
The objective of this study was to utilize a case report to review the use of physostigmine for jimsonweed intoxication. A 15-year-old girl was found at school hallucinating and incoherent. Upon presentation to the emergency department, she was found to be tachycardic and confused with dilated pupils and dry, flushed, hot skin. She was admitted to our institution. Hallucinations and symptoms resolved after the use of physostigmine. She subsequently admitted to ingesting 'moonflower seeds,' which are derived from Jimsonweed (Datura stramonium). She was discharged when she got well. Jimsonweed is known to contain high concentrations of anticholinergic substances; hence, ingestion can result in the anticholinergic toxidrome. Signs and symptoms include hallucinations, tachycardia, dilated pupils, and disorientation. In our patient, the use of the physostigmine as an antidote resulted in a favorable outcome without any complications. Ingestion of the Datura species can result in severe toxicity. Each plant varies in the concentrations of alkaloid substances. For this reason, it is very important for individuals to become educated on the toxicities and potential risks associated with recreational use of these plants. The use of physostigmine can help in both the diagnosis and management of patients intoxicated with these substances.


Cannabis is one of the most widely used illicit drugs among adolescents, and most users first experiment with it in adolescence. Adolescence is a critical phase for brain development, characterized by neuronal maturation and rearrangement processes, such as myelination, synaptic pruning and dendritic plasticity. The endocannabinoid system plays an
important role in fundamental brain developmental processes such as neuronal cell proliferation, migration and differentiation. Therefore changes in endocannabinoid activity during this specific developmental phase, induced by the psychoactive component of marijuana, Delta(9)-tetrahydrocannabinol, might lead to subtle but lasting neurobiological changes that can affect brain functions and behaviour. In this review, we outline recent research into the endocannabinoid system focusing on the relationships between adolescent exposure to cannabinoids and increased risk for certain neuropsychiatric diseases such as schizophrenia, as highlighted by both human and animal studies. Particular emphasis will be given to the possible mechanisms by which adolescent cannabis consumption could render a person more susceptible to developing psychoses such as schizophrenia.

3. Panlilio LV, Justinova Z, Goldberg SR. Animal models of cannabinoid reward. Br J Pharmacol. 2010;160(3):499-510. The endogenous cannabinoid system is involved in numerous physiological and neuropsychological functions. Medications that target this system hold promise for the treatment of a wide variety of disorders. However, as reward is one of the most prominent of these functions, medications that activate this system must be evaluated for abuse potential. Meanwhile, cannabis is already being used chronically by millions of people, many of whom eventually seek treatment for cannabis dependence. Therefore, there is a need for procedures that can be used to: (i) better understand the mechanisms of cannabinoid reward; (ii) evaluate the abuse potential of new medications; and (iii) evaluate the effectiveness of medications developed for treating cannabis dependence. Animal models of cannabinoid reward provide a means of accomplishing these goals. In this review, we briefly describe and evaluate these models, their advantages and their shortcomings. Special emphasis is placed on intravenous cannabinoid self-administration in squirrel monkeys, a valid, reliable and flexible model that we have developed over the past decade. Although the conditions under which cannabinoid drugs have rewarding effects may be more restricted than with other drugs of abuse such as cocaine and heroin, work with these models indicates that cannabinoid reward involves similar brain mechanisms and produces the same kinds of reward-related behaviour. By continuing to use these animal models as tools in the development of new medications, it should be possible to take advantage of the potential benefits provided by the endocannabinoid system while minimizing its potential for harm.

The blood-brain barrier (BBB) is a key determinant for drug transport through brain vessels. It restricts the pharmacological efficacy in numerous neurological diseases, including brain tumors. A major functional constituent of BBB is P-glycoprotein, which is also a major obstacle for effective chemotherapy of brain tumors. An appealing strategy is to selectively modulate BBB function using P-glycoprotein inhibitors. We assessed 57 chemically defined compounds derived from medicinal plants used in traditional Chinese medicine for their potential to inhibit P-glycoprotein. Nine phytochemicals inhibited P-glycoprotein in porcine brain capillary endothelial cells (PBCECs) and multidrug-resistant CEM/ADR5000 cells as shown by a calcein fluorescence assay. The cytotoxicity of the 57 phytochemicals was measured by a growth inhibition assay. Seven compounds inhibiting P-glycoprotein at lower doses were cytotoxic to drug-sensitive parental CCRF-CEM cells at higher doses. Of them, five were not cross-resistant to CEM/ADR5000 cells (baicalein, bufalin, glybomine B, deoxyserofendic acid, and shogaol). Bufalin was chosen as a lead compound. Of a further six bufalin-related compounds, scillarenin showed improved features in comparison to bufalin. It was cytotoxic to cancer cells at a nanomolar range. COMPARE and hierarchical cluster analyses of microarray-based mRNA expression were used to investigate determinants of sensitivity or resistance of the bufalin-related compounds downstream of P-glycoprotein. CEM/ADR5000 cells were not cross-resistant, but were collaterally sensitive towards scillarenin. Finally, scillarenin inhibited P-glycoprotein in PBCECs. Taken together, these data show that scillarenin is a potential novel candidate for P-glycoprotein inhibition at BBB, and, thereby, may improve the efficacy of therapy regimens in treating brain diseases.

Methylmercury is a widely distributed environmental toxicant with detrimental effects on the developing and adult nervous system. Due to its accumulation in the food chain, chronic exposure to methylmercury via consumption of fish and sea mammals is still a major concern for human health, especially developmental exposure that may lead to neurological alterations, including cognitive and motor dysfunctions. Mercury-induced neurotoxicity and the identification of the underlying mechanisms has been a main focus of research in the neurotoxicology field. Three major mechanisms have been identified as critical in methylmercury-induced cell damage including (i) disruption of calcium homeostasis, (ii) induction of oxidative stress via overproduction of reactive oxygen species or reduction of antioxidative defenses and (iii)
interactions with sulfhydryl groups. In vivo and in vitro studies have provided solid evidence for the occurrence of neural cell death, as well as cytoarchitectural alterations in the nervous system after exposure to methylmercury. Signaling cascades leading to cell death induced by methylmercury involve the release of mitochondrial factors, such as cytochrome c and AIF with subsequent caspase-dependent or -independent apoptosis, respectively; induction of calcium-dependent proteases calpains; interaction with lysosomes leading to release of cathepsins. Interestingly, several pathways can be activated in parallel, depending on the cell type. In this paper, we provide an overview of recent findings on methylmercury-induced neurotoxicity and cell death pathways that have been described in neural and endocrine cell systems.

Despite clinical experience that spans more than half a century, chelation for toxic heavy metals represents one of the most controversial and misapplied interventions in clinical toxicology. The prompt use of chelating agents to treat acute, life-threatening intoxication is an indication that is largely supported by experimental animal data and limited clinical research. Although chelating agents administered for chronic intoxication may accelerate the excretion of heavy metals, their therapeutic efficacy in terms of decreased morbidity and mortality is largely unestablished. Recent investigations suggest that their use in such settings might be associated with deleterious effects. Careful attention to risk-benefit issues is warranted, particularly in clinical situations in which the etiological role of heavy metals in the patient's illness is in question.

This article reviews the evidence supporting the efficacy of antidotes used or recommended for the potential chemical warfare agents of most concern. Chemical warfare agents considered include cyanide, vesicants, pulmonary irritants such as chlorine and phosgene, and nerve agents. The strength of evidence for most antidotes is weak, highlighting the need for additional research in this area.

INTRODUCTION: In Mediterranean countries, intoxication by Atractylis gummifera L. is frequent and characterized
principally by hepatorenal injury, often fatal. Its toxicity after a cutaneous application is unknown. We report a case of poisoning by *A. gummifera* L. induced by repeated cutaneous application. **CASE REPORT:** A 30-month-old boy was admitted in our pediatric intensive care unit in coma (Glasgow Coma Scale 8). Investigations showed hepatic cellular injury, cholestasis, decreased prothrombin level, and increased creatinine. History from the parents revealed repeated and occlusive cutaneous application of *A. gummifera* L. on a skin burn. Qualitative analysis of urine confirmed the diagnosis of *A. gummifera* poisoning. The child was discharged after 16 days of hospitalization with residual renal insufficiency. **DISCUSSION:** Poisoning by *A. gummifera* L. after cutaneous application has not previously been reported in the literature. The prevention of this poisoning, particularly frequent in Mediterranean countries, is mainly based on the education of the public concerning the dangers of this plant.


**CONTEXT:** Cyanide is a rapidly acting cellular poison, primarily targeting cytochrome c oxidase, and is a common occupational and residential toxin, mostly via smoke inhalation. Cyanide is also a potential weapon of mass destruction, with recent credible threats of attacks focusing the need for better treatments, as current cyanide antidotes are limited and impractical for rapid deployment in mass casualty settings. **OBJECTIVE:** We have used mouse models of cyanide poisoning to compare the efficacy of cobinamide (Cbi), the precursor to cobalamin (vitamin B(12)), to currently approved cyanide antidotes. Cbi has extremely high affinity for cyanide and substantial solubility in water. **MATERIALS AND METHODS:** We studied Cbi in both an inhaled and intraperitoneal model of cyanide poisoning in mice. **RESULTS:** We found Cbi more effective than hydroxocobalamin, sodium thiosulfate, sodium nitrite, and the combination of sodium thiosulfate–sodium nitrite in treating cyanide poisoning. Compared to hydroxocobalamin, Cbi was 3 and 11 times more potent in the intraperitoneal and inhalation models, respectively. Cobinamide sulfite (Cbi–SO(3)) was rapidly absorbed after intramuscular injection, and mice recovered from a lethal dose of cyanide even when given at a time when they had been apneic for over 2 min. In range-finding studies, Cbi–SO(3) at doses up to 2000 mg/kg exhibited no clinical toxicity. **DISCUSSION AND CONCLUSION:** These studies demonstrate that Cbi is a highly effective cyanide antidote in mouse models, and suggest it could be used in a mass casualty setting, because it can be given rapidly as an intramuscular injection when administered as Cbi–SO(3). Based on these animal data Cbi–SO(3) appears to be an antidote worthy of further
testing as a therapy for mass casualties.


The use of neem-based products is widespread in the Indian Subcontinent. Neem-based pesticides obtained from neem kernels are considered natural and safe. The toxic effects of ingestion and overdose of this pesticide in adults have not been described in this literature. We report the case of a 35-year-old lady who had consumed Azadirachtin in an attempt of deliberate self-harm. The patient had features of neurotoxicity because of Azadirachtin requiring intensive medical care with mechanical ventilation. The patient survived the overdose with no long-lasting side effects of the toxin.


**BACKGROUND:** Some mushrooms in the genus Cortinarius are well known to cause acute and chronic renal failure. Until now, there have been no confirmed cases of renal failure due to the ingestion of a Cortinarius mushroom in North America. We describe a case of a woman who ingested mushrooms found under an oak tree in western Michigan and developed chronic renal failure. **METHODS:** Phylogenetic analysis of the internal transcribed spacer (ITS) regions of nuclear-encoded ribosomal RNA was performed between an unconsumed sample of the Michigan specimens, a control sample of Cortinarius orellanus (JFA9859) from Europe, and other closely related ITS sequences of Cortinarius retrieved from GenBank. An additional gene region, rpb2, was also sequenced for comparison. **RESULTS:** Phylogenetic analysis revealed the Michigan material to be closely related to, but distinct from, other ITS sequences of the Orellanii clade in Cortinarius. Divergence is less at the rpb2 locus. No historical taxa from North America are known to match the identification of the Michigan material. **CONCLUSION:** The mushrooms ingested by the patient were confirmed to be a new species of Cortinarius closely related to C. orellanus. We introduce a newly described North American species, Cortinarius orellanosus, capable of causing renal failure after ingestion.


**CONTEXT:** Radiolabeling and dose fixation study of alpha-ketoglutarate (A-KG). **OBJECTIVE:** A-KG is a potential oral
antidote for cyanide poisoning. Its protective efficacy in animals was best exhibited at a dose of 2.0 g/kg body weight, which when extrapolated to human is very high. The objective of this study was to reduce the dose of A-KG in humans with concomitant increase in its bioavailability, employing pharmacoscintigraphic techniques to assess kinetics in man.

MATERIALS AND METHODS: A-KG was radiolabeled with technetium-99m pertechnetate (Tc-99m) and its purity, labeling efficiency, and stability in vitro were determined by instant thin layer chromatography. Time-dependent bio-absorption of the drug in rats and rabbits was assessed by gamma scintigraphy after oral administration of a tracer dose of (99m)Tc-A-KG mixed with nonradioactive A-KG at a concentration of 0.1-2.0 g/kg in the presence or absence of aqueous dilution. Furthermore, scintigraphy and radiometry studies were performed in healthy human volunteers using 5-20 g of A-KG, given in single or split doses followed by different quantity of water. Drug bioavailability was estimated periodically. RESULTS: High radiolabeling (>97%) of A-KG with a stability of 24 h in vitro was obtained. Less than 1% absorption of the drug occurred within 20 min after A-KG was administered in animals at a concentration of 2.0 g/kg body weight. One-tenth reduction in dose increased the bioavailability to 15%. Significant improvement in gastric emptying of the drug was achieved when the drug was administered along with 1-5 mL of water. In humans, two doses of 10 g A-KG given at an interval of 10 min, followed by 300 mL of water, increased the drug bioavailability to 40% as compared to a single dose of 20 g. DISCUSSION: Significant reduction in A-KG dose was achieved in humans as compared to the recommended dose in animals. CONCLUSION: Aqueous dilution improves the bioavailability of A-KG in humans.


BACKGROUND: Grayanotoxins (GTX), also known as andromedotoxins, are produced by plants of the Ericaceae family. This toxin is responsible for "mad honey" intoxication, which can present with fatal cardiac bradyarrhythmias and circulatory collapse. GTXs lead to cardiac toxicity because they increase sodium channel permeability and activate the vagus nerve. OBJECTIVE: We evaluated 42 patients (33 males) prospectively who had been hospitalized with diagnosis of "mad honey" intoxication in a state hospital setting. METHODS AND RESULTS: The median age of patients was 48.5 years and all patients were admitted with complaints of nausea, vomiting, dizziness, fainting, and sweating. Five of the patients had syncope before admission. On admission, the mean systolic blood pressure was 73.1 +/- 12.7 mmHg, the mean diastolic blood pressure was 52.1 +/- 11.3 mmHg, mean heart rate was 38 +/- 7 bpm. On initial
electrocardiograms, 18 patients had sinus bradycardia, 15 patients had complete atrioventricular block, and 9 patients had nodal rhythm. All patients were monitored in a coronary care unit and treated symptomatically with atropine, intravenous fluids, and dopamine. None of the patients needed temporary pacing and all were discharged without complications. CONCLUSION: "Mad honey," which is produced widely in northern parts of Turkey can be toxic. This intoxication should be considered in patients admitted to emergency department with bradycardia and hypotension especially in regions where this honey is produced.

A large number of herbal remedies (e.g. garlic, mistletoe, Essiac, Lingzhi, and astragalus) are used by cancer patients for treating the cancer and/or reducing the toxicities of chemotherapeutic drugs. Some herbal medicines have shown potentially beneficial effects on cancer progression and may ameliorate chemotherapy-induced toxicities. However, there is no or weak scientific basis for the clinical use of these herbal medicines in cancer management and almost none of these plant medicines have been tested in rigorous clinical trials.
There are increased reports on the interaction of herbal medicines and anticancer drugs that is becoming a safety concern. For example, a clinical study in cancer patients reported that treatment of St John's wort at 900 mg/day orally for 18 days decreased the plasma levels of the active metabolite of irinotecan, SN-38, by 42%. In healthy subjects, 2 weeks of treatment with St John's wort at 900 mg/day significantly decreased the systemic exposure of imatinib by 32%. In women with advanced breast cancer, coadministration of garlic supplement reduced the clearance of docetaxol by 23.1-35.1%, although the difference did not achieve statistical significance. Most anticancer drugs undergo Phase I and/or II metabolism and are substrates of P-glycoprotein, breast cancer resistance protein, multidrug resistance associated proteins, and/or other transporters. Induction and inhibition of these enzymes and transporters is considered an important mechanism for herb-anticancer drug interactions. Further studies are warranted to investigate potentially harmful herbal interactions with anticancer drugs in patients.

This article presents evidence demonstrating that the historical use of leaded gasoline and lead (Pb) in exterior paints in Australia has contaminated urban soils in the older
inner suburbs of large cities such as Sydney and Melbourne. While significant attention has been focused on Pb poisoning in mining and smelting towns in Australia, relatively little research has focused on exposure to Pb originating from inner-city soil dust and its potential for childhood Pb exposures. Due to a lack of systematic blood lead (PbB) screening and geochemical soil Pb mapping in the inner cities of Australia, the risks from environmental Pb exposure remain unconstrained within urban population centres.


As factors affecting neonatal neurodevelopment, methylmercury, polychlorinated biphenyls (PCBs), and maternal seafood intake reflecting n-3 polyunsaturated fatty acids (PUFAs) are believed to have adverse or beneficial effects, but there are a few reports addressing such factors simultaneously. We carried out a birth cohort study to clarify the effects of these three factors on the Neonatal Behavioral Assessment Scale (NBAS), administered 3 days after birth. In a total of 498 mother-neonate pairs, the total mercury level (median, 1.96 μg/g) in maternal hair at parturition and the summation operator PCB level (45.5 ng/g-lipid) in cord blood were analyzed, and maternal seafood intake was estimated using a semi-quantitative food frequency questionnaire. A negative relationship between the hair mercury level and the motor cluster of NBAS was observed, even after adjusting for PCBs, maternal seafood intake, and possible confounders such as maternal age, birth weight, and parity. The summation operator PCB level was negatively correlated with the motor cluster, but this association was attenuated after adjusting for mercury and the confounders. There was seen to be a positive association between maternal seafood intake and the motor cluster when considering the effects of mercury and PCBs. In conclusion, our data suggest that prenatal exposure to methylmercury adversely affects neonatal neurobehavioral function; in contrast, maternal seafood intake appears to be beneficial. The neurobehavioral effect of prenatal exposure to PCBs remains unclear in our study. Further research is necessary to elucidate interactive effects of methylmercury, PCBs, and n-3 PUFAs, originating from fish, on child neurodevelopment.


We developed a probabilistic model to characterize the plausible distribution of health and economic benefits that
would accrue to the U.S. population following reduction of methyl mercury (MeHg) exposure. MeHg, a known human developmental neurotoxicant, may increase fatal heart attack risks. Model parameters reflect current understanding of the relationships between MeHg intake, health risks, and societal valuation of these risks. The expected monetary value of the annual health benefits generated by a 10% reduction in U.S. population exposure to MeHg for one year is $860 million; 80% of this is associated with reductions in fatal heart attacks and the remainder with IQ gains. The plausible distribution of the benefits is quite broad with 5th and 95th percentile estimates of approximately $50 million and $3.5 billion, respectively. The largest source of uncertainty is whether epidemiological associations between MeHg exposure and fatal heart attacks reflect causality. The next largest sources of uncertainty concern the slope of the relationship between maternal MeHg exposure and reduced intelligence among children and whether this relationship exhibits a threshold. Our analysis suggests that the possible causal relationship between MeHg exposure and fatal heart attacks should be better characterized, using additional epidemiological studies and formally elicited expert judgment.


Mercury has a number of unique and fascinating properties. It is present in the environment in several forms, both organic and inorganic. Each of these forms has somewhat unique properties that differentiate them from the other forms, but all are toxic to humans in one way or the others. Mercury has been proven to be a potential source of poisoning in children as a result of the inappropriate handling of a liquid mercury. The cases of metallic mercury vapor intoxication not associated with occupational exposure may occur in school science laboratories, from mercury dust and powders, from latex paint containing a mercury-based fungicide, and from normal wear or installation of dental amalgam fillings. Another source of toxic mercury exposure can be broken thermometers, barometers, or sphygmomanometers that may occur in the home, and children are often victims of environmental exposure. In this paper, we present three members of a family who were exposed to mercury brought home from school by a family member. Since the mercury exposure was not known, the initial presentation and clinical picture suggested a misdiagnosis, a contagious infectious disease, because the onset of symptoms occurred at different times in the same family members. A subsequent change to a diagnosis of mercury intoxication and chelation therapy with meso-2,3-dimercaptosuccinic acid was started.

A sensitive and specific liquid chromatography-electrospray ionization mass spectrometry (LC/ESI-MS) method was developed for the analysis of 18 drugs used for the treatment of anti-hypertension, including diuretics, calcium antagonists, and angiotensin-converting enzyme inhibitors (ACEI) as adulterants in dietary supplements and traditional Chinese medicines. Separation was accomplished on a Xtimate C18 reversed-phase column using a mixture of methanol, acetonitrile and 20 mM ammonium formate buffer (pH 3.2) as mobile phase. The method demonstrated linearity from 0.03 to 21.52 mg kg\(^{-1}\). Limits of detection ranged from 6.5 to 86.0 microg kg\(^{-1}\). The recoveries of spiked samples ranged from 71% to 109%. The procedure was successfully applied in routine inspection analysis.


Twenty herbal medicines or dietary supplements marketed as natural slimming products were analysed by diffusion ordered spectroscopy (DOSY) 1H-nuclear magnetic resonance (NMR) and DOSY-COSY 1H-NMR. The method allows analysis of the whole sample with the detection of both active and inactive ingredients in these complex matrices. Among the 20 formulations analysed, two were strictly herbal and four had a composition corresponding to declared ingredients on the packaging or the leaflet. The others were all adulterated. Eight formulations contain sibutramine alone at doses ranging from 4.4 to 30.5 mg/capsule. Five formulations contain sibutramine (from 5.0 to 19.6 mg/capsule or tablet) in combination with phenolphthalein (from 4.4 to 66.1 mg/capsule), and the last formulation was adulterated with synephrine (19.5 mg/capsule). Quantification of the actives was carried out with 1H-NMR. Several other compounds were also characterized including methylsynephrine, vitaberin, sugars, vitamins, etc. DOSY NMR is thus proposed as a useful tool for detection of unexpected adulteration.


BACKGROUND/AIMS: To report the recently 7 cases of drug induced hepatitis patients in our department. METHODOLOGY: From October 2008 to December 2008, 7 patients were enrolled in our
department for drug induced hepatitis caused by Zhixue capsules administration. The Zhixue capsule is composed of cortex dictam and radices sophorae flavescentis. There were 4 female and 3 male patients. The patients were of age 31 to 52 years old. Of those, 6 patients belonged to the hepatocellular injury type and one to the mixed type. The time period Zhixue capsule was administered was from 6 to 18 days. When the patients enrolled into our department, they were treated for jaundice and protective liver function. RESULTS: When the patients were discharged the symptoms were all improved evidently and liver function became normal. One patient with mixed type was hospitalized for 63 days and he was treated with glucocorticoid to help his recovery. CONCLUSIONS: Zhixue capsule could induce acute hepatitis of various types, but mainly hepatocellular injury type. The patients of all types could be recovered with proper treatment. The combined type may need glucocorticoid administration to help recovery.


23. Moon JM, Chun BJ. The efficacy of high doses of vitamin C in patients with paraquat poisoning. Hum Exp Toxicol. 2010. Paraquat (PQ) poisoning is an extremely difficult condition to manage clinically because of the lack of effective treatments. The purpose of this study was to assess the effect of high doses of vitamin C in combination with anti-inflammatory and immunosuppressant therapy in patients with PQ poisoning. The medical records of 134 patients who presented to the emergency department within 24 hours after PQ poisoning were reviewed retrospectively. The 57 patients presented between January 2004 and September 2005 were group 1; they received pulse therapy, which included cyclophosphamide and methylprednisolone, followed by the administration of dexamethasone over 2 weeks. The 77 patients that presented between October 2005 and January 2008 were group 2; they received the above-mentioned therapy and high-dose vitamin C for 2 weeks. There was no difference in the distribution of baseline variables between the 2 groups. However, group 2 showed a significant reduction in acute kidney injury related to PQ. Furthermore, a multivariate logistic regression analysis showed that the addition of vitamin C to the treatment was significantly associated with an increased survival of the patients. Larger trials will be needed to verify the effect of high-dose vitamin C on survival in patients with PQ poisoning.


There has been much debate about the use of activated charcoal in patients who have taken overdoses and then present to
Emergency Departments. There are clinical trials, research and position statements that have examined the effectiveness of activated charcoal in a number of overdoses of different medications, but there is still a debate surrounding the evidence based practice of administering activated charcoal in patients who have taken a drug overdose due to lack of evidence. This article will examine on the two main guidelines on activated charcoal, one produced by the National Institute for Clinical Excellence and the second produced by American Academy of Clinical Toxicology. It will discuss the methods of administration on activated charcoal, contraindications and the difficulties or challenges in adhering to these guidelines in the clinical setting.

With the rapid development of nanotechnology, there is a growing interest on the application of nanoparticles in various fields such as photonics, catalysis, magnetics, and biotechnology including cosmetics, pharmaceutics, and medicines. However, little is known about their potential toxicity to human health. Owing to their special properties, nanoparticles have the capacity to bypass the blood–brain barrier (BBB). However, the toxic effects of nanoparticles on central nervous system (CNS) function are still lacking. And the interactions of nanoparticles with the cells and tissues in CNS are poorly understood. Thus, neurotoxicity induced by nanoparticles is still a new topic that requires more attention. In this review, we summarized the pathways by which the nanoparticles could enter into the CNS and the recent investigations on the neurotoxicity of nanoparticles both in vitro and in vivo, as well as the potential mechanisms. Furthermore, the future direction in the neurotoxicity studies of nanoparticles is also discussed.


BACKGROUND: Traditional Chinese Medicine (TCM) is popular for treatment of fibromyalgia (FM) although there is a lack of comprehensive evaluation of current clinical evidence for TCM's therapeutic effect and safety. Objective: To review systematically the beneficial and harmful effects of TCM therapies for FM. METHODS: We searched six English and Chinese electronic databases for randomized clinical trials (RCTs) on
TCM for treatment of FM. Two authors extracted data and assessed the trial quality independently. RevMan 5 software was used for data analyses with an effect estimate presented as mean difference (MD) with a 95% confidence interval (CI).

RESULTS: Twenty-five RCTs were identified with 1516 participants for this review. Seven trials (28%) were evaluated as having a low risk of bias and the remaining trials were identified as being as unclear or having a high risk of bias. Overall, ten trials were eligible for the meta-analysis, and data from remaining 15 trials were synthesized qualitatively. Acupuncture reduced the number of tender points (MD, -3.21; 95% CI -4.23 to -2.11; p < 0.00001, I(2) = 0%), and pain scores compared with conventional medications (MD, -1.78; 95% CI, -2.24 to -1.32; p < 0.00001; I(2) = 0%). Acupuncture showed no significant effect, with a random-effect model, compared with sham acupuncture (MD, -0.55; 95% CI, -1.35-0.24; p = 0.17; I(2) = 69%), on pain reduction. A combination of acupuncture and cupping therapy was better than conventional medications for reducing pain (MD, -1.66; 95% CI, -2.14 to -1.19; p < 0.00001; I(2) = 0%), and for improving depression scores with related to FM (MD, -4.92; 95% CI, -6.49 to -3.34; p < 0.00001; I(2) = 32%). Other individual trials demonstrated positive effects of Chinese herbal medicine on pain reduction compared with conventional medications. There were no serious adverse effects reported that were related to TCM therapies in these trials.

CONCLUSIONS: TCM therapies appear to be effective for treating FM. However, further large, rigorously designed trials are warranted because of insufficient methodological rigor in the included trials.


OBJECTIVE: The objective of this study was to systematically evaluate the effects of Traditional Chinese Medicine (TCM) therapy including acupuncture, tu'ina, oral herbal medicine, herbal bathing, and collateral–channels conduct therapy for treating children with cerebral palsy (CP). METHODS: We included randomized controlled trials (RCTs) on TCM for children with CP. We searched the China National Knowledge Infrastructure, Database for Chinese Technical Periodicals, Chinese Biomedical Literature Database, databases of Chinese biomedical journals/Chinese Medical Current Contents, Wan Fang Data, PubMed, MEDLINE, Embase, and the Cochrane Library until the end of July 2009, and searched the reference list of retrieved papers. Data were extracted by 1 author and checked for validation by another author, and data were analyzed using RevMan 4.3.2. Only one meta-analysis was performed due to the heterogeneity among the trials. RESULTS: Thirty-five (35) RCTs
involving 3286 children with CP using TCM therapy and conventional therapy (CT) including physical, occupational, and speech therapy, hyperbaric oxygen, cranial nerves nutrition agents, or any combination of above were included. The methodological quality was generally low in terms of allocation concealment, blinding, and intention-to-treat analysis. Meta-analysis showed acupuncture combine with CT improved activities of daily living (mean difference: 6.38, 95% confidence interval 5.15-7.61; p < 0.00001, n = 160) compared with CT alone. Acupuncture plus tu'ina, or plus herbal medicine and CT showed significant beneficial effects on comprehensive function in terms of both physical and mental aspects, independence, and verbal function compared with CT alone. The combination of radix Astragali injection with CT showed significant benefit on gross motor function and social behavior adaptation comparing with CT. There are six trials reported adverse events that were not associated with acupuncture, tu'ina, and/or herbal medicine. CONCLUSIONS: Acupuncture with or without CT or other conventional therapy, tu'ina, herbal medicine, and collateral channels conduct treatment combined with CT may have benefit in children with CP. However, due to insufficient evidence, further rigorous trials are warranted.

29. Byard RW. A review of the potential forensic significance of traditional herbal medicines. J Forensic Sci. 2010;55(1):89-92. Traditional herbal substances may contain highly toxic chemicals and heavy metals, in addition to naturally occurring organic toxins. These substances may cause illness, exacerbate pre-existing ill health or result in death, particularly if taken in excess or in an unusual manner (e.g., injected rather than ingested). Lack of regulation of the content and quality of herbal medicines may result in contamination and adulteration with prescription medications. As there may be no history of the specific use of these products their contribution to death may not be fully appreciated during a standard autopsy. Even when their existence is known or suspected, it may be difficult to identify these substances on standard toxicologic screening. Herbal medicines may also be responsible for a range of symptoms and signs that may confuse the clinical presentation of cases. Given these issues the role of herbal medicines in forensic practice needs to be more clearly defined as deaths may be occurring where herbal medicines have made a significant, but as-yet unrecognized, contribution.

30. Chen WH, Wang R, Shi YP. Flavonoids in the poisonous plant Oxytropis falcata. J Nat Prod. 2010;73(8):1398-403. Three new flavonoids, oxytropisoflavans A (1) and B (2) and (6aR,11aR)-3,8-dihydroxy-9,10-dimethoxypterocarpan (3), together with 30 known flavonoids (4-33), were isolated from
the aerial parts and roots of Oxytropis falcata. The absolute configurations of 3 and C-3 in 1 and 2 were deduced by circular dichroism. The structure of flavonoid 2 was confirmed by single-crystal X-ray diffraction analysis and that of flavonoid 3 by total synthesis of its racemate. Oxytropisoflavan A (1) is an unprecedented chalcone-isoflavan biflavonoid, whereas oxytropisoflavan B (2) possesses a rare modified A-ring. Pterocarpan 3 has good radical-scavenging activity in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay.


OBJECTIVE: To investigate whether the lack of knowledge of toxic agents in households is a risk factor for individual unintentional childhood poisoning. METHODS: The case group (n = 25) was composed of caregivers of children under 60 months of age who underwent accidental oral poisoning and were treated at two reference hospitals in Porto Alegre, southern Brazil, and recorded in the Toxicology Information Center database. The control group (n = 25) was composed of caregivers of children matched for sex, age, and presence in their homes of the same toxic agents found in the case group, who sought emergency medical care at the same hospitals, but for other reasons. A structured questionnaire was administered to verify the following questions: sociodemographic data, clinical history, behavioral antecedents of caregivers, storage of toxic agents, history of previous poisoning accidents. RESULTS: The children's mean age was 31.8 months (+/-0.97) and mean height was 93 cm (+/-11). Families, in both groups, were aware of the toxic action of agents available in their homes; however, caregivers in the control group were twice as likely to have such knowledge compared to the case group. Distraction was 15 times more likely to occur among caregivers of children who underwent poisoning compared to the control group. Storage of toxic agents below 150 cm was approximately 17 times more likely to occur in the group of children who underwent poisoning compared to children in the control group. CONCLUSIONS: Lack of knowledge of the toxic action of agents stored in households is not a risk factor for childhood poisoning. The attributable risks described in this study indicated that the elimination of other factors, such as distraction and storage below 150 cm, would lead to the prevention of 13 and 19% of poisonings in childhood, respectively.


33. Kovacic P. How safe is bisphenol A? Fundamentals of toxicity:
The FDA recently announced concern about the safety of bisphenol A (BPA) and the need for more research. In the current controversy, scant attention is being paid to toxicity at the fundamental, molecular level, which is the topic of this report. Important information is provided by extensive studies on metabolism. The principal pathway is detoxification, mainly by conjugation leading to a glucuronide. A minor route entails oxidation by hydroxylation to a catechol followed by further transformation to an o-quinone. The catechol-o-quinone couple is capable of redox cycling with generation of reactive oxygen species (ROS) and oxidative stress (OS). o-Quinones are highly electron affinic with very favorable reduction potentials that permit electron transfer (ET) under physiological conditions. Only small amounts are sufficient to generate large quantities of ROS catalytically. There is extensive evidence for production of ROS, which buttresses ET by o-quinone as a plausible source. In addition, there are numerous reports on toxicity to body constituents by BPA. Those adversely affected include the liver, DNA, genes, CNS, reproductive system and kidney. Since a plethora of prior studies links ROS-OS with toxicity, it is reasonable to propose a similar connection for BPA. Cell signaling also plays a role. There are various other factors involved with toxic responses, including age, with the fetus and infants being the most vulnerable. A report concludes that human exposure to BPA is not negligible. The present overview represents a novel, integrated approach to BPA toxicity. A similar article was recently published in this journal which deals with toxicity of prevalent phthalate plasticizers.


RATIONALE AND OBJECTIVE: Studies in laboratory animals strongly suggest reciprocal modulation of the opioidergic and endocannabinoid systems, a relationship that has not been demonstrated in humans. This study sought to clarify this interaction by assessing how a range of naltrexone doses
altered the subjective, cognitive, and cardiovascular effects of marijuana. MATERIAL AND METHODS: Daily marijuana smokers (n = 29) participated in this within-subject, randomized, double-blind, placebo-controlled study. Naltrexone (0, 12, 25, 50, or 100 mg) was administered before active or inactive marijuana (3.27 or 0% THC) was smoked. RESULTS: Active marijuana increased subjective ratings of marijuana 'Strength,' 'High,' and positive subjective ratings of marijuana quality and drug effect including 'Liking,' 'Good,' and 'Take Again' compared to inactive marijuana. Naltrexone alone decreased ratings of 'Liking,' 'Take Again,' and 'Stimulated' compared with placebo, but increased ratings of drug 'Strength,' 'High,' 'Good,' 'Liking,' 'Stimulated,' and 'Take Again' when administered under active marijuana conditions. Active marijuana did not affect performance on cognitive tasks relative to inactive marijuana, whereas naltrexone decreased performance when administered alone or in combination with active marijuana. Active marijuana increased heart rate compared to inactive marijuana under placebo naltrexone conditions. Although naltrexone alone decreased heart rate, it further increased marijuana's cardiovascular effect. CONCLUSIONS: In heavy marijuana smokers opioid-receptor blockade enhanced the subjective and cardiovascular effects of marijuana, suggesting that endogenous opioids dampen cannabinoid effects in this population. These findings demonstrate that a broad range of clinically used doses of naltrexone potentially increases the abuse liability and cardiovascular risks of cannabinoids.


RATIONALE: Caffeine exacerbates the acute toxicity of 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy') in rats characterised by hyperthermia, tachycardia and lethality. Depletion of central catecholamine stores and dopamine D(1) receptor blockade have been reported to attenuate the ability of caffeine to exacerbate MDMA-induced hyperthermia.

OBJECTIVES: Here, we investigate whether dopamine D(1) and D(2) receptors mediate the effects of caffeine on MDMA-induced changes in body temperature, heart rate and locomotor activity.

METHODS: All parameters were recorded continuously in individually housed rats using bioradiotelemetry from 1 h prior to 4 h following caffeine (10 mg/kg, s.c.) and/or MDMA (10 mg/kg, s.c.) administration. RESULTS: Co-administration of caffeine with MDMA provoked a switch from MDMA-induced hypothermia and bradycardia to hyperthermia and tachycardia without influencing MDMA-induced hyperlocomotion. Pre-treatment with a specific dopamine D(1/5) antagonist SCH 23390 (1 mg/kg) enhanced MDMA-induced hypothermia and blocked the ability of
caffeine to provoke a switch from MDMA-induced hypothermia to hyperthermia. Furthermore, SCH 23390 blocked MDMA-induced hyperactivity and the ability of caffeine to promote a tachycardic response to MDMA. By contrast, pre-treatment with the selective D(2) antagonist, sulphiride (100 mg/kg) blocked MDMA-induced hypothermia, failed to influence the ability of caffeine to promote tachycardia whilst enhancing MDMA-induced hyperactivity. CONCLUSIONS: Our results highlight the importance of dopamine D(1) and D(2) receptors in shaping the behavioural and physiological response to MDMA and suggest that the ability of caffeine to provoke MDMA-induced toxicity is associated with the promotion of dopamine D(1) over D(2) receptor-related responses.

39. Micozzi MS, Pribitkin EA. Common herbal remedies, adverse reactions, and dermatologic effects. Skinmed. 2010;8(1):30-6. Herbal remedies (phytomedicines) possess significant biological activity and pharmacologic efficacy. Consequently, they may manifest potential adverse effects and drug interactions. The expansion in sales of herbal remedies has brought products to the marketplace that do not always conform to the standards of safety and efficacy that physicians and patients have come to expect. Relatively few physicians inquire about herbal medicine use, and up to 70% of patients do not reveal their use of herbal medicines to their physicians and pharmacists. All physicians should question patients regarding their use of herbal remedies and document their responses in the medical record. Patients should be aware that potentially limited standardization and quality control, and somewhat circumscribed regulation, may result in variability in content, efficacy, and potential contamination of herbal remedies. Physicians in general, and specifically dermatologists, should be aware of potential adverse reactions related to the use of certain herbal remedies. Specific cautions exist with regard to dermatologic side effects such as contact dermatitis, blisters, urticaria, angioedema, ulceration, photosensitization, and changes in skin pigmentation.

40. Schoeman K, Bend JR, Koren G. Hair methylmercury: a new indication for therapeutic monitoring. Ther Drug Monit. 2010;32(3):289-93. Maternal exposure to methylmercury can adversely affect fetal neurodevelopment. Long-term mercury exposure is best estimated by hair measurement of the metal. The authors analyzed the appropriateness of therapeutic monitoring of hair mercury in women of reproductive age using widely accepted criteria for therapeutic drug monitoring. The analysis reveals that such monitoring can help protect babies from long-term adverse effects, while ensuring appropriate maternal fish consumption.

Methylmercury (MeHg), an environmental toxicant primarily found in fish and seafood poses a dilemma to both consumers and regulatory authorities given the nutritional benefits of fish consumption vs. possible adverse neurological damage caused by MeHg. The present study addresses whether supplementation with 6-hydroxy-2,5,7,8-tetramethylchromane-2-carboxylic acid (Trolox), alters the neuro-oxidative effects of MeHg in C6-glioma and B35-neuronal cell lines. As indicators of cytotoxicity, reduced glutathione (GSH), reactive oxygen species (ROS) and mitochondrial activity (MTT) were measured. The cellular mercury (Hg) content was measured with high resolution-inductively coupled plasma mass spectrometry (HR-ICPMS). The amount of MeHg-induced ROS was significantly reduced (p<0.05) after treatment with 50muM Trolox in C6 glial cell line. However, treatment with Trolox did not induce any significant increase in GSH levels or MTT activity in either of the cell lines. In addition, treatment with Trolox did not induce any significant changes in intracellular MeHg levels. The MeHg and Trolox treated C6 glial cell line differed significantly (p<0.05) from the B35 cell line for MTT, ROS and GSH activity. These findings provide experimental evidence that preincubation with Trolox prevents MeHg-induced ROS generation in C6 glial cell line by quenching of free radicals and not by changes in intracellular GSH or MeHg content.


OBJECTIVE: Poisoning events, including exposures to hazardous materials, can involve multiple victims. Regional poison centers often are contacted in such events involving multiple victims. METHODS: We searched our poison center database over a nine-year time period for all calls involving a poisoning event in which more than two people were exposed to the same substance. We then matched each product to the generic category used by the National Poison Data System. We analyzed this data to find the most frequent substances reported as primary substances in the multiple exposures. RESULTS: We identified 6,695 calls between 2000 and 2008 that had more than two people exposed to the same substance. In these calls, 25,926 people were exposed (3.6% of the 715,701 human exposure calls for this period). These calls involved 64 of the 67 NPDS substance group codes. Some substances were much more commonly involved than others. The top three categories causing the most exposures were Fumes/Gases/Vapors, Food Products/Food Poisoning and Pesticides. Of the patients exposed, 69.4% were not followed due to minimal effects possible or judged as nontoxic, 0.3% had
major effects, 8.6% had no effects, and 9.3% had minimal to moderate effects. Eight people expired. CONCLUSION: Fumes, gases, and vapors make up the majority of multi-exposure calls. The overall mortality from multi-exposures, based on our data, is low. Analysis of these calls can help poison centers better understand these events and direct training.