

**American Academy of Clinical Toxicology**  
**Special Interest Group: Herbs & Dietary Supplements**  
**Abstracting Service**  
**April 13, 2008**

1. Landelle C, Francony G, Sam-Lai NF, Gaillard Y, Vincent F, Wroblewski I, Danel V. **Poisoning** by lavandin extract in a 18-month-old boy. *Clin Toxicol (Phila)*. 2008;46(4):279-81. PMID: 18363117  
An 18-month-old boy ingested a small amount of homemade lavandin extract. The child developed a central nervous system depression and a confused state three hours after ingestion. The electroencephalogram showed fast rhythm disorders consistent with a toxic etiology. The outcome was favorable. **Poisoning** was confirmed by headspace-gas chromatography-mass spectrometry. Linalyl acetate, linalyl formate, and acetone were identified in pure lavandin extract and in the child's blood and urine. We report the only case of lavandin extract **poisoning** confirmed by **toxicological** analysis.
2. Freeman K. Mitigating methylmercury exposure. *Environ Health Perspect*. 2008;116(1):A36. PMID: 18197288
3. Kasper S, Gastpar M, Muller WE, Volz HP, Dienel A, Kieser M, Moller HJ. Efficacy of St. John's wort extract WS 5570 in acute treatment of mild depression: a reanalysis of data from controlled clinical trials. *Eur Arch Psychiatry Clin Neurosci*. 2008;258(1):59-63. PMID: 18084790  
Based on the original data from two double-blind, randomized, placebo-controlled clinical trials and the acute phase of a long-term study that investigated the antidepressant efficacy of St. John's wort extract WS 5570, we present a re-analysis of a subset of patients suffering from an acute episode of mild depression according to DSM criteria. Out of a total of more than 1,200 patients included into these trials 217 had a pre-treatment total score  $\leq$  20 points on the 17-item Hamilton Rating Scale for Depression (HAM-D) and were eligible for our re-analysis. They received 600, 900, or 1,200 mg/day WS 5570 or placebo for 6 weeks. In patients treated with WS 5570 the HAM-D total score decreased by averages of 10.8 (600 mg/day), 9.6 (900 mg/day), and 10.7 (1,200 mg/day) points between the pre-treatment baseline value and the end of acute treatment, compared to 6.8 points in the placebo group ( $p < 0.01$  for all pairwise comparisons of WS 5570 against placebo). This corresponded to average relative decreases by 49-57% for WS 5570 and by 36% for placebo. The rates of responders (i.e., patients with a HAM-D total score decrease  $\geq$  50%) were 73%, 64%, 71%, and 37% for WS 5570 600 mg/day, 900 mg/day and 1,200 mg/day, and placebo, respectively. At the end of acute treatment 57% of the patients treated with WS 5570 600 mg/day, 33% in the 900 mg/day group and 62% in the 1,200 mg/day group, as well as 25% in the placebo group were in remission (HAM-D total score  $\leq$  7 points). The analysis shows that St. John's wort extract WS 5570 has a meaningful beneficial effect during acute treatment of patients suffering from mild depression and leads to a substantial increase in the probability of remission.
4. Mortelmans LJ, Van Loo M, De Cauwer HG, Merlevede K. Seizures and hyponatremia after excessive intake of diet coke. *Eur J Emerg Med*. 2008;15(1):51. PMID: 18180668  
We describe a case of epileptic seizures after a massive intake of diet coke. Apart from the hyponatremia due to water intoxication the convulsions can be potentiated by the high dose of caffeine and aspartame from the diet coke. To our knowledge this is the first report of seizures due to excessive diet coke intake.
5. Abate P, Pueta M, Spear NE, Molina JC. Fetal learning about ethanol and later ethanol responsiveness: evidence against "safe" amounts of prenatal exposure. *Exp Biol Med (Maywood)*. 2008;233(2):139-54. PMID: 18222969  
Near-term fetuses of different mammalian species, including humans, exhibit functional sensory and learning capabilities. The neurobiological literature indicates that the unborn organism processes

sensory stimuli present in the amniotic fluid, retains this information for considerable amounts of time, and is also capable of associating such stimuli with biologically relevant events. This research has stimulated studies aimed at the analysis of fetal and neonatal learning about ethanol, a topic that constitutes the core of the present review. Ethanol has characteristic sensory (olfactory, taste, and trigeminal) attributes and can exert pharmacologic reinforcing effects. The studies under examination support the hypothesis that low to moderate levels of maternal ethanol intoxication during late pregnancy set the opportunity for fetal learning about ethanol. These levels of prenatal ethanol exposure do not generate evident morphologic or neurobehavioral alterations in the offspring, but they exert a significant impact upon later ethanol-seeking and intake behaviors. Supported by preclinical and clinical findings, this review contributes to strengthening the case for the ability of prenatal ethanol exposure to have effects on the postnatal organism.

6. Burdock GA, Carabin IG. Safety assessment of sandalwood oil (*Santalum album* L.). *Food Chem Toxicol.* 2008;46(2):421-32. PMID: 17980948  
Sandalwood (*Santalum album* L.) is a fragrant wood from which oil is derived for use in food and cosmetics. Sandalwood oil is used in the food industry as a flavor ingredient with a daily consumption of 0.0074 mg/kg. Over 100 constituents have been identified in sandalwood oil with the major constituent being alpha-santalol. Sandalwood oil and its major constituent have low acute oral and dermal toxicity in laboratory animals. Sandalwood oil was not mutagenic in spore Rec assay and was found to have anticarcinogenic, antiviral and bactericidal activity. Occasional cases of irritation or sensitization reactions to sandalwood oil in humans are reported in the literature. Although the available information on toxicity of sandalwood oil is limited, it has a long history of oral use without any reported adverse effects and is considered safe at present use levels.
7. Krenova M, Pelcova D, Navratil T. Survey of *Amanita phalloides* poisoning: clinical findings and follow-up evaluation. *Hum Exp Toxicol.* 2007;26(12):955-61. PMID: 18375639  
The aim of our study was to evaluate the severity of hepatic and kidney damage with a focus on their reversibility, and to analyze the prognostic factors following *Amanita phalloides* poisoning based on calls made to the Czech Toxicological Information Centre. A variety of clinical and laboratory parameters were collected. Student's t-test and Fisher's test were used for statistical analysis. *Amanita phalloides* poisoning was verified in 34 cases (5 children, 29 adults). The following findings emerged: vomiting (76%), diarrhea (62%), hepatic failure (24%), and renal failure (11%). Two patients died on the fifth day after mushroom ingestion. In 18 patients, all serum levels normalized by the time of discharge; in 10 patients up to 7.3 months on average after discharge. Five patients did not comply with follow-up. Renal damage persisted in only one patient, 19 months after discharge. In conclusion, the interval to recovery from hepatic and renal damage by the time of discharge depended on a decrease in the prothrombin index and an increase in serum transaminase and bilirubin levels. Recovery was favorable in all subjects who survived the acute phase of poisoning, except in one patient with a solitary kidney.
8. Saatcioglu O, Ugur Z, Kamberyan K, Yanik M. A psychotic disorder related to use of herbal preparation: case report. *Int J Psychiatry Med.* 2007;37(3):279-82. PMID: 18314856  
This article deals with the increasing frequency with which herbal preparations are being used in Turkey. The ingredients of herbal preparations are multiple and include a variety of herbal seed and leaf-related components. Thus, it is not possible to pinpoint a specific chemical culprit without careful analysis of each. In this article, we present a case of psychotic manic state due to the herbal preparations.
9. Final report on the safety assessment of Hexamidine and Hexamidine Diisethionate. *Int J Toxicol.* 2007;26 Suppl 3(79-88. PMID: 18273451  
Hexamidine Diisethionate functions as a biocide in cosmetics at concentrations of 0.03% to 0.1% in

38 cosmetic products. Hexamidine functions as a biocide and preservative in cosmetics, but is not in current use in cosmetics, but it is used in over-the-counter (OTC) drug products. Hexamidine was poorly absorbed by human cadaver skin when in water-oil formulations or in a gel that simulated a cosmetic product formulation. Hexamidine Diisethionate was poorly absorbed by the skin of live rats and was not stored in any tissue type. Hexamidine Diisethionate given to rats intravenously was rapidly metabolized to Hexamidine. Excretion was primarily via the feces, with a small amount excreted in the urine. Acute oral LD(50) values of Hexamidine Diisethionate were 0.71 to 2.5 g/kg in mice and 0.75 g/kg in rats. Dermal exposure to 4 g/kg Hexamidine Diisethionate in rats or up to 9.4 ml/kg of a 0.1% Hexamidine Diisethionate solution under occlusion in rabbits produced no mortality or other signs of toxicity. The no-observed-effect level (NOEL) for oral subchronic toxicity of Hexamidine Diisethionate in rats was 50 mg/kg/day. No signs of toxicity were observed with 2% Hexamidine Diisethionate in subchronic studies using rabbits. Application of 0.1 ml of 0.11% Hexamidine Diisethionate in aqueous solution to the eyes of rabbits produced transient reactions; 0.05% produced no reactions. Slight erythema was observed with 0.10% Hexamidine Diisethionate applied to the abraded skin of 1/11 albino rabbits. A 40% solution of Hexamidine Diisethionate applied to 10% of the body surface of rats produced slight erythema, slight edema, and scabbing in some animals at varying times after treatment. Hexamidine Diisethionate was not a sensitizer in the guinea pig maximization test or in an intracutaneous guinea pig sensitization test. Hexamidine Diisethionate was not a photosensitizer in albino rabbits. Hexamidine Diisethionate was not mutagenic in a bacterial reverse mutagenicity assay or clastogenic in mammalian cells. Hexamidine Diisethionate at 0.10% did not provoke primary irritation, inflammation, or sensitization in a clinical test of 200 human subjects. One case report of photosensitivity to Hexamidine and one of contact sensitivity to Hexamidine were reported. There were nine case reports of contact sensitivity to Hexamidine Diisethionate. A European safety assessment recommended a limit of 0.1% Hexamidine Diisethionate in leave-on and rinse-off cosmetic products. In considering the available data, the Cosmetic Ingredient Review (CIR) Expert Panel acknowledged the lack of carcinogenicity and reproductive/developmental toxicity data. Because genotoxicity studies were negative, and there were no structural alerts, the Panel concluded that it was unlikely that these ingredients would be carcinogenic. Because the rate of absorption of Hexamidine and Hexamidine Diisethionate is slow, there is no tissue accumulation, and excretion is rapid and complete, and there was no toxicity in a subchronic study, the Panel concluded that dermal exposures would not likely present a risk of reproductive/developmental toxicity. The Panel noted that a guinea pig maximization study using Hexamidine Diisethionate produced no dermal reactions and that a clinical test at 0.1% produced no irritation or sensitization. The Panel also expressed concern regarding the possible presence of 1,4-dioxane as an impurity, and stressed that the cosmetic industry should continue to use the necessary purification procedures to remove these impurities from the ingredient before blending into cosmetic formulations. The Panel noted that there are no data for concentration of use for eye makeup and baby products, and was concerned that there should not be unrestricted concentration levels in these product categories. Although there are gaps in knowledge about product use, the overall information available on the types of products in which these ingredients are used and at what concentration indicate a pattern of use. Within this overall pattern of use, the Expert Panel considers all ingredients in this group to be safe at concentrations up to and including 0.1%.

10. Final report on the amended safety assessment of Propyl Gallate. *Int J Toxicol*. 2007;26 Suppl 3(89-118). PMID: 18080874  
Propyl Gallate is the n-propyl ester of gallic acid (3,4,5-trihydroxybenzoic acid). It is soluble in ethanol, ethyl ether, oil, lard, and aqueous solutions of polyethylene glycol (PEG) ethers of cetyl alcohol, but only slightly soluble in water. Propyl Gallate currently is used as an antioxidant in a reported 167 cosmetic products at maximum concentrations of 0.1%. Propyl Gallate is generally recognized as safe (GRAS) antioxidant to protect fats, oils, and fat-containing food from rancidity that results from the formation of peroxides. Data on dermal absorption are not available, but Propyl Gallate is absorbed when ingested, then methylated, conjugated, and excreted in the urine. The

biological activity of Propyl Gallate is consistent with its free-radical scavenging ability, with effects that include antimicrobial activity, enzyme inhibition, inhibition of biosynthetic processes, inhibition of the formation of nitrosamines, anesthesia, inhibition of neuromuscular response to chemicals, ionizing/ultraviolet (UV) radiation protection, chemoprotection, antimutagenesis, anticarcinogenesis and antitumorogenesis, antiteratogenesis, and anticariogenesis. Animal toxicity studies indicate that Propyl Gallate was slightly toxic when ingested, but no systemic effects were noted with dermal application. Propyl Gallate is a strong sensitizer when tested intradermally, less sensitizing when tested topically, and nonsensitizing topically at 0.1% in one study. In a second study, Propyl Gallate (15 mg dissolved in 8 ml vehicle) was sensitizing to guinea pigs. Acute eye irritation tests conducted on nine cosmetic formulations, each containing less than 1% Propyl Gallate, were negative. A phototoxicity study conducted on a cosmetic formulation containing 0.003% Propyl Gallate determined that the product was not phototoxic to guinea pigs. In one study, female rats fed 0.5 g Propyl Gallate had substantially increased fetal resorption rates when compared to controls, but in four other studies, Propyl Gallate at doses up to 2.04 g/kg was nonteratogenic in rats, rabbits, mice, and hamsters. In clinical cumulative irritancy tests, Propyl Gallate was nonirritating at concentrations up to 10%. Patch tests at concentrations less than 1% yielded positive elicitation responses. Repeat-insult patch tests using cosmetic formulations with 0.003% Propyl Gallate produced no irritation or sensitization. Propyl Gallate at a concentration of 10% in alcohol was nonphototoxic in 25 subjects. Cosmetic formulations, each containing 0.003% Propyl Gallate, produced no signs of photosensitization or phototoxicity in a total of 371 subjects. Although Propyl Gallate is not a skin irritant in clinical tests, the available data demonstrate that it is a skin sensitizer and that it may be a sensitizer at lower concentrations than originally thought, i.e., at concentrations less than 1%. In actual practice, cosmetic formulations contain Propyl Gallate at concentrations up to 0.1% and usage has increased over the past 20 years. In spite of the increased exposure associated with increased use, it is the clinical experience of the Panel that the use of Propyl Gallate in cosmetics has not resulted in sensitization reactions. Therefore, the Panel believes that a concentration limitation of 0.1% in cosmetics is necessary (given the evidence of sensitization at concentrations less than 1%) and sufficient (given that current products are not producing adverse reactions).

11. Sheibani S, Gerson LB. Chemical colitis. *J Clin Gastroenterol*. 2008;42(2):115-21. PMID: 18209577

Chemical colitis can occur as a result of accidental contamination of endoscopes or by intentional or accidental administration of enemas containing various chemicals. Most cases have occurred after accidental contamination of endoscopes with glutaraldehyde and/or hydrogen peroxide. There have been multiple case reports of chemical colitis resulting from unintentional administration of caustic chemicals. Intentional administration of corrosive enemas has been implicated in sexual practices, bowel cleansing, or in suicide attempts. Patients present with nonspecific symptoms including abdominal pain, rectal bleeding, and/or diarrhea. As chemical colitis remains rare, the literature consists of scattered case reports and small series. Agents implicated in chemical colitis that are covered in this review include alcohol, radiocontrast agents, glutaraldehyde, formalin, ergotamine, hydrofluoric acid, sulfuric acid, acetic acid, ammonia, soap, sodium hydroxide, hydrogen peroxide, herbal medicines, chloro-m-xyleneol, and potassium permanganate. Clinical, endoscopic, and histologic features are outlined for each agent in addition to the existing literature. Given the nonspecific presentation of many cases of chemically induced colitis, the diagnosis can be challenging if the pertinent history is not obtained. Most patients demonstrate the resolution of chemical-induced colitis after conservative or medical therapy. Depending on the depth and extent of injury, patients rarely require colectomy for ischemic colitis and/or peritonitis. Other postingestion complications include colonic strictures and rectovaginal fistulae. The benefits of medical therapy compared with conservative therapy are not known, as comparative clinical management trials have not been performed.

12. Vojdani JD, Beuchat LR, Tauxe RV. Juice-associated outbreaks of human illness in the United States, 1995 through 2005. *J Food Prot.* 2008;71(2):356-64. PMID: 18326187  
Outbreaks of illness associated with consumption of fruit juice have been a growing public health problem since the early 1990s. In response to epidemiologic investigations of outbreaks in which juice was implicated, the U.S. Food and Drug Administration implemented process control measures to regulate the production of fruit juice. The final juice regulation, which became effective in 2002, 2003, and 2004, depending on the size of the business, requires that juice operations comply with a hazard analysis critical control point (HACCP) plan. The Centers for Disease Control and Prevention (CDC) receives reports of food-associated outbreaks of illness. We reviewed fruit juice-associated outbreaks of illness reported to the CDC's Foodborne Outbreak Reporting System. From 1995 through 2005, 21 juice-associated outbreaks were reported to CDC; 10 implicated apple juice or cider, 8 were linked to orange juice, and 3 involved other types of fruit juice. These outbreaks caused 1,366 illnesses, with a median of 21 cases per outbreak (range, 2 to 398 cases). Among the 13 outbreaks of known etiology, 5 were caused by Salmonella, 5 by Escherichia coli O157:H7, 2 by Cryptosporidium, and one by Shiga toxin-producing E. coli O111 and Cryptosporidium. Fewer juice-associated outbreaks have been reported since the juice HACCP regulation was implemented. Some juice operations that are exempt from processing requirements or do not comply with the regulation continue to be implicated in outbreaks of illness.
13. Ragothaman M, Kulkarni G, Ashraf VV, Pal PK, Chickabasavaiah Y, Shankar SK, Govindappa SS, Satishchandra P, Muthane UB. Elemental mercury **poisoning** probably causes cortical myoclonus. *Mov Disord.* 2007;22(13):1964-8. PMID: 17708573  
Mercury toxicity causes postural tremors, commonly referred to as "mercurial tremors," and cerebellar dysfunction. A 23-year woman, 2 years after injecting herself with elemental mercury developed disabling generalized myoclonus and ataxia. Electrophysiological studies confirmed the myoclonus was probably of cortical origin. Her deficits progressed over 2 years and improved after subcutaneous mercury deposits at the injection site were surgically cleared. Myoclonus of cortical origin has never been described in mercury **poisoning**. It is important to ask patients presenting with jerks about exposure to elemental mercury even if they have a progressive illness, as it is a potentially reversible condition as in our patient.
14. Seneviratne CJ, Wong RW, Samaranyake LP. Potent anti-microbial activity of traditional Chinese medicine herbs against Candida species. *Mycoses.* 2008;51(1):30-4. PMID: 18076592  
Anti-candidial activities of eight traditional Chinese medicinal (TCM) herbs were evaluated against six different Candida species. TCM preparations were screened for antifungal activity using a standard agar diffusion assay. Following identification of potential candidate herbs, their minimum inhibitory concentration (MIC) values were determined using the standardised NCCLS M-27A broth microdilution assay. Among TCM herbs, Rhizoma Coptidis had potent antifungal activity against Candida glabrata, Candida krusei and Candida tropicalis, but not against Candida albicans, Candida dubliniensis and Candida parapsolosis. The MIC values of the Rhizoma Coptidis against C. glabrata, C. krusei and C. tropicalis were 50, 50 and 100 microg ml(-1) respectively. We report here, for the first time, the potent antifungal activity of Rhizoma Coptidis and Cortex phellodendri Chinesis on three different non-albicans Candida species, C. glabrata, C. krusei and C. tropicalis and hence their possible use as therapeutic agents.
15. Busse F, Omid L, Leichtle A, Windgassen M, Kluge E, Stumvoll M. Lead **poisoning** due to adulterated marijuana. *N Engl J Med.* 2008;358(15):1641-2. PMID: 18403778
16. Greene S, Harris C, Singer J. Gastrointestinal decontamination of the **poisoned** patient. *Pediatr Emerg Care.* 2008;24(3):176-86; quiz 187-9. PMID: 18347499  
Gastrointestinal decontamination has been a historically accepted modality in the emergency management of oral intoxicants. Theoretically, gastric and whole-bowel emptying procedures hinder

absorption, remove toxic substances, prevent clinical deterioration, and hasten recovery. This article presents a current overview of gastrointestinal decontamination. It challenges the accepted precepts of gut decontamination and assesses the utility of syrup of ipecac-induced emesis, orogastric lavage, single-dose-activated charcoal, cathartics, and whole-bowel irrigation.

17. Holst L, Nordeng H, Haavik S. Use of herbal drugs during early pregnancy in relation to maternal characteristics and pregnancy outcome. *Pharmacoepidemiol Drug Saf.* 2008;17(2):151-9. PMID: 17992658  
PURPOSE: To study characteristics of women using herbal drugs and the possible impact of use in early pregnancy on pregnancy outcome. METHODS: Data on the use of herbal drugs during pregnancy were obtained from the Swedish Medical Birth Register during the period 1st July 1995 to end of 2004. Women who reported use of herbal drugs were compared to all women giving birth during the period. Outcome variables were prematurity, birth weight, Apgar score, number of infants in delivery and congenital malformations. RESULTS: Among the 860 215 women in the register, 787 (0.9%) reported use of herbal drugs during early pregnancy. The most frequently used herbal drugs were Floradix (iron-rich herbs), ginseng and valerian. Use of such drugs was independently associated with high maternal age, normal weight and 14-15 years of education. Risk factors for valerian differed from those for other herbal drugs, for example with respect to maternal smoking and country of birth. Concomitant drug use was common and the most frequently used drugs were multivitamins, folic acid, cardiovascular drugs (mainly antihypertensive drugs), non-steroid anti-inflammatory drugs (NSAIDs), analgesics and psycholeptics. None of the infant characteristics studied were influenced significantly by the mother's use of the examined herbal drugs during early pregnancy. CONCLUSIONS: The most commonly reported herbal drugs used during pregnancy were Floradix (iron-rich herbs), ginseng and valerian. No signs of unfavourable effect on pregnancy outcome were seen. The number of exposures, however, was low and therefore effects on rare outcomes (e.g. specific malformations) cannot be excluded.
18. Angelova N, Kong HW, van der Heijden R, Yang SY, Choi YH, Kim HK, Wang M, Hankemeier T, van der Greef J, et al. Recent methodology in the phytochemical analysis of ginseng. *Phytochem Anal.* 2008;19(1):2-16. PMID: 18058794  
This review summarises the most recent developments in ginseng analysis, in particular the novel approaches in sample pre-treatment and the use of high-performance liquid-chromatography-mass spectrometry. The review also presents novel data on analysing ginseng extracts by nuclear magnetic resonance spectroscopy and high-resolution mass spectrometry (Fourier transform mass spectrometry) in the context of metabolomics.
19. Prozialeck WC, Edwards JR, Nebert DW, Woods JM, Barchowsky A, Atchison WD. The vascular system as a target of metal toxicity. *Toxicol Sci.* 2008;102(2):207-18. PMID: 17947343  
Vascular system function involves complex interactions among the vascular endothelium, smooth muscle, the immune system, and the nervous system. The toxic metals cadmium (Cd), arsenic (As), and lead (Pb) can target the vascular system in a variety of ways, ranging from hemorrhagic injury to subtle pathogenic remodeling and metabolic changes. Acute Cd exposure results in hemorrhagic injury to the testis, although some strains of animals are resistant to this effect. A comparison of Cd-sensitive with Cd-resistant mouse strains showed that expression of the Slc39a8 gene, encoding the ZIP8 transporter, in the testis vasculature endothelium is responsible for this difference. Endogenously, ZIP8 is a Mn(2+)/HCO(3)(-)-symporter that may also contribute to Cd damage in the kidney. Chronic Cd exposure is associated with various cardiovascular disorders such as hypertension and cardiomyopathy and it is reported to have both carcinogenic and anticarcinogenic activities. At noncytotoxic concentrations of 10-100nM, Cd can inhibit chemotaxis and tube formation of vascular endothelial cells. These angiostatic effects may be mediated through disruption of vascular endothelial cadherin, a Ca(2+)-dependent cell adhesion molecule. With regard to As, ingestion of water containing disease-promoting concentrations of As promotes capillarization of the

liver sinusoidal endothelium. Because capillarization is a hallmark precursor for liver fibrosis and contributes to an imbalance of lipid metabolism, this As effect on hepatic endothelial cells may be a pathogenic mechanism underlying As-related vascular diseases. With regard to Pb, perinatal exposure may cause sustained elevations in adult blood pressure, and genetically susceptible animals may show enhanced sensitivity to this effect. Taken together, these data indicate that the vascular system is a critical target of metal toxicity and that actions of metals on the vascular system may play important roles in mediating the pathophysiologic effects of metals in specific target organs.