   Since their discovery, the safety of artificial sweeteners has been controversial. Artificial sweeteners provide the sweetness of sugar without the calories. As public health attention has turned to reversing the obesity epidemic in the United States, more individuals of all ages are choosing to use these products. These choices may be beneficial for those who cannot tolerate sugar in their diets (e.g., diabetics). However, scientists disagree about the relationships between sweeteners and lymphomas, leukemias, cancers of the bladder and brain, chronic fatigue syndrome, Parkinson's disease, Alzheimer's disease, multiple sclerosis, autism, and systemic lupus. Recently these substances have received increased attention due to their effects on glucose regulation. Occupational health nurses need accurate and timely information to counsel individuals regarding the use of these substances. This article provides an overview of types of artificial sweeteners, sweetener history, chemical structure, biological fate, physiological effects, published animal and human studies, and current standards and regulations.

   The purpose of this systemic review is to assess the efficacy of Er-xian decoction (EXD), a formula of Chinese medicine, in relieving menopausal symptoms. Seven databases were extensively retrieved. The Chinese electronic databases include VIP Information, CBMdisc, and CNKI. The English electronic databases include AMED, CINAHL, Cochrane Library, and MEDLINE. Randomized controlled trials using EXD as a main intervention were included in the study selection. The quality of studies was assessed by Jadad scale and the criteria referred in Cochrane reviewers' handbook. Two independent reviewers were responsible for data extraction and assessment. Discrepancies were rectified referring to the original articles. The efficacy of EXD treatment for menopausal symptoms was evaluated by meta-analysis. There were 154 articles retrieved according to the search strategy, 677 participants involved in the 5 studies that satisfied the selection criteria. Meta-analysis indicated that administration of EXD significantly relieved at least one menopausal symptom when compared to the control group at a 95% confidence interval (p<0.01). The curing effect of EXD with all symptoms relieved was significant as compared with the control groups (p<0.01). The results also indicated that the efficacy of EXD was better than the other non-menopausal hormone therapy (p<0.01), while there was no significant difference between the EXD and menopausal hormone therapy groups. The EXD is effective in treating menopausal symptoms. However, owing to the low quality of the investigated studies, more randomized controlled trials are needed before evidence-based recommendation regarding the effectiveness of EXD in the management of menopausal symptoms can be provided.

   Lead intoxication affects the central nervous system and produces structural disorders and behavioral deficits in several animal species. Although lead neurotoxicity is a well-reported phenomenon, studies on the developmental neurotoxicity induced by this metal in avian are scarce. The aim of this study was to evaluate how a single dose of 28 mug lead acetate administered into the yolk sac on the fifth incubation day of Gallus domesticus can affect the behavior and the brain tissue in the first postnatal week. Several behavioral tests, mainly those related to the motor and exploratory functions were evaluated at fifth and sixth postnatal days (PN). The lead deposition into mesencephalon and
cerebellum was investigated by autometallography (AMG) method. Congenital anomalies, as failure on closure of body's ventral midline and leg dysfunction, were observed in treated chicks. During the first postnatal week, inactivity and anomalous movements were significantly high in lead treated chicks in comparison to control animals. Lead impregnation was observed in both mesencephalon and cerebellum and the cerebellar molecular layer presented higher lead deposition in comparison to granular layer and Purkinje cells. Our results indicate that the in ovo exposure to lead induces important deficits on motor behavior of chicks during the first postnatal week and such phenomena are related to lead deposition in the cerebellar tissue during embryonic development. The proposed exposure schedule represents an interesting experimental approach for studying behavioral and cellular mechanisms related to lead-induced developmental neurotoxicity.

4. Tanne JH. FDA says that bisphenol A in food is safe, despite controversy. BMJ. 2008;337(a1429. PMID: 18728075


Mad-honey disease or honey intoxication is caused by consuming honey produced from leaves and flowers of the Rhododendron family. Here a case of honey intoxication with cardiac involvement is reported.


Objective. To describe the toxidromes associated with plant poisonings in Taiwan. Methods. Retrospective review of acute single-plant exposures with clinical signs and symptoms reported between January 1987 and December 2006 by hospitals to the network of Taiwan Poison Control Centers. Recorded data included demographic data, intent of exposures, exposure routes, clinical findings, and therapeutic strategies. Results. There were 389 cases that met the criteria. Each case was placed into one of the expected toxidromes: anticholinergic, mucosal inflammation, gastroenteritis, acute multisystem organ failure, delayed multisystem organ failure, cholinergic, cardiac dysrhythmia, hepatotoxicity, dermatitis, seizures, and dyspnea. Anticholinergic poisoning was the most common toxidrome. Conclusion. Plant poisonings can be classified into recognizable toxicologic syndromes. These toxidromes may guide a clinician's evaluation and management before a botanist can confirm the actual plant identity.


Introduction. In traditional Chinese medicine, Melia azedarach (Ku-lian) is used orally and topically as an antiparasitic and antifungal agent. Although toxicity of this plant has been widely described in veterinary literature, human poisoning is rarely reported. We describe five patients with M. azedarach poisoning who recovered with supportive care. Case series. Five patients were identified retrospectively from the database of the Taiwan National Poison Center at the Taipei Veterans General Hospital. Three cases were on-site patients, and two were telephone consultations from outside hospitals. Neurological symptoms were the major manifestation in four cases: weakness, myalgia, numbness, and ptosis. Treatment was symptomatic and supportive; all patients recovered without sequelae. Discussion. It is not known which limonoids are responsible for human toxicity. In the Chinese medical literature, human M. azedarach poisoning is said to occur if six to nine fruits, 30 to 40 seeds, or 400 g of the bark is consumed. Onset of symptoms typically occurs within 4-6 h, but as short as 0.5 h had been documented. In our patients, the onset of M. azedarach poisoning was variable, ranging from a few hours to up to 3 weeks after consumption of the herb. Conclusions. M. azedarach poisoning may result in gastrointestinal, cardiovascular, respiratory, or neurological effects, and death in severe cases.

Introduction. Poisoning from Abrus precatorius is attributed to a toxalbumin (abrin) that acts by inhibiting protein synthesis and rarely can cause immuno-mediated demyelination. We report a case of abrin poisoning with demyelination. Case report. A 19-year-old man presented with a history of ingesting crushed Abrus precatorius seeds following a family quarrel. He developed vomiting, abdominal pain, and bloody diarrhea, followed by a seizure and an altered sensorium. Magnetic resonance imaging (MRI) of the brain showed demyelination in the bilateral-medial temporal lobes. The patient was treated with supportive care, and intravenous methylprednisolone followed by oral prednisone, and recovered fully. Discussion. Abrin is an immuno-modulator that may cause immuno-mediated demyelination. We report the clinical course of a patient with demyelination after abrin poisoning, treated with corticosteroids, and document his clinical recovery. Conclusion. Demyelination is a rare complication of Abrus precatorius poisoning. In our case, the demyelination was demonstrated by MRI. Although our patient appeared to recover completely following methylprednisolone therapy, the suggestion that methylprednisolone or other corticosteroids might be useful in treating this demyelination needs experimental verification and clinical validation before concluding that it is a beneficial therapy.


Traditional medicine use is common in developing countries and increasingly popular in the western world. Despite the popularity of traditional medicines, scientific research on safety and efficacy is limited. However documented fatalities and severe illness due to lead poisoning are increasingly recognized to be associated with traditional medicine use. As society becomes more globalized, it is imperative for pharmacists and health care providers to learn about the safety of traditional medical practices. The information presented educates and alerts pharmacists and health care providers about the potential of traditional medicines to cause lead encephalopathy. Case reports were located through systematic literature searches using MEDLINE, CINAHL, AMED, CISCOM, EMBASE and The Cochrane library from 1966 to the February 2007. Reference lists of identified articles and the authors' own files were also searched. Inclusion criteria were cases of human lead encephalopathy associated with traditional medical practices. There were no restrictions regarding the language of publication. Data were subsequently extracted and summarized in narrative and tabular form. We found 76 cases of lead encephalopathy potentially associated with traditional medicine. Ayurvedic medicines were associated with 5 cases (7%), Middle eastern traditional medicines with 66 cases (87%) and 5 cases (7%) with other traditional medicines. Of the 76 cases, 5% were in adults and 95% were in infants and young children. Of the 4 adult cases, at least one was left with residual neurological impairment. In infants and young children, among 72 cases 8 (11%) were fatal, and at least 15 (21%) had residual neurological deficits. Traditional medicine users should be screened for lead exposure and strongly encouraged to discontinue metal-containing remedies. Therefore, the United States Food and Drug Administration and corresponding agencies in other countries should require and enforce heavy metal testing for all imported traditional medicines and "dietary supplements".


PURPOSE OF REVIEW: We remain far from achieving the goal of eliminating lead-associated neurodevelopmental morbidities in children. New evidence regarding the blood lead levels at which morbidities occur have led to calls for the Centers for Disease Control and Prevention to reduce the current screening guideline of 10 microg/dl. The review evaluates the basis for these calls. RECENT FINDINGS: Adverse outcomes, such as reduced intelligence quotient and academic deficits, occur at levels below 10 microg/dl. Some studies suggest that the rate of decline in performance is greater at
levels below 10 microg/dl than above 10 microg/dl, although a plausible mechanism has not been identified. Increased exposure is also associated with neuropsychiatric disorders such as attention deficit hyperactivity disorder and antisocial behavior. Functional imaging studies are beginning to provide insight into the neural substrate of lead's neurodevelopmental effects. Current protocols for chelation therapy appear ineffective in preventing such effects, although environmental enrichment might do so. SUMMARY: No level of lead exposure appears to be 'safe' and even the current 'low' levels of exposure in children are associated with neurodevelopmental deficits. Primary prevention of exposure provides the best hope of mitigating the impact of this preventable disease.


**BACKGROUND:** Few studies have examined factors related to the time required for children's blood lead levels (BLLs) > or = 10 microg/dL to decline to < 10 microg/dL. **OBJECTIVES:** We used routinely collected surveillance data to determine the length of time and risk factors associated with reducing elevated BLLs in children below the level of concern of 10 microg/dL. **METHODS:** From the North Carolina and Vermont state surveillance databases, we identified a retrospective cohort of 996 children < 6 years of age whose first two blood lead tests produced levels > or = 10 microg/dL during 1996-1999. Data were stratified into five categories of qualifying BLLs and analyzed using Cox regression. Survival curves were used to describe the time until BLLs declined below the level of concern. We compared three different analytic methods to account for children lost to follow-up. **RESULTS:** On average, it required slightly more than 1 year (382 days) for a child's BLL to decline to < 10 microg/dL, with the highest BLLs taking even longer. The BLLs of black children [hazard ratio (HR) = 0.84; 95% confidence interval (CI), 0.71-0.99], males (HR(male) = 0.83; 95% CI, 0.71-0.98), and children from rural areas (HR(rural) = 0.83; 95% CI, 0.70-0.97) took longer to fall below 10 microg/dL than those of other children, after controlling for qualifying BLL and other covariates. Sensitivity analysis demonstrated that including censored children estimated a longer time for BLL reduction than when using linear interpolation or when excluding censored children. **CONCLUSION:** Children with high confirmatory BLLs, black children, males, and children from rural areas may need additional attention during case management to expedite their BLL reduction time to < 10 microg/dL. Analytic methods that do not account for loss to follow-up may underestimate the time it takes for BLLs to fall below the recommended target level.


**OBJECTIVES:** To evaluate adverse effects of herbal remedies consumed by menopausal women for control of the climacteric syndrome. **METHODS:** We examined the long term safety and herb-drug interactions of commonly used herbal therapy such as soy, black cohosh, dong quai, ginseng and vitamin E. **RESULTS:** Even carefully designed studies on herbal treatments for vasmotor menopausal symptoms never addressed specifically safety issues. Sporadic reports show dangerous adverse effects of these herbal preparations as well as hazardous interactions between botanic compounds and conventional medications. **CONCLUSIONS:** The unrestricted sale of plant products constitutes a new situation for physicians with little training in phytotherapy. The qualitative and quantitative diversity of the commercially available preparations, the absence of precise prescribing guidelines, and the risk of self-prescribed medication justify the introduction of 'phyto-vigilance'. Physicians should warn their patients about the lack of evidence regarding safety and possible interactions of herbal remedies with concurrent medications.


Extracts of the leaves of the stevia plant (Stevia rebaudiana Bertoni) are used to sweeten food and
beverages in South America, Japan and China. The components responsible for the sweet properties of the plant are glycosides of steviol, primary stevioside (ent-13-hydroxykaur-16-en-18-oic acid), which is 250-300 times sweeter than sucrose and rebaudiosides A and C. Stevioside and steviol have been subjected to extensive genetic testing. The majority of the findings show no evidence of genotoxic activity. Neither stevioside nor its aglycone steviol have been shown to react directly with DNA or demonstrate genotoxic damage in assays relevant to human risk. The mutagenic activity of steviol and some of its derivatives, exhibited in strain TM677, was not reproduced in the same bacteria having normal DNA repair processes. The single positive in vivo study measuring single-strand DNA breaks in Wistar rat tissues by stevioside, was not confirmed in experiments in mice and appears to be measuring processes other than direct DNA damage. Neither stevioside nor steviol-induced clastogenic effects at extremely high dose levels in vivo. Application of a Weight-of-Evidence approach to assess the genetic toxicology database concludes that these substances do not pose a risk of genetic damage following human consumption.


The safety of the stevia-derived sweetener, rebaudioside A (CAS No. 58543-16-1), was evaluated in two oral toxicity studies. In a 4-week study, Wistar rats were administered rebaudioside A at dietary concentrations of 0, 25,000, 50,000, 75,000 and 100,000ppm. The NOAEL, including an evaluation of testes histopathology, was determined to be 100,000 ppm. In the 13-week study, Wistar rats were administered rebaudioside A at dietary concentrations of 0, 12,500, 25,000 and 50,000ppm. Reductions in body weight gain attributable to initial taste aversion and lower caloric density of the diet were observed in high-dose male and females groups. Inconsistent reductions in serum bile acids and cholesterol were attributed to physiological changes in bile acid metabolism due to excretion of high levels of rebaudioside A via the liver. All other hepatic function test results and liver histopathology were within normal limits. Significant changes in other clinical pathology results, organ weights and functional observational battery test results were not observed. Macroscopic and microscopic examinations of all organs, including testes and kidneys, were unremarkable with respect to treatment-related findings. The NOAEL in the 13-week toxicity study was considered to be 50,000ppm or approximately 4161 and 4645mg/kg body weight/day in male and female rats, respectively.

15. Storelli MM. Potential human health risks from metals (Hg, Cd, and Pb) and polychlorinated biphenyls (PCBs) via seafood consumption: estimation of target hazard quotients (THQs) and toxic equivalents (TEQs). *Food Chem Toxicol.* 2008;46(8):2782-8. PMID: 18584931

Edible marine species (fish, cephalopod molluscs, crustaceans) from the Adriatic Sea were analyzed for content in heavy metals (Hg, Cd and Pb) and polychlorinated biphenyls (PCBs). Health risks to human via dietary intake of seafood were assessed by the target hazard quotients (THQs) and the toxic equivalent factors (TEFs). Mercury maximum concentrations corresponded to fish (0.07-1.56 microg g(-1)w.w.), followed by cephalopod molluscs (0.10-0.55 microg g(-1)w.w.), and crustaceans (0.27-0.33 microg g(-1)w.w.). Cadmium levels in cephalopods (0.18-0.59 microg g(-1)w.w.) were higher than those in fish (0.01-0.05 microg g(-1)w.w.) and crustaceans (0.02-0.04 microg g(-1)w.w.), while for Pb the concentrations were generally low (fish: ND-1.18 microg g(-1)w.w., cephalopods: ND-0.17 microg g(-1)w.w., crustaceans: ND-0.03 microg g(-1)w.w.). For PCBs, concentrations in fish, cephalopods and crustaceans ranged between 141 and 3,406 ng g(-1)l.w., 190 and 542 ng g(-1)l.w., and 202 and 429 ng g(-1)l.w., respectively. Cd and Pb THQ values as well as estimates of PCB TEQ exposure indicated the absence of health risks through consumption of the various seafood. In contrast, mercury TEQs values due to consumption of certain fish species (albacore, rosefish and thornback ray) indicated that human health risk might be of concern.

Toxicological studies constitute an essential part of the effort in developing an herbal medicine into a drug product. The US food and drug administration (FDA) published a guidance to assist academic and industry sponsors in the development of this unique group of drug products, and has recently approved an new drug application (NDA) based on green tea extract (Veregen) for topical treatment of genital and perianal warts. In this article, current regulatory views on issues related to requirements and recommendations on various types of nonclinical toxicity studies in support of clinical trials and filing an NDA for a herbal medicine, including pharm/tox aspects of green tea extract (Veregen) NDA, are discussed. Topics include nonclinical pharmacology/toxicology perspectives on herbal nomenclature and its identification, previous human experience and initial clinical trial proposal, regulatory aspects of acute toxicity studies, chronic toxicity studies, mutagenicity studies, reproductive toxicity studies, and carcinogenicity studies on botanicals. Certain regulatory review-related issues are also presented. It is anticipated that through a proactive two-way communication between the Agency and the sponsor, toxicological development of botanical drug product can be significantly facilitated.


HC Red No. 7 functions as a semipermanent (direct) hair colorant in one cosmetic product at 1%. Analytical studies found the relative purity of HC Red No. 7 to be > 98.5%. Impurities may include 2-nitro-benzene-1,4-diamine; 3-(4-amin0-3-nitro-phenoxy)-oxazolin-2-one; 2-chloroethyl 4-amino-3-nitrophenylcarbamate; residual solvents ethanol, DMF, or isopropyl acetate; chloride ions; and heavy metals. Around 0.10% of the applied HC Red No. 7 was absorbed in human dermatomed skin samples. In an acute oral toxicity study in rats, the maximum nonlethal dose was 300 mg/kg. The no observed effect level (NOEL) in a subchronic oral toxicity study in rats was 50 mg/kg day(-1). HC Red No. 7 was not a dermal or ocular irritant in rabbits, but lymphoproliferative responses in mice indicated that HC Red No. 7 should be considered a moderate sensitizer. The NOEL for maternal toxicity was 50 mg/kg/day and the no observed adverse effect level (NOAEL) for embryonic development was 200 mg/kg/day in a prenatal toxicity study of HC Red No. 7 using rats. HC Red No. 7 was nonmutagenic at the hprr locus but mutagenic at the TK locus in mouse lymphoma cells, was mutagenic in several Salmonella typhimurium strains, was not active in an unscheduled DNA synthesis assay, and was unclear in a micronucleus assay in human lymphocyte cultures. No carcinogenicity studies were available, nor were any clinical tests reported. Available hair dye epidemiology studies are insufficient to conclude a causal relationship between hair dye use and cancer or other diseases, but more relevant is that direct hair dyes, although not the focus in all investigations, appear to have little evidence of an association with adverse events as reported in epidemiology studies. As reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel, HC Red No. 7 appears to be a moderate sensitizer in animals. No human sensitivity data concerning this ingredient have been reported. However, hair dyes containing HC Red No. 7, as coal tar hair dye products, are exempt from the principal adulteration provision and from the color additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes contact dermatitis. The Expert Panel expects that following this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures. The CIR Expert Panel also noted that mutagenicity studies available for HC Red No. 7 gave both positive and negative results. Based on the available data, it was concluded that, at most, this ingredient is a weak mutagen. Due to its low dermal absorption potential and its use as a semipermanent hair dye, the CIR Expert Panel believes there is low risk of genotoxicity and that HC Red No. 7 is safe as a hair dye ingredient in the practices of use and concentrations as described in this safety assessment.

18. Final report of the safety assessment of Alcohol Denat., including SD Alcohol 3-A, SD Alcohol 30, SD Alcohol 39, SD Alcohol 39-B, SD Alcohol 39-C, SD Alcohol 40, SD Alcohol 40-B, and SD

Alcohol Denat. is the generic term used by the cosmetics industry to describe denatured alcohol. Alcohol Denat. and various specially denatured (SD) alcohols are used as cosmetic ingredients in a wide variety of products. Many denaturants have been previously considered, on an individual basis, as cosmetic ingredients by the Cosmetic Ingredient Review (CIR) Expert Panel, whereas others, including Brucine and Brucine Sulfate, Denatonium Benzoate, and Quassin, have not previously been evaluated. Quassin is a bitter alkaloid obtained from the wood of Quassia amara. Quassin has been used as an insect antifeedant and insecticide and several studies demonstrate its effectiveness. At oral doses up to 1000 mg/kg using rats, Quassin was not toxic in acute and short-term tests, but some reversible piloerection, decrease in motor activity, and a partial loss of righting reflex were found in mice at 500 mg/kg. At 1000 mg/kg given intraperitoneally (i.p.), all mice died within 24 h of receiving treatment. In a cytotoxicity test with brine shrimp, 1 mg/ml of Quassin did not possess any cytotoxic or antiplasmodial activity. Quassin administered to rat Leydig cells in vitro at concentrations of 5-25 ng/ml inhibited both the basal and luteinizing hormone (LH)-stimulated testosterone secretion in a dose-related fashion. Quassin at doses up to 2.0 g/kg in drinking water using rats produced no significant effect on the body weights, but the mean weights of the testes, seminal vesicles, and epididymides were significantly reduced, and the weights of the anterior pituitary glands were significantly increased. The sperm counts and levels of LH, follicle-stimulating hormone (FSH), and testosterone were significantly lower in groups treated with Quassin. Brucine is a derivative of 2-hydroxystrychnine. Swiss-Webster mice given Brucine base, 30 ml/kg, had an acute oral LD(50) of 150 mg/kg, with central nervous system depression followed by convulsions and seizures in some cases. In those animals that died, respiratory arrest was the cause. The acute i.p. LD(50) for 15 ml/kg of Brucine base was 62.0 mg/kg, with central nervous system depression prior to the onset of convulsions, just as with oral Brucine. The acute intravenous (i.v.) LD(50) was 12.0 mg/kg. Brucine was nonmutagenic in an Ames assay at levels up to 6666 mg/plate, with and without metabolic activation. In a repeat-insult patch test, for a hair care product containing 47% SD Alcohol 40 (95%), it was reported that Brucine Sulfate may be considered a nonprimary irritant and a nonprimary sensitizer. Three different sunscreen products (35% SD Alcohol 40-B, 72.4% SD Alcohol 40, and 74.5% SD Alcohol 40) did not show any signs of photoallergy in human subjects. Also, these three formulas did not exhibit any evidence of phototoxicity in humans. Denatonium Benzoate is a bitter substance detectable at a concentration of 10 ppb, discernibly bitter at 50 ppb, and unpleasantly bitter at 10 ppm. The distribution of topically applied lidocaine, a topical anesthetic chemically related to Denatonium Benzoate demonstrated that virtually no lidocaine appears in the plasma, suggesting that the larger Denatonium Benzoate molecule also would have little or no systemic exposure. Denatonium Benzoate (0.1%) did not show adverse effects in 10 rats in an acute inhalation toxicity test and 0.005% to 0.05% was nonirritating to ocular mucosa in 6 albino rabbits. The acute oral LD(50) for the male rats was 640 mg/kg and for females, 584 mg/kg. The LD(50) for the male rabbits was 508 mg/kg and for the female rabbits, 640 mg/kg. In two chronic toxicity studies, Denatonium Benzoate was administered (by gavage) at 1.6, 8, and 16 mg/kg/day, one using cynomologus monkeys and the other rats, resulted in no compound-related toxicity. The toxicity of SD Alcohols has also been tested, with implications for the particular denaturant used. An irritation test of 55.65% SD Alcohol 40-B denatured with Denatonium Benzoate using rabbits produced minimal effects. A spray formula containing 12% SD Alcohol 40-B was found to be nonirritating when evaluated for vaginal mucosal irritation in New Zealand white rabbits. Cosmetic formulations containing SD Alcohol 40-B (denatured with Denatonium Benzoate) were not sensitizers in repeated insult patch tests. A gel formula containing 29% SD Alcohol 40-B and a spray liquid containing 12% SD Alcohol 40-B did not induce photoallergy, dermal sensitization, or phototoxic response in human subjects. Although the absorption of ethanol (aka Alcohol for purposes of cosmetic ingredient labeling) occurs through skin, ethanol does not appear to affect the integrity of the skin barrier nor reach a very high systemic concentration following dermal exposure. Ethanol may be found in the bloodstream as a result of inhalation exposure and ingestion. Topically applied, ethanol can act as a
penetration enhancer. Most of the systemic toxicity of ethanol appears to be associated with chronic abuse of alcohol. Although ethanol is denatured to make it unfit for consumption, there have been reports of intentional and unintentional consumption of products containing denatured alcohol. Ethanol is a reproductive and developmental toxicant. Ethanol is genotoxic in some test systems and it has been proposed that the genotoxic effects of ethanol are mediated via its metabolite, acetaldehyde. A brief summary is provided of the effects of chronic ingestion of alcohol including intoxication, liver damage, brain damage, and possible carcinogenicity. The CIR Expert Panel recognizes that certain ingredients in this group are reportedly used in a given product category, but the concentration of use is not available. Because dermal application or inhalation of cosmetic products containing these ingredients will not produce significant systemic exposure to ethanol, the CIR Expert Panel concluded that safety of the ingredients should be predicated on the safety of the denaturants used. The Panel considered that the adverse effects known to be associated with Alcohol ingestion included in this safety assessment do not suggest a concern for Alcohol Denat. or SD Alcohols because of the presence of the denaturants, which are added for the express purpose of making the Alcohol unpotable. The CIR Expert Panel has previously conducted safety assessments of t-Butyl Alcohol, Diethyl Phthalate, Methyl Alcohol, Salicylic Acid, Sodium Salicylate, and Methyl Salicylate, in which each was affirmed safe or safe with qualifications. Given their use as denaturants are at low concentrations of use in Alcohol, the CIR Expert Panel determined that Alcohol Denat. denatured with t-Butyl Alcohol, Diethyl Phthalate, Methyl Alcohol, Salicylic Acid, Sodium Salicylate, and Methyl Salicylate is safe as used in cosmetic formulations with no qualifications. Likewise, because they are denatured with either t-Butyl Alcohol, Diethyl Phthalate, or Methyl Alcohol, SD Alcohols 3-A, 30, 39-B, 39-C, and 40-C all are considered safe as used. The Panel considered the available data for Denatonium Benzoate and SD Alcohol 40-B to be sufficient to support the safety of these ingredients in cosmetics. Denatonium Benzoate is sufficiently bitter that it is an effective denaturant at only 0.0006%. The Panel recognized that data on dermal penetration of Denatonium Benzoate were not available, but considered that the available data on lidocaine, a smaller structurally related chemical, indicates that dermal exposure does not result in measurable systemic exposure. The available data, however, were not sufficient to support the safety of Quassin, Brucine, and Brucine Sulfate, Alcohol Denat. denatured with those denaturants, or SD Alcohol 39 and SD Alcohol 40 (SD Alcohols denatured with Quassin, Brucine, and/or Brucine Sulfate), and in order for the Expert Panel to reach a conclusion for these denaturants, additional data are needed.


Kampo is Japan's traditional herbal medicine and it is an integral part of the official Westernized medical system in Japan. We describe the Kampo approach to premenstrual symptoms. We present 3 clinical cases of women treated for premenstrual discomforts in a Kampo clinic in Japan. Each of these women reported improvement in their conditions. We argue that Kampo is well-suited for treatment of premenstrual symptoms in Japan and deserves the attention of Western clinicians for three reasons: (1) patient-centered Kampo diagnosis allows physicians to handle subjective and culture-bound symptoms that are often ignored by Western medicine; (2) Kampo herbal formulas are regulated by the Japanese government, and are pure and of high quality; and (3) the settings in which Kampo is practiced set a stage for therapeutic collaboration between the doctor and the patient.


Hyperprolactinemia is a common adverse effect that occurs as a result of antipsychotic therapies, which often results in discontinuation. Empirical evidence has shown that some herbal medicines have suppressive effects on prolactin (PRL) hyperactivities. This study was designed to compare the
herbal preparation called Peony-Glycyrrhiza Decoction (PGD) with bromocriptine (BMT), a dopamine agonist widely used for PRL-secreting disorders, in the treatment of risperidone-induced hyperprolactinemia. Twenty schizophrenic women who were under risperidone maintenance treatment, diagnosed with hyperprolactinemia (serum PRL levels >50 mug/L), and currently experiencing oligomenorrhea or amenorrhea were selected for the study. Subjects were randomized to additional treatment with PGD (45 g/d) followed by BMT (5 mg/d) or BMT followed by PGD at the same doses for 4 weeks each, with an interval of 4-week washout period between 2 treatment sessions. The severity of psychotic symptoms, adverse events, serum PRL, estradiol, testosterone, and progesterone levels were examined at baseline and endpoint. Peony-Glycyrrhiza Decoction treatment produced a significant baseline-end point decrease in serum PRL levels, without exacerbating psychosis and changing other hormones, and the decreased amplitudes were similar to those of BMT (24% vs 21%-38%). Moreover, there was a significantly greater proportion of patients during PGD treatment than BMT treatment showing improvements on adverse effects associated with hyperprolactinemia (56% vs 17%, P = 0.037). These results suggest that the herbal therapy can yield additional benefits while having comparable efficacy in treating antipsychotic-induced hyperprolactinemia in individuals with schizophrenia.


We report a case of complicated cataract aggravated after taking herbal medication for atopic dermatitis. An 11-yr-old boy was referred for the evaluation of decreased visual acuity in both eyes for 2 months. Past history showed that he had been diagnosed with atopic dermatitis when he was 1 yr old. He had been treated only with herbal medication for a period of 8 months prior to visiting our clinic. He had his visual acuity checked in a local ophthalmic clinic one year before, and the visual acuity was 20/20 in both eyes at that time. When attending our clinic the ophthalmologic examination showed that his best corrected visual acuity was 20/200 in both eyes. Lenses of both eyes had severe posterior subcapsular and posterior capsular opacity. Phacoemulsification, posterior chamber intraocular lens implantation, and posterior continuous curvilinear capsulectomy were performed in both eyes. After 3 months postoperatively, the best corrected visual acuity was recovered to 20/20 in both eyes without any complication. Our case suggests that there may be a risk of aggravation of cataract or development of cataract after treatment with some unidentified herbal medication in a patient with atopic dermatitis.


OBJECTIVE: Black cohosh [Actaea racemosa L., formerly Cimicifuga racemosa (L.) Nutt.] is a botanical used mainly for the management of menopausal symptoms. Recently, regulatory agencies in Australia, Canada, and the European Union have released statements regarding the "potential association" between black cohosh and hepatotoxicity. In response, the Dietary Supplement Information Expert Committee of the US Pharmacopoeia's Council of Experts reviewed safety information for black cohosh products. DESIGN: The Expert Committee analyzed information from human clinical case reports, adverse event reports, animal pharmacological and toxicological data, historical use, regulatory status, and contemporaneous extent of use. Reports were obtained from diverse sources, including the European Medicines Agency, Health Canada, the Australian Therapeutic Goods Administration, and the US Food and Drug Administration. Case reports pertaining to liver damage were evaluated according to the Naranjo causality algorithm scale. RESULTS: Thirty nonduplicate reports on use of black cohosh products concerning liver damage were analyzed. All the reports of liver damage were assigned possible causality, and none were
probable or certain causality. The clinical pharmacokinetic and animal toxicological information did not reveal unfavorable information about black cohosh. CONCLUSIONS: Based on this safety review, the Dietary Supplement Information Expert Committee determined that black cohosh products should be labeled to include a cautionary statement. This is a change from the Expert Committee's decision of 2002, which required no such statement. With this decision, the US Pharmacopeia's Botanical Expert Committee may develop monographs for black cohosh, and the US Pharmacopeia may offer its verification programs to dietary supplement ingredient and product manufacturers.

The purpose of this study was to find out whether the effect of acute exposure to lead on memory processes in mice could be exacerbated by cerebral oligemia. Adult mice were subjected to 30 min of bilateral clamping of carotid arteries (BCCA) and then treated intraperitoneally with lead acetate at a single dose of: 29.3 mg/kg, 58.6 mg/kg or 87.9 mg/kg. Long-term memory was assessed in the passive avoidance task while spontaneous alternation was evaluated using the Y-maze task. Performance of the tasks was tested on the 2nd, 7th and 14th post-surgical day. On the 14th post-surgical day, significant retention deficits in passive avoidance performance were only observed in BCCA mice injected with the 87.9 mg/kg lead. Co-exposure to cerebral oligemia and lead did not change spontaneous alternation in the Y-maze task. These results show that cerebral oligemic hypoxia combined with acute lead exposure may cause selective and long-lasting impairment in memory function.

We present a case of acute cholestatic liver injury associated with the combination of whey protein and creatine supplements. The difficulty of diagnosing drug-induced liver injury is emphasized. The patient is a healthy, 27-year-old man who presented with painless jaundice. He had no occupational exposures to solvents, was not taking prescription medications, and did not use recreational drugs or alcohol. He was an enthusiastic weight-lifter and had been taking creatine for 8 to 9 months and whey protein supplements for 4 weeks prior to the development of symptoms. Laboratory tests revealed elevated total bilirubin (54.7 mg/dL) and alkaline phosphatase (436 U/L), minimally elevated transaminases, and a creatinine of 3.1 mg/dL. Serologic work-up was negative for viral hepatitis and autoimmune liver disease, and Wilson's disease was ruled out. Magnetic resonance cholangiopancreatogram was unremarkable, but a liver biopsy showed marked cholestasis with ductular proliferation. He had dramatic clinical improvement with intravenous fluids and discontinuation of the nutritional supplements. In patients with acute liver injury, clinicians should inquire about dietary supplement usage and consider immediate discontinuation of all unnecessary products. We describe a case of profound jaundice related to a commonly used and reportedly safe combination of such supplements.

Oxidative damage of biomolecules and antioxidant status in erythrocytes of humans from an outbreak of argemone oil (AO) poisoning in Kannauj (India) and AO intoxicated experimental animals was investigated. Erythrocytes of the dropsy patients and AO treated rats were found to be more susceptible to 2,2'-azobis (2-amidinopropane) dihydrochloride (AAPH) induced peroxidative stress. Significant decrease in RBC glutathione (GSH) levels (46, 63%) with concomitant enhancement in oxidized glutathione (172, 154%) levels was noticed in patients and AO intoxicated animals. Further, depletion of glutathione reductase (GR), glucose-6-phosphate dehydrogenase (G-6-PDH) and glutathione-S-transferase (GST) (42-52%) was observed in dropsy patients. Oxidation of
erythrocyte membrane lipids and proteins was increased (120-144%) in patients and AO treated animals (112-137%) along with 8-OHdG levels in whole blood (180%) of dropsy patients. A significant reduction in alpha-tocopherol content (68%) was noticed in erythrocytes of dropsy patients and hepatic, plasma and RBCs of AO treated rats (59-70%) thereby indicating the diminished antioxidant potential to scavenge free radicals or the limited transport of alpha-tocopherol from liver to RBCs leading to enhanced oxidation of lipids and proteins in erythrocytes. These studies implicate an important role of erythrocyte degradation in production of anemia and breathlessness in epidemic dropsy.


OBJECTIVE: To study the effects of BSO, GSH, Vit-C and DMPS on the nephrotoxicity of mercury. METHODS: The rats in groups 1, 2 and 3 were sc injected with 0.75, 1.5 and 2.5 mg/kg HgCl2, respectively. Fourth group rats were ip injected with 0.5 mmol/kg BSO and 4h later sc administrated with 0.75 mg/kg HgCl2. The rats in groups 5, 6 and 7 were ip injected with 3 mmol/kg GSH, 4 mmol/kg Vit-C, 200 micromol/kg DMPS, respectively, and 2 h later sc administrated with 2.5 mg/kg HgCl2. Eighth group rats were sc injected with saline as a control. Mercury concentrations in the liver, renal cortex and urine, urinary NAG, ALP, LDH activities, protein and BUN contents were determined. RESULTS: Urinary NAG, ALP activities, protein and BUN contents in the rats of BSO pretreatment group were significantly higher than that of 0.75 mg/kg HgCl2 alone group and control group. As compared with 2.5 mg/kg HgCl2 alone group, urinary NAG, ALP, LDH activities, urinary protein and BUN contents decreased significantly. CONCLUSION: BSO pretreatment could enhance the renal toxicity of mercury and GSH, Vit-C and DMPS pretreatment had antagonistic effects on nephrotoxicity of mercury.