinese gall. The effective anti-Candida principals were identified to be berberine, palmatine, allincin, pseudolaric acid A and B, magnolol, honokiol, and galangin. Thus, traditional Chinese medicinal herbs provide abundant choices for the treatment of refractory candidiasis commonly seen in HIV/AIDS patients. However, there remains a need for further screening of effective extracts and for study of the antifungal mechanisms involved. Importantly, ahead of clinical application, the safety of these compounds must be firmly established.

3. Nriagu J, Senthamarai-Kannan R, Jamil H, Fakhori M, Korponic S. Lead Poisoning Among Arab American and African American Children in the Detroit Metropolitan Area, Michigan. *Bull Environ Contam Toxicol*. 2011. PMID: 21725626

This study explored the hypothesis that acculturation is a risk factor for childhood lead poisoning in the Detroit area of Michigan. Blood lead levels (BLLs) were determined in 429 Arab American and African American children, aged 6 months to 15 years, who were receiving well-child examination in three Women, Infant, and Children (WIC) clinics in the city. Mean BLL was 3.8 +/- 2.3 mug/dL (range: 1-18 mug/dL) and 3.3% of the children tested had blood lead values above the 10 mug/dL level of concern. Neither the age of the dwelling units nor ethnicity of the child was significantly associated with the BLL. Multivariable analyses instead identified a number of acculturation-related factors that are associated with elevation in blood lead including paternal education, language spoken at home (English only, English and Arabic, or Arabic only), home ownership, smoking in the home, and exposure of child to home health remedies. The difference in blood lead between Arab American children from families where Arabic only versus Arabic and English is spoken at home was found to be statistically significant. This study provides information showing that immigrant children are at heightened risk of being poisoned by lead which can be useful in identifying groups at risk of atypical exposures.

4. Chen XW, Serag ES, Sneed KB, Zhou SF. Herbal bioactivation, molecular targets and the toxicity relevance. *Chem Biol Interact*. 2011;192(3):161-76. PMID: 21459083

There have been increasing reports on the adverse reactions associated with herbal consumption. For many of these adverse reactions, the underlying biochemical mechanisms are unknown, but bioactivation of herbal compounds to generate reactive intermediates have been implicated. This minireview updates our knowledge on metabolic activation of herbal compounds, molecular targets and the toxicity relevance. A number of studies have documented that some herbal compounds can be converted to toxic or even carcinogenic metabolites by Phase I [e.g. cytochrome P450s (CYPs)] and less frequently by Phase II enzymes. For example, aristolochic acids (AAs) in *Aristolochia* spp, which undergo reduction of the nitro group by hepatic CYP1A1/2 or peroxidases in extrahepatic tissues to generate highly reactive cyclic nitrenium ions. The latter can react with macromolecules (DNA and protein), resulting in activation of H-ras and myc oncogenes and gene mutation in renal cells and finally carcinogenesis of the kidneys. Teucrin A and teuchamaedryn A, two diterpenoids found in germander (*Teuchrium chamaedrys*) used as an adjuvant to slimming herbal supplements that caused severe hepatotoxicity, are converted by CYP3A4 to reactive epoxide which reacts with proteins such as CYP3A and epoxide hydrolase and inactivate them. Some naturally occurring alkenylbenzenes (e.g. safrole, methyleugenol and estragole) and flavonoids (e.g. quercetin) can undergo bioactivation by sequential 1-hydroxylation and sulfation, resulting in reactive intermediates capable of forming DNA adducts. Extensive pulegone metabolism generated p-cresol that is a glutathione depletory. The hepatotoxicity of kava is possibly due to intracellular glutathione depletion and/or quinone formation. Moreover, several herbal compounds including capsaicin from chili peppers, diallyl sulfone in garlic, methysticin and dihydromethysticin in kava, oleuropein in olive oil, and resveratrol found in grape seeds are mechanism-based (suicide) inhibitors of various CYPs. Together with advances of proteomics, metabolomics and toxicogenomics, an integrated systems toxicological approach may provide deep insights into mechanistic aspects of herb-induced toxicities, and contribute to bridging the relationships between herbal bioactivation, protein/DNA adduct formation and the toxicological consequences.

5. Heng XP, Chen KJ, Hong ZF, He WD, Chu KD, Chen WL, et al. Anticolchicine cytotoxicity enhanced by Dan Gua-Fang, a Chinese herb prescription in ECV304 in mediums. *Chin J Integr Med.* 2011;17(2):126-33. PMID: 21390579

**OBJECTIVE:** To study the effect of anticolchicine cytotoxicity of Dan Gua-Fang, a Chinesea Chinese), a Chinese herbal compound prescription on endothelial cells of vein (ECV304) cultivated in mediums of different glucose concentrations as well as the proliferation of those cells in the same conditions, in order to reveal the value of Dan Gua-Fang in preventing and treating endothelial damage caused by hyperglycemia in diabetes mellitus. **METHODS:** The research was designed as three stages. The growing state and morphological changes were observed when ECV304 were cultivated in the culture mediums, which have different glucose concentrations with or without Dan Gua-Fang and at the same

time with or without colchicine. RESULTS: (1) Dan Gua-Fang at all concentrations reduced the floating cell population of ECV304 cultivated in hyperglycemia mediums. (2) Dan Gua-Fang at all concentrations and hyperglycemia both had a function of promoting "pseudopod-like" structure formation in cultivated ECV304, but the function was not superimposed in mediums containing both hyperglycemia and Dan Gua-Fang. (3) Colchicine reduced and even vanished the "pseudopod-like" structure of the endotheliocyte apparently cultivated in mediums of hyperglycemia or with Dan Gua-Fang. The "pseudopod-like" structure of the endotheliocyte emerged quickly in Dan Gua-Fang groups after colchicine was removed, but it was not the case in hyperglycemia only without Dan Gua-Fang groups. (4) Dan Gua-Fang reduced the mortality of cells cultivated in mediums containing colchicine. The cell revived to its normal state fast after colchicine was removed. CONCLUSION: Dan Gua-Fang has the functions of promoting the formation of cytoskeleton and fighting against colchicine cytotoxicity.

6. Chan A, Crankshaw DL, Monteil A, Patterson SE, Nagasawa HT, Briggs JE, et al. The combination of cobinamide and sulfanegen is highly effective in mouse models of cyanide poisoning. *Clin Toxicol (Phila)*. 2011;49(5):366-73. PMID: 21740135

Context. Cyanide is a component of smoke in residential and industrial fires, and accidental exposure to cyanide occurs in a variety of industries. Moreover, cyanide has the potential to be used by terrorists, particularly in a closed space such as an airport or train station. Current therapies for cyanide poisoning must be given by intravenous administration, limiting their use in treating mass casualties. Objective. We are developing two new cyanide antidotes - cobinamide, a vitamin B(12) analog, and sulfanegen, a 3-mercaptopyruvate prodrug. Both drugs can be given by intramuscular administration, and therefore could be used to treat a large number of people quickly. We now asked if the two drugs would have an augmented effect when combined. Materials and methods. We used a non-lethal and two different lethal models of cyanide poisoning in mice. The non-lethal model assesses neurologic recovery by quantitatively evaluating the innate righting reflex time of a mouse. The two lethal models are a cyanide injection and a cyanide inhalation model. Results. We found that the two drugs are at least additive when used together in both the non-lethal and lethal models: at doses where all animals died with either drug alone, the combination yielded 80 and 40% survival in the injection and inhalation models, respectively. Similarly, drug doses that yielded 40% survival with either drug alone, yielded 80 and 100% survival in the injection and inhalation models, respectively. As part of the inhalation model, we developed a new paradigm in which animals are exposed to cyanide gas, injected intramuscularly with an antidote, and then re-exposed to cyanide gas. This simulates cyanide exposure of a large number of people in a closed space, because people would remain exposed to cyanide, even after receiving an antidote. Conclusion. The combination of cobinamide and

sulfanegen shows great promise as a new approach to treating cyanide poisoning.

7. Fuchs J, Rauber-Luthy C, Kupferschmidt H, Kupper J, Kullak-Ublick GA, Ceschi A. Acute plant poisoning: Analysis of clinical features and circumstances of exposure. *Clin Toxicol (Phila)*. 2011. PMID: 21809910

Introduction. Human contact with potentially toxic plants, which may occur through abuse or by accident or attempted suicide, is frequent and sometimes results in clinically significant toxicity. Objective. The aim of the present study was to identify which plants may lead to severe poisoning, and to define the clinical relevance of plant toxicity for humans in Switzerland. Methods. We analyzed 42 193 cases of human plant exposure and 255 acute moderate, severe, and lethal poisonings, which were reported to the Swiss Toxicological Information Centre between January 1995 and December 2009. Results. Plant contact was rarely responsible for serious poisonings. Lethal intoxications were extremely rare and were caused by plants with cardiotoxic (*Taxus baccata*) or mitosis-inhibiting (*Colchicum autumnale*) properties. Conclusions. Most often, plant contact was accidental and patients remained asymptomatic or developed mild symptoms, which fully resolved within a short time.

8. Horowitz BZ. The ripe olive scare and hotel Loch Maree tragedy: Botulism under glass in the 1920's. *Clin Toxicol (Phila)*. 2011;49(4):345-7. PMID: 21563914

Botulism was believed to be a rare disease in both the US and UK in the 1920's, until two deadly outbreaks altered that view and launched public health measures to control it. In the United States, the ripe olive scare of 1920 found glass-packaged olives linked to multiple deaths. In the United Kingdom, eight deaths from glass-potted duck paste, in the summer of 1922 at Loch Maree, Scotland will always be associated with botulism.

9. Krul J, Girbes AR. Gamma-hydroxybutyrate: experience of 9 years of gamma-hydroxybutyrate (GHB)-related incidents during rave parties in The Netherlands. *Clin Toxicol (Phila)*. 2011;49(4):311-5. PMID: 21563907

**OBJECTIVE.** The objective of this study was to determine the health disturbances and to assess the severity of the incidents as reported during a 9-year experience of gamma-hydroxybutyrate (GHB)-related First Aid Attendees attending First Aid Stations at rave parties. **DESIGN.** This study was a prospective observational study of self-referred patients from the year 2000 to 2008. During rave parties, First Aid Stations were staffed with specifically trained medical and paramedical personnel. Patients were diagnosed and treated, and data were recorded using standardized methods. **RESULTS.** During a 9-year period with 202 rave parties, involving approximately three million visitors, 22 604 First Aid Attendees visited the First Aid Stations, of which 771 reported GHB-related health problems. The mean age of the GHB-using First Aid Attendees

was 25.7 +/- 6.1 years, most of them (66.4%) were male. Approximately one-third (32.7%) of them used one substance, while 48.1% combined GHB with ecstasy, alcohol, or cannabis. One of five (19.2%) combined GHB with other substances or more than one substance. One case was categorized as severe/life-threatening and 202 (26.2%) cases as moderate, requiring further medical care. In total, 43 (5.6%) First Aid Attendees needed hospital care. The most encountered health disturbance was altered consciousness. Combinations of altered consciousness, vomiting, and/or low body temperature were found in 186 cases (24.1%) and considered to be potentially dangerous. GHB-related First Aid Attendees required a longer stay at the First Aid Stations than the total group First Aid Attendees did (median 45 min vs 10 min). **CONCLUSION.** We found very little, severe short-term GHB-related health disturbances during rave parties in The Netherlands. Hospital referrals were rare. The most found symptom was altered consciousness, sometimes accompanied by vomiting and low body temperature. At events where the visitors use GHB, a well-trained and qualified medical team, including nurses and physicians, is recommendable. They must be able to recognize GHB intake and prevent secondary problems such as aspiration and hypothermia.

10. Liu ZL, Liu JP, Zhang AL, Wu Q, Ruan Y, Lewith G, et al. Chinese herbal medicines for hypercholesterolemia. *Cochrane Database Syst Rev.* 2011(7):CD008305. PMID: 21735427

**BACKGROUND:** Hypercholesterolemia is an important key contributory factor for ischemic heart disease and is associated with age, high blood pressure, a family history of hypercholesterolemia, and diabetes. Chinese herbal medicines have been used for a long time as lipid-lowering agents. **OBJECTIVES:** To assess the effects of Chinese herbal medicines on hypercholesterolemia. **SEARCH STRATEGY:** We searched the following databases: The Cochrane Library (issue 8, 2010), MEDLINE (until July 2010), EMBASE (until July 2010), Chinese BioMedical Database (until July 2010), Traditional Chinese Medical Literature Analysis and Retrieval System (until July 2010), China National Knowledge Infrastructure (until July 2010), Chinese VIP Information (until July 2010), Chinese Academic Conference Papers Database and Chinese Dissertation Database (until July 2010), and Allied and Complementary Medicine Database (until July 2010). **SELECTION CRITERIA:** We considered randomized controlled clinical trials in hypercholesterolemic participants comparing Chinese herbal medicines with placebo, no treatment, and pharmacological or non-pharmacological interventions. **DATA COLLECTION AND ANALYSIS:** Two review authors independently extracted data and assessed the risk of bias. We resolved any disagreements with this assessment through discussion and a decision was achieved based by consensus. We assessed trials for the risk of bias against key criteria: random sequence generation, allocation concealment, blinding of participants, incomplete outcome data, selective outcome reporting and other sources of bias. **MAIN RESULTS:** We included 22 randomized trials (2130 participants). The mean treatment duration was 2.3 +/- 1.3 months

(ranging from one to six months). Twenty trials were conducted in China and 18 trials were published in Chinese. Overall, the risk of bias of included trials was high or unclear. Five different herbal medicines were evaluated in the included trials, which compared herbs with conventional medicine in six comparisons (20 trials), or placebo (two trials). There were no outcome data in any of the trials on cardiovascular events and death from any cause. One trial each reported well-being (no significant differences) and economic costs. No serious adverse events were observed. Xuezhikang was the most commonly used herbal formula investigated. A significant effect on total cholesterol (two trial, 254 participants) was shown in favor of Xuezhikang when compared with inositol nicotinate (mean difference (MD) -0.90 mmol/L, 95% confidence interval (CI) -1.13 to -0.68) .  
AUTHORS' CONCLUSIONS: Some herbal medicines may have cholesterol-lowering effects. Our findings have to be interpreted with caution due to high or unclear risk of bias of the included trials.

11. Qu HB, Dengfeng W, Wu T, Marjoribanks J, Ying S, Haijun J, et al. Chinese herbal medicine in the treatment of ectopic pregnancy. *Cochrane Database Syst Rev.* 2011(7):CD006224. PMID: 21735404

**BACKGROUND:** Traditionally Chinese herbal medicine (CHM) has been used widely in Chinese hospitals to treat ectopic pregnancy. Many studies have been published supporting its use but the evidence has not been systematically reviewed. This is an update of the review published in 2007. **OBJECTIVES:** To determine the effectiveness and safety of CHM in the treatment of ectopic pregnancy. **SEARCH STRATEGY:** Computerised databases (CENTRAL (The Cochrane Library), MEDLINE, EMBASE, Chinese Biomedical Database, China National Knowledge Infrastructure, VIP, Traditional Chinese Medicine Database System) were searched from their inception to November 2010 for relevant trials. **SELECTION CRITERIA:** Randomised controlled trials (RCT) on the use of CHM for the treatment of ectopic pregnancy. **DATA COLLECTION AND ANALYSIS:** Original authors of the identified studies were contacted to determine the trial design and identify authentic RCTs. Two review authors extracted and analysed the data. **MAIN RESULTS:** The search identified 281 trials. Only two studies involving a total of 157 participants were confirmed to be authentic RCTs (Li 2004c; Zhao 2000). Both were of poor methodological quality with a high risk of conflicted interest and potential for bias in favour of the intervention. We could not reach a definitive conclusion from the results. The pooled result showed that adding a Western medicine to CHM resulted in a significantly higher treatment success rate than with CHM alone (RR 1.33, 95% CI 1.08 to 1.63). When CHM plus Western medicine was compared to CHM alone for the time to disappearance of abdominal pain, again the results favoured the arm that included Western medicine (RR -2.09, 95% CI -4.14 to -0.04). Results were inconsistent for the time required for human chorionic gonadotropin (beta-hCG) to return to normal. One study favoured CHM plus Western medicine over Western medicine (with or without placebo) (MD -6.68, 95% CI -11.49 to -1.87); when CHM plus Western medicine was compared to CHM alone the results

favoured the arm that included Western medicine (MD -8.12, 95% CI -10.89 to -5.53). **AUTHORS' CONCLUSIONS:** We have not found any well-designed trials investigating Chinese herbal medicines in the treatment of ectopic pregnancy. We cannot support or refute any CHM preparation for clinical use on the basis of evidence from randomised controlled trials.

12. Braun JM, Hauser R. Bisphenol A and children's health. *Curr Opin Pediatr.* 2011;23(2):233-9. PMID: 21293273

**PURPOSE OF REVIEW:** Bisphenol A (BPA) is a widely used chemical that has been shown to adversely affect health outcomes in experimental animal studies, particularly following fetal or early life exposure. Despite widespread human exposure in the United States and developed countries, there are limited epidemiological studies on the association of BPA with adverse health outcomes. This review briefly summarizes the epidemiological literature with special emphasis on childhood health outcomes. **RECENT FINDINGS:** Several studies report correlations between urinary BPA and serum sex steroid hormone concentrations in adults. Two studies report weak associations between urinary BPA concentrations and delayed onset of breast development in girls. One study found a relationship between prenatal BPA exposure and increased hyperactivity and aggression in 2-year-old female children. **SUMMARY:** Additional large prospective cohort studies are needed to confirm and validate findings from animal studies. Even in the absence of epidemiological studies, concern over adverse effects of BPA is warranted given the unique vulnerability of the developing fetus and child. Healthcare providers are encouraged to practice primary prevention and counsel patients to reduce BPA exposures.

13. Saokaew S, Suwankesawong W, Permsuwan U, Chaiyakunapruk N. Safety of herbal products in Thailand: an analysis of reports in the Thai health product vigilance center database from 2000 to 2008. *Drug Saf.* 2011;34(4):339-50. PMID: 21417506

**BACKGROUND:** The use of herbal products continues to expand rapidly across the world and concerns regarding the safety of these products have been raised. In Thailand, Thai Vigibase, developed by the Health Product Vigilance Center (HPVC) under the Thai Food and Drug Administration, is the national database that collates reports from health product surveillance systems and programmes. Thai Vigibase can be used to identify signals of adverse events in patients receiving herbal products. **OBJECTIVES:** The purpose of the study was to describe the characteristics of reported adverse events in patients receiving herbal products in Thailand. **METHODS:** Thai Vigibase data from February 2000 to December 2008 involving adverse events reported in association with herbal products were used. This database includes case reports submitted through the spontaneous reporting system and intensive monitoring programmes. Under the spontaneous reporting system, adverse event reports are collected nationwide via a national network of 22 regional centres covering more than 800 public and private hospitals, and health service centres. An intensive monitoring programme

was also conducted to monitor the five single herbal products listed in the Thai National List of Essential Medicines (NLEM), while another intensive monitoring programme was developed to monitor the four single herbal products that were under consideration for inclusion in the NLEM. The database contained patient demographics, adverse events associated with herbal products, and details on seriousness, causality and quality of reports. Descriptive statistics were used for data analyses. RESULTS: A total of 593 reports with 1868 adverse events involving 24 different products were made during the study period. The age range of individuals was 1-86 years (mean 47 years). Most case reports were obtained from the intensive monitoring programme. Of the reports, 72% involved females. The herbal products for which adverse events were frequently reported were products containing turmeric (44%), followed by andrographis (10%), veld grape (10%), pennywort (7%), plai (6%), jewel vine (6%), bitter melon (5%) and snake plant (5%). Gastrointestinal problems were the most common adverse effect reported. Serious adverse events included Stevens-Johnson syndrome, anaphylactic shock and exfoliative dermatitis. CONCLUSIONS: Adverse event reports on herbals products were diverse, with most of them being reported through intensive monitoring programmes. Thai Vigibase is a potentially effective data source for signal detection of adverse events associated with herbal products.

14. Jin Y, Yu F, Liao Y, Liu S, Liu M, Xu J, et al. Therapeutic efficiency of succimer used with calcium and ascorbic acid in the treatment of mild lead-poisoning. *Environ Toxicol Pharmacol.* 2011;31(1):137-42. PMID: 21787678

The aim of this study was to explore therapeutic efficiency of succimer used with calcium and ascorbic acid in the treatment of mildly lead-poisoned mice and preschool children. Mice were exposed to lead by drinking water, and then treated with saline solution, 50mg/kg body weight (b.w.) succimer, 100mg/kg b.w. succimer, or 50mg/kg b.w. succimer plus calcium and ascorbic acid by gavage. Seventy-two children aged 48-72 months were randomly assigned into combined treatment or nutritional intervention group. Lead levels in blood and bone were analyzed by atomic absorption spectrophotometry. Activities of aminolevulinic acid dehydratase (ALAD) in blood were determined by colorimetric method. Results of animal experiment showed that succimer used alone could reduce lead levels in blood and bone and reverse activities of ALAD in blood, however, a better therapeutic efficiency in mobilizing bone lead could be achieved by succimer used with calcium and ascorbic acid. Findings from the clinical study showed that reduction of blood lead levels (BLLs) between the end and initiation of therapy in the combined treatment group was significantly greater than that in the nutritional intervention group. Percentage of children with BLLs less than 10µg/dL at the end of therapy and the eighth week after therapy in the combined treatment group was significantly higher than that in the nutritional intervention group. In conclusion, combined use of succimer with calcium and ascorbic acid seemed to be a choice in the treatment of mildly lead poisoned children.

15. Lu L, Wang X, Lang L, Fu F. Protective effect of reduced glutathione on the liver injury induced by acute omethoate poisoning. *Environ Toxicol Pharmacol.* 2010;30(3):279-83. PMID: 21787660

Omethoate is an organophosphate insecticide with high toxicity. The aim of this study was to investigate the protective effect of exogenous reduced glutathione (GSH) on omethoate-induced liver injury. Sprague-Dawley rats were randomly divided into three groups: control, OM (omethoate poisoning), and OM+GSH (omethoate poisoning treated with GSH). The activities of acetylcholinesterase (AChE), aspartate aminotransferase (AST), alanine aminotransferase (ALT) in plasma, free organophosphate (FOP) in the liver were determined, and the histopathological changes in the liver were observed. Furthermore, TNF-alpha and NO in liver homogenate were assayed. The results showed that AChE activity was significantly inhibited by omethoate, but was not altered by GSH treatment. GSH was able to prevent hepatocellular edema and fatty degeneration, decrease liver FOP, attenuate the increased AST and ALT activity, and decline the increase of TNF-alpha and NO induced by omethoate. These results indicate GSH can attenuate liver injury, and suggest that GSH may be administered to protect the organ from injury in patients with acute organophosphate poisoning.

16. Watanabe T, Ohnuki K, Kobata K. Studies on the metabolism and toxicology of emerging capsinoids. *Expert Opin Drug Metab Toxicol.* 2011;7(5):533-42. PMID: 21355789

**INTRODUCTION:** Capsinoids are nonpungent compounds that are found in almost all pungent peppers and are abundant in the sweet pepper cultivar CH-19 Sweet. Since the discovery of capsinoids 13 years ago, various physiological effects of these compounds - especially reduction of visceral fat - have been observed both in rodents and humans. Recently, capsules containing capsinoids have become commercially available and comprehensive studies have been performed on the metabolism and toxicity of capsinoids. **AREAS COVERED:** This article reviews all the literature from 1998 to date providing details on the nature and physiological effects of capsinoids. In addition to this, the article also looks at their metabolism as well as their acute and chronic toxicity including their genotoxicity and teratology. **EXPERT OPINION:** Capsinoids are the most promising compounds among all known transient receptor potential vanilloid 1 agonists. The physiological activities of capsinoids are similar to those of capsaicin, the most pungent food component of red pepper, but appear to be much safer to use as a therapeutic compound. That said, there is still a need for further research into the capsinoid mechanism of action before it can be 'green-lighted' for therapeutic use.

17. Padilha RQ, Riera R, Atallah AN. Homeopathic Plumbum metallicum for lead poisoning: a randomized clinical trial. *Homeopathy*. 2011;100(3):116-21. PMID: 21784327

**INTRODUCTION:** Poisoning due to lead and its compounds has short and long-term effects primarily on the nervous, hematopoietic, gastrointestinal, cardiovascular, musculoskeletal, renal and reproductive systems. It can manifest in acute or chronic symptoms. Measuring serum concentration is the primary method for diagnosing and monitoring exposed workers. Presently, elevated lead levels are treated by drugs whose effectiveness is contested on various fronts. Experimental studies suggest that homeopathic preparations may be in controlling blood lead levels in laboratory animals, creating the need for controlled studies to evaluate the effectiveness and safety of these preparations in humans. **OBJECTIVE:** To evaluate the effectiveness of the homeopathic preparation Plumbum metallicum in reducing the blood lead level of workers exposed to this metal. **DESIGN:** Double-blind randomized trial. **SETTING:** Workers' clinic in the Ajax battery plant, which employs 900 workers with varying degrees of lead exposure in Bauru, Sao Paulo State, Brazil. **SUBJECTS:** 131 workers exposed to lead. **INTERVENTION:** Plumbum metallicum 15cH or placebo, orally for 35 days. **RESULTS:** The percentage of workers who demonstrated a reduction in lead counts by a percentage greater than or equal to 25% following treatment was the same for both groups: 20.3% in the homeopathic groups versus 21% in the control group [Relative Risk (RR)=0.95, confidential interval (CI) 95%: 0.47-1.92]. Analysis by intention-to-treat also did not show any difference between the groups: 18.2% in the treated group versus 20% in the placebo group (RR=0.91, CI 95%: 0.45-1.84). **CONCLUSION:** The homeopathic preparation Plumbum metallicum had no effect, in this study, in terms of reducing serum lead in workers exposed to lead.

18. Fan KL, Chan CK, Lau FL. Mercury exposure: the experience of the Hong Kong Poison Information Centre. *Hong Kong Med J*. 2011;17(4):292-6. PMID: 21813897

**OBJECTIVES.** To review the characteristics of the consultation about the management of mercury exposure and identify the controversial issues on the clinical management of individuals with a history of mercury exposure. **DESIGN.** Descriptive case series. **SETTING.** Hong Kong Poison Information Centre, Hong Kong. **PARTICIPANTS.** Persons consulting the Hong Kong Poison Information Centre about individuals with possible or definitive mercury exposure. **MAIN OUTCOME MEASURES.** Characteristics of the consultations, including: the demographics of affected individuals, source and reason for the consultation, tissue mercury levels, the source of mercury exposure, specific intervention if any, and clinical outcomes. **RESULTS.** Forty-one consultations were analysed. Most consultations were from the public sector. Reasons of the consultation were very variable. Individuals with abnormal tissue mercury levels were uncommon. There was only one case of acute mercury poisoning. The majority of identified

individuals were not subjected to specific interventions. Chelation therapy was given to three patients, but in one of them it was considered to be contra-indicated. CONCLUSION. The management of mercury exposure is highly variable. Recommendations were made on the approach to an individual with potential mercury exposure or poisoning.

19. Sasan MS, Hadavi N, Afshari R, Mousavi SR, Alizadeh A, Balali-Mood M. Metal mercury poisoning in two boys initially treated for brucellosis in Mashhad, Iran. *Hum Exp Toxicol*. 2011. PMID: 21803782

Elemental mercury (Hg) is the only metal which evaporates in room temperature and its inhalation may cause toxicity. Hg poisoning may occur by mishandling the metal, particularly in children who play with it. Wide-spectrum of the clinical presentations of chronic Hg poisoning may cause misdiagnosis, particularly when history of exposure is unknown. We report two cases of accidental Hg poisoning, which initially had been diagnosed and treated for brucellosis. The patients were two brothers (7 and 14 years old) who presented with pain in their lower extremities, sweating, salivation, weight loss, anorexia and mood changes on admission. Meticulous history taking revealed that they had played with a ball of Hg since 3 months before admission. The level of urinary Hg was 125.9 and 54.29 g/L in the younger and older brother, respectively (normal  $\leq 25$  g/L). The patients were successfully treated by dimercaprol and discharged in good condition 24 days after admission. These cases are being reported to emphasize the importance of acrodynia as a differential diagnosis for brucellosis in endemic areas.

20. Persico A, Bacis G, Uberti F, Panzeri C, Di Lorenzo C, Moro E, et al. Identification of taxine derivatives in biological fluids from a patient after attempted suicide by ingestion of yew (*Taxus baccata*) leaves. *J Anal Toxicol*. 2011;35(4):238-41. PMID: 21513618

The yew tree (*Taxus baccata*) is an evergreen conifer that is widespread over central and southern Europe. The toxic effects of this conifer and its leaves have been known since ancient times. The seeds are generally responsible for accidental intoxications in childhood, whereas the bark and the leaves are mainly used for homicidal or suicidal attempts. We investigated the metabolic pattern of taxines in a healthy 44-year-old male farmer who was admitted to Bergamo Emergency Department after attempting suicide. High-performance liquid chromatography was used to separate and identify taxine metabolites. Data reported in this paper confirmed that the patient attempted suicide by ingesting *Taxus baccata* leaves, which had been suggested by clinical examination. The most abundant free and conjugated taxine metabolites were characterized. The high concentration of conjugated metabolites found in urine underscores the critical role that conjugation in the liver plays in eliminating taxines and increasing the probability of the patient's survival.

21. Teske J, Weller JP, Albrecht UV, Fieguth A. Fatal intoxication due to brucine. *J Anal Toxicol.* 2011;35(4):248-53. PMID: 21513620

A sensitive method for identifying and quantifying brucine by means of liquid chromatography-tandem mass spectrometry is presented in this article. Based on a solid-phase extraction for human serum, the validation indicated limits of detection and quantification of 0.12 and 0.23 ng/mL, respectively. In one case of lethal suicidal brucine monointoxication, brucine concentrations of 1.51 mug/mL, 1.69 mug/mL, 9.94 mug/mL, 16.4 mug/g, 0.99 mug/g, 0.75 mug/g, and 1.95 mg/g were determined in femoral blood, urine, bile collected from the gallbladder, liver tissue, cerebellum, cerebrum, and stomach contents, respectively.

22. Schneir AB, Cullen J, Ly BT. "Spice" girls: synthetic cannabinoid intoxication. *J Emerg Med.* 2011;40(3):296-9. PMID: 21167669

**BACKGROUND:** "Spice" refers to various synthetic cannabinoid-containing products that seem to have rapidly become popular recreational drugs of abuse. Very little medical literature currently exists detailing the adverse effects and emergency department (ED) presentations associated with "spice" use. **OBJECTIVES:** To describe the presentation of 2 patients who recreationally used a "spice" product and to briefly summarize what is known about "spice" and synthetic cannabinoids. **CASE REPORT:** Two patients presented to the ED with, predominantly, anxiety after recreationally using a "spice" product that we subsequently confirmed to contain the synthetic cannabinoids, JWH-018 and JWH-073. **CONCLUSION:** We suspect that use of "spice" products may increase. Although anxiety was a prominent presentation in both of the patients described here, undoubtedly, future studies will describe the manifestations of intoxication and toxicity with the various synthetic cannabinoids.

23. Larrey D, Faure S. Herbal medicine hepatotoxicity: a new step with development of specific biomarkers. *J Hepatol.* 2011;54(4):599-601. PMID: 21167851

24. Stickel F, Kessebohm K, Weimann R, Seitz HK. Review of liver injury associated with dietary supplements. *Liver Int.* 2011;31(5):595-605. PMID: 21457433

Dietary supplements (DS) are easily available and increasingly used, and adverse hepatic reactions have been reported following their intake. To critically review the literature on liver injury because of DSs, delineating patterns and mechanisms of injury and to increase the awareness towards this cause of acute and chronic liver damage. Studies and case reports on liver injury specifically because of DSs published between 1990 and 2010 were searched in the PubMed and EMBASE data bases using the terms 'dietary/nutritional supplements', 'adverse hepatic reactions', 'liver injury'; 'hepatitis', 'liver failure',

'vitamin A' and 'retinoids', and reviewed for yet unidentified publications. Significant liver injury was reported after intake of Herbalife and Hydroxycut products, tea extracts from *Camellia sinensis*, products containing usnic acid and high contents of vitamin A, anabolic steroids and others. No uniform pattern of hepatotoxicity has been identified and severity may range from asymptomatic elevations of serum liver enzymes to hepatic failure and death. Exact estimates on how frequent adverse hepatic reactions occur as a result of DSs cannot be provided. Liver injury from DSs mimicking other liver diseases is increasingly recognized. Measures to reduce risk include tighter regulation of their production and distribution and increased awareness of users and professionals of the potential risks.

25. Seely KA, Prather PL, James LP, Moran JH. Marijuana-based drugs: innovative therapeutics or designer drugs of abuse? *Mol Interv*. 2011;11(1):36-51. PMID: 21441120

The principal psychoactive component of marijuana, Delta(9)-tetrahydrocannabinol (THC), activates CB1 cannabinoid receptors (CB1Rs). Unfortunately, pharmacological research into the design of effective THC analogs has been hampered by psychiatric side effects. THC-based drug design of a less academic nature, however, has led to the marketing of "synthetic marijuana," labeled as K2 or "Spice," among other terms, which elicits psychotropic actions via CB1R activation. Because of structural dissimilarity to THC, the active ingredients of K2/Spice preparations are widely unregulated. The K2/Spice "phenomenon" provides a context for considering whether marijuana-based drugs will truly provide innovative therapeutics or merely perpetuate drug abuse.

26. Alvarez Tundidor S, Gonzalez Lopez A, Nava Rebollo A, Andres Martin B, Diego Martin JV, Santana Zapatero H, et al. Mushroom poisoning: Orellanus syndrome. *Nefrologia*. 2011;31(4):495-496. PMID: 21738256

27. Lee CH, Wang JD, Chen PC. Risk of liver injury associated with Chinese herbal products containing radix bupleuri in 639,779 patients with hepatitis B virus infection. *PLoS One*. 2011;6(1):e16064. PMID: 21264326

**BACKGROUND:** Chinese herbal products (CHPs) containing radix bupleuri are often prescribed for chronic hepatitis. There have been no epidemiological studies in populations with hepatitis B virus (HBV) infection. Our study was conducted to determine the association between the use of CHPs containing radix bupleuri and the risk of hospitalisation related to liver injury among HBV-infected patients in Taiwan. **METHODS:** From a total of 639,779 patients with diagnoses related to HBV infection, we included hospitalised adult cases with a primary diagnosis of liver injury in the database of Taiwan's national health insurance during the period 1997-2004. Case-control and case-crossover designs were used to assess the risk of hospitalisation with conditional logistic regression models constructed and adjusted for 270 conventionally hepatotoxic

drugs. Cumulative doses of these CHPs and radix bupleuri were assessed for any dose-response relationship. FINDINGS: In total, we collected 1,080 cases fulfilled the inclusion criteria. In the case-control design, the adjusted odds ratio was 1.90 (95% confidence interval [CI]: 1.30 to 2.77). The risks from prescribing the CHPs Xiao-Chai-Hu-Tang and Long-Dan-Xie-Gan-Tang were significantly high, and dose-response relationships were found. The risk of adding each 19 gm dose of radix bupleuri was 2.19 (95% CI: 1.66 to 2.89). The results using the case-crossover design remained similar. CONCLUSIONS: Prescribing Xiao-Chai-Hu-Tang, Long-Dan-Xie-Gan-Tang, or CHPs containing more than 19 gram of radix bupleuri in HBV-infected patients might increase their risks of liver injury. Further studies are indicated to corroborate the above findings.

28. Barregard L, Rekić D, Horvat M, Elmberg L, Lundh T, Zachrisson O. Toxicokinetics of mercury after long-term repeated exposure to thimerosal-containing vaccine. *Toxicol Sci.* 2011;120(2):499-506. PMID: 21252391

The preservative thimerosal contains ethyl mercury (EtHg). Concerns over possible toxicity have re-emerged recently due to its presence in (swine and other) flu vaccines. We examined the potential accumulation of mercury in adults given repeated injections of a thimerosal-preserved vaccine for many years. Fifteen female patients were recruited from an outpatient clinic running a clinical trial with repeated injections (1 ml every 3-4 weeks) of a staphylococcus toxoid vaccine containing 0.01% thimerosal to treat chronic fatigue syndrome. Fifteen untreated female patients with the same diagnoses served as controls. Blood samples were taken before injecting the vaccine, 1 day later, about 2 weeks later, and just before the next injection. In the 15 controls, samples were taken twice. Blood was analyzed for total mercury and EtHg. The toxicokinetics were assessed for each patient separately as well as with a population-based pharmacokinetic model. Total mercury in blood increased on Day 1 in all treated patients (median: 0.33, range: 0.17-1.3 µg/l), as did EtHg (median: 0.14 µg/l, range: 0.06-0.43 µg/l). After a few weeks, levels were back to normal and similar to those in controls. Levels of methyl mercury (MeHg; from fish consumption) were much higher than those of EtHg. After exclusion of an outlier, the mean half-life in a population-based model was 5.6 (95% CI: 4.8-6.3) days. The results indicate that mercury from thimerosal is not accumulated in blood in adults. This is in accordance with short half-lives and rapid metabolism of EtHg to inorganic mercury.

29. Bellocchi M, Sala GL, Prandi S. The cytolytic and cytotoxic activities of palytoxin. *Toxicon.* 2011;57(3):449-59. PMID: 21194542

Palytoxin (PITX) is one of the largest compound present in nature and, with its strong ability to modify the normal function of different biological systems, is also classified as one of the most potent biotoxins. Many alterations are triggered by PITX, directly or indirectly related to its interaction with Na(+),K(+)-ATPase and the consequent conversion of this ion pump into a non-specific cation channel.

The resulting perturbation of Na(+), K(+), Ca(2+) and H(+) ion fluxes is the driving force of PITX-induced cytotoxic events, culminating with system disruption and, finally, cell death. The modifications in the distribution of these ions across the plasma membrane play key roles in the promotion of the PITX-induced cytolytic and cytotoxic responses. In this scenario, PITX-specific cytolysis can be part, but might not necessarily represent a unique aspect of the cytotoxic effects of the toxin. Owing to the complex array of responses, some of them being cell-type-specific and/or affected by experimental conditions, the distinction between cytolytic and cytotoxic events becomes ill-defined, but the two responses show distinct features, whose further characterization could contribute to a better understanding of the molecular mechanism of cellular effects induced by PITX.