



The American Academy of Clinical Toxicology

Uniting scientists and clinicians in the advancement of research, education, prevention and treatment of diseases caused by chemicals, drugs and other toxins.

Herbs & Dietary Supplements Special Interest Group Scientific Abstracting Service

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1. Ghannoum M, Nolin TD, Lavergne V, Hoffman RS. Blood purification in toxicology: nephrology's ugly duckling. *Adv Chronic Kidney Dis.* 2011;18(3):160-6
Contrary to popular opinion, application of extracorporeal therapies for poisonings predates their use for ESRD. Despite this observation, the science of blood purification in toxicology remains desperately stagnant today. In fact, much of our current knowledge is derived from George Schreiner's 1958 review. Original publications are almost exclusively composed of case reports and case series, from which good inference is impossible. Until randomized controlled trials become available, the medical community would be well served by a group mandated to systematically review available literature, extract relevant information, provide recommendations based on current evidence, and propose research initiatives. The EXtracorporeal TReatments In Poisoning workgroup, formed by several international experts in different medical fields and represented by over 20 societies, now has this mission.
2. Winchester JF, Harbord NB. Intoxications amenable to extracorporeal removal. *Adv Chronic Kidney Dis.* 2011;18(3):167-71
Extracorporeal removal of drugs was first attempted in 1913, by John Jacob Abel. Previously known to be a rarity, dialysis and to a lesser extent hemoperfusion have now become obvious tools for nephrologists in treating life-threatening cases of poisoning. Moreover, for dialysis patients, dialysis along with chelation therapy for removal of aluminum, once known to be common in the United States, is resurging in some countries. This article will discuss the principles of drug removal, the indications for dialysis, and give a brief outline of poisons amenable to dialysis.
3. Wells DL, Ott CA. The "new" marijuana. *Ann Pharmacother.* 2011;45(3):414-7
Synthetic cannabinoid-induced toxicity is increasing in frequency across the US, with more than 1057 reported cases as of August 2010. There is a paucity of literature on synthetic cannabinoid toxicity; however, there are various reports of adverse effects including tachycardia, hypertension, tachypnea, chest pain, heart palpitations, hallucinations, racing thoughts, and seizures. While reports suggest that toxic symptoms last no longer than 3-4 hours, with no residual adverse effects in many cases, there is concern about serious acute and long-term toxicities. This article reviews the development, abuse, toxicity, treatment, and legal status of synthetic cannabinoids. It is important for health-care professionals to recognize and appropriately treat synthetic cannabinoid-induced toxicity.
4. Parveen R, Baboota S, Ali J, Ahuja A, Vasudev SS, Ahmad S. Effects of silymarin nanoemulsion against carbon tetrachloride-induced hepatic damage. *Arch Pharm Res.* 2011;34(5):767-74

Silymarin is a complex mixture of four flavonolignan isomers (silybin, isosilybin, silydianin and silychristin) obtained from 'milk thistle' (*Silybum marianum*). This plant compound is used almost exclusively for hepatoprotection. Because of its low and poor oral bioavailability, silymarin was formulated as a nanoemulsion to increase its solubility (and so its oral bioavailability) as well as therapeutic activity. The present study assessed the hepatoprotective activity on Wistar rats by determining biochemical parameters and histopathological properties of the nanoemulsion formulation of silymarin against carbon tetrachloride (CCl₄)-induced hepatotoxicity. Hepatoprotective activity was evaluated by the activity of serum alkaline phosphatase, alanine transaminase and aspartate transaminase; antioxidative defence markers (concentration of reduced glutathione); oxidative stress parameter (thiobarbituric acid reactive substances) and liver histopathology. The nanoemulsion-treated group showed significant decreases in glutamate oxaloacetate transaminase, pyruvate transaminase, alkaline phosphatase, total bilirubin and tissue lipid peroxides and increased total protein, albumin, globulin and tissue glutathione as compared to toxicant. The results indicate an excellent potential of the nanoemulsion formulation for the reversal of CCl₄-induced liver toxicity in rats as compared to standard silymarin.

5. Sang AGP, Guharat S, Wananukul W. A mass cyanide poisoning from pickling bamboo shoots. *Clin Toxicol (Phila)*. 2011
Context. Bamboo shoots contain cyanogenic glycosides named taxiphyllin. Cyanide poisoning from cyanogenic glycosides commonly occurs following ingestion. However, toxicity caused by inhalation of hydrogen cyanide gas (HCN) produced from pickled shoots has never been reported. Objective. To describe cyanide poisoning in eight victims who were exposed to HCN produced in a well containing pickling bamboo shoots. Materials and methods. Due to a series of botched rescue attempts, a total of eight patients entered into a 27 m³ well containing pickled bamboo shoots and immediately lost consciousness. After rescue, two patients developed cardiac arrest, metabolic acidosis and died. Four other patients suffered metabolic acidosis, but recovered after supportive care. The remaining two regained consciousness and recovered soon after the event. Ambient air study and cyanide content of bamboo shoots helped confirm the diagnosis. Results. All patients had high anion gap metabolic acidosis with normal oxygenation. Blood cyanide levels ranged from 2.66 to 3.30 mcg/ml (taken after about 18 h of incident). Ambient air study (21 h after incident) revealed oxygen 20.9%, and sulfur dioxide 19.4 ppm. The instrument was unfortunately not equipped to detect HCN. A simulation study revealed HCN and sulfur dioxide in the ambient air at 10 ppm and 7.5 ppm, respectively. Cyanide content in the bamboo shoots ranged from 39 to 434 mg/kg in the wet shoots. Discussion. This series of patients developed sudden onset of alteration of consciousness and metabolic acidosis upon exposure, and cyanide was confirmed in all victims. The simulation study confirmed the presence of HCN in the ambient air of the well containing bamboo shoots. Conclusion. We have reported mass acute cyanide poisoning with two fatalities. The source of HCN was unusual as it was produced from pickling bamboo shoot.
6. Albuquerque UP, Melo JG, Medeiros MF, Menezes IR, Moura GJ, Asfora El-Deir AC, et al. Natural products from ethnodirected studies: revisiting the ethnobiology of the zombie poison. *Evid Based Complement Alternat Med*. 2012;2012:202508
Wade Davis's study of Haitian "zombification" in the 1980s was a landmark in ethnobiological research. His research was an attempt to trace the origins of reports of "undead" Haitians, focusing on the preparation of the zombification poison. Starting with this influential ethnopharmacological research, this study examines advances in the pharmacology of natural products, focusing especially on those of animal-derived products. Ethnopharmacological,

pharmacological, and chemical aspects are considered. We also update information on the animal species that reportedly constitute the zombie poison. Several components of the zombie powder are not unique to Haiti and are used as remedies in traditional medicine worldwide. This paper emphasizes the medicinal potential of products from zootherapy. These biological products are promising sources for the development of new drugs.

7. Zhao YL, Zhou GD, Yang HB, Wang JB, Shan LM, Li RS, et al. Rhein protects against acetaminophen-induced hepatic and renal toxicity. *Food Chem Toxicol.* 2011;49(8):1705-10
This study investigated the possible protective effects and mechanism of rhein on Acetaminophen (APAP)-induced hepatotoxicity and nephrotoxicity in rats. Treatment of rats with APAP resulted in severe liver and kidney injuries, as demonstrated by drastic elevation of serum glutamate-pyruvate transaminase (GPT), glutamate-oxaloacetic transaminase (GOT), total bilirubin (TBIL), creatinine (CREA), urea nitrogen (UREA) levels and typical histopathological changes including necrosis, phlogocyte infiltration and fatty degeneration in liver, tubules epithelium swelling and severe vacuolar degeneration in kidney. APAP caused oxidative stress, as evidenced by increased reactive oxygen species (ROS) production, nitric oxide (NO) and malondiadehyde (MDA) levels, together with depleted glutathione (GSH) concentration in the liver and kidney of rats. However, rhein can attenuate APAP-induced hepatotoxicity and nephrotoxicity in a dose-dependent manner. Our results showed that GPT, GOT, UREA and CREA levels and ROS production were reduced dramatically, NO, MDA, GSH contents were restored remarkably by rhein administration, as compared to the APAP alone treated rats. Moreover, the histopathological damage of liver and kidney were also significantly ameliorated by rhein treatment. These findings suggested that the protective effects of rhein against APAP-induced liver and kidney injuries might result from the amelioration of APAP-induced oxidative stress.
8. Lin CC, Phua DH, Deng JF, Yang CC. Aconitine intoxication mimicking acute myocardial infarction. *Hum Exp Toxicol.* 2011;30(7):782-5
INTRODUCTION: Cardiotoxicity in acute aconitine intoxication is well known; however, elevation of troponin I level and abnormal scintigraphy findings had not previously been reported. CASE REPORT: A 60-year-old man developed chest tightness, syncope and convulsion after ingesting processed *Aconitum carmichaeli* (Chuanwu) extract for treatment of headache. Electrocardiogram showed first degree atrioventricular (AV) block. Troponin I level was elevated at 14.8 ng/mL 13 hours post-ingestion. Creatine kinase was also increased to 414 U/L. However, echocardiography did not show any abnormal cardiac wall motion. Tc-99m-PYP scintigraphy revealed diffusely increased uptake in the myocardium, suggesting the presence of myocardial necrosis or myocarditis. DISCUSSION: Aconitine poisoning can mimic acute myocardial infarction with chest tightness and elevated cardiac enzymes. Increased cardiac markers and myocardial insult seen in this patient were likely to be related to the toxicity of aconitine. Care should be taken in making the diagnosis in such instances. Management is primarily supportive.
9. Venkatesh C, Adhisivam B. Hypocalcemia in *Cleistanthus collinus* Poisoning. *Indian Pediatr.* 2011;48(9):741
10. Sychev DA, Semenov AV, Polyakova IP. A case of hepatic injury suspected to be caused by *Canephron N*, a *Centaurium Hill* containing phytotherapeutics. *Int J Risk Saf Med.* 2011;23(1):5-6

11. Liang Q, Wu Q, Jiang J, Duan J, Wang C, Smith MD, et al. Characterization of sparstolonin B, a Chinese herb-derived compound, as a selective Toll-like receptor antagonist with potent anti-inflammatory properties. *J Biol Chem.* 2011;286(30):26470-9
Blockade of excessive Toll-like receptor (TLR) signaling is a therapeutic approach being actively pursued for many inflammatory diseases. Here we report a Chinese herb-derived compound, sparstolonin B (SsnB), which selectively blocks TLR2- and TLR4-mediated inflammatory signaling. SsnB was isolated from a Chinese herb, Spaganium stoloniferum; its structure was determined by NMR spectroscopy and x-ray crystallography. SsnB effectively inhibited inflammatory cytokine expression in mouse macrophages induced by lipopolysaccharide (LPS, a TLR4 ligand), Pam3CSK4 (a TLR1/TLR2 ligand), and Fsl-1 (a TLR2/TLR6 ligand) but not that by poly(I:C) (a TLR3 ligand) or ODN1668 (a TLR9 ligand). It suppressed LPS-induced cytokine secretion from macrophages and diminished phosphorylation of Erk1/2, p38a, I κ B, and JNK in these cells. In THP-1 cells expressing a chimeric receptor CD4-TLR4, which triggers constitutive NF- κ B activation, SsnB effectively blunted the NF- κ B activity. Co-immunoprecipitation showed that SsnB reduced the association of MyD88 with TLR4 and TLR2, but not that with TLR9, in HEK293T cells and THP-1 cells overexpressing MyD88 and TLRs. Furthermore, administration of SsnB suppressed splenocyte inflammatory cytokine expression in mice challenged with LPS. These results demonstrate that SsnB acts as a selective TLR2 and TLR4 antagonist by blocking the early intracellular events in the TLR2 and TLR4 signaling. Thus, SsnB may serve as a promising lead for the development of selective TLR antagonistic agents for inflammatory diseases.
12. Lee MR. The history of Ephedra (ma-huang). *J R Coll Physicians Edinb.* 2011;41(1):78-84
Ephedra is a Chinese shrub which has been used in China for medicinal purposes for several thousand years. The pure alkaloid ephedrine was first isolated and characterised by Nagai in 1885. It was then forgotten until it was rediscovered by Chen and Schmidt in the early 1920s. Its actions on the adrenoceptors could be classified into separate alpha and beta effects--a defining moment in the history of autonomic pharmacology. Ephedrine became a highly popular and effective treatment for asthma, particularly because, unlike adrenaline (until then the standard therapy), it can be given by mouth. Ephedrine as a treatment for asthma reached its zenith in the late 1950s, since when there has been a gradual and inevitable decline in its therapeutic use. From mainstream medicine, ephedrine moved into the twilight zone of street drugs and nutritional supplements. Ephedra and ephedrine products are now banned in many countries, as they are a major source for the production of the addictive compound methamphetamine (crystal meth).
13. Shandley K, Austin DW. Ancestry of pink disease (infantile acrodynia) identified as a risk factor for autism spectrum disorders. *J Toxicol Environ Health A.* 2011;74(18):1185-94
Pink disease (infantile acrodynia) was especially prevalent in the first half of the 20th century. Primarily attributed to exposure to mercury (Hg) commonly found in teething powders, the condition was developed by approximately 1 in 500 exposed children. The differential risk factor was identified as an idiosyncratic sensitivity to Hg. Autism spectrum disorders (ASD) have also been postulated to be produced by Hg. Analogous to the pink disease experience, Hg exposure is widespread yet only a fraction of exposed children develop an ASD, suggesting sensitivity to Hg may also be present in children with an ASD. The objective of this study was to test the hypothesis that individuals with a known hypersensitivity to Hg (pink disease survivors) may be more likely to have descendants with an ASD. Five hundred and twenty-two participants who had previously been diagnosed with pink disease completed a survey on the health outcomes of their descendants. The prevalence rates of ASD and a variety of other

clinical conditions diagnosed in childhood (attention deficit hyperactivity disorder, epilepsy, Fragile X syndrome, and Down syndrome) were compared to well-established general population prevalence rates. The results showed the prevalence rate of ASD among the grandchildren of pink disease survivors (1 in 22) to be significantly higher than the comparable general population prevalence rate (1 in 160). The results support the hypothesis that Hg sensitivity may be a heritable/genetic risk factor for ASD.

14. Schonthal AH. Adverse effects of concentrated green tea extracts. *Mol Nutr Food Res.* 2011;55(6):874-85

A myriad of health claims are being made in favor of the consumption of green tea. However, mostly due to the easy availability and greater than ever popularity of highly concentrated green tea extracts, sometimes combined with an attitude of more-is-better, certain health risks of green tea consumption have begun to emerge. Among such risks are the possibility of liver damage, the potential to interact with prescription drugs to alter their therapeutic efficacy, and the chance to cause harm when combined with other highly popular herbal remedies. This review will summarize documented examples of adverse effects of green tea in humans, and will discuss risks of copious consumption of highly concentrated green tea extracts as indicated by studies in animals. While there is no intention to minimize any of the scientifically established benefits of the use of green tea, the purpose of this review is to focus primarily on the potential for adverse effects and raise awareness of the rare, yet under-appreciated risks.

15. Kumar A, Singh CK, Lavoie HA, Dipette DJ, Singh US. Resveratrol restores Nrf2 level and prevents ethanol-induced toxic effects in the cerebellum of a rodent model of fetal alcohol spectrum disorders. *Mol Pharmacol.* 2011;80(3):446-57

In humans, ethanol exposure during pregnancy produces a wide range of abnormalities in infants collectively known as fetal alcohol spectrum disorders (FASD). Neuronal malformations in FASD manifest as postnatal behavioral and functional disturbances. The cerebellum is particularly sensitive to ethanol during development. In a rodent model of FASD, high doses of ethanol (blood ethanol concentration 80 mM) induces neuronal cell death in the cerebellum. However, information on potential agent(s) that may protect the cerebellum against the toxic effects of ethanol is lacking. Growing evidence suggests that a polyphenolic compound, resveratrol, has antioxidant and neuroprotective properties. Here we studied whether resveratrol (3,5,4'-trihydroxy-trans-stilbene), a phytoalexin found in red grapes and blueberries, protects the cerebellar granule neurons against ethanol-induced cell death. In the present study, we showed that administration of resveratrol (100 mg/kg) to postnatal day 7 rat pups prevents ethanol-induced apoptosis by scavenging reactive oxygen species in the external granule layer of the cerebellum and increases the survival of cerebellar granule cells. It restores ethanol-induced changes in the level of transcription factor nuclear factor-erythroid derived 2-like 2 (nfe2l2, also known as Nrf2) in the nucleus. This in turn retains the expression and activity of its downstream gene targets such as NADPH quinone oxidoreductase 1 and superoxide dismutase in cerebellum of ethanol-exposed pups. These studies indicate that resveratrol exhibits neuroprotective effects in cerebellum by acting at redox regulating proteins in a rodent model of FASD.

16. Viegi L, Vangelisti R. Toxic plants used in ethnoveterinary medicine in Italy. *Nat Prod Commun.* 2011;6(7):999-1000

This study was conducted to document the use of toxic or potentially toxic plants for the treatment of ailments in livestock and pets in ethnoveterinary practice in Italy. More than 250 of the entities used (81% for curative purposes) can be toxic unless dosed appropriately. Many

(55%) are dietary supplements. The list included 186 species (45%) for internal and 175 (55%) for external use, many used in places where animals are kept. The species belong to 71 families, among which the Fabaceae predominate. The purpose of the study was to provide information that can be validated and associated with correct determination, permitting even potentially dangerous plants to be used in veterinary practice.

17. Kirchmair M, Carrilho P, Pfab R, Haberl B, Felgueiras J, Carvalho F, et al. Amanita poisonings resulting in acute, reversible renal failure: new cases, new toxic Amanita mushrooms. *Nephrol Dial Transplant*. 2011
BACKGROUND: Renal failure as a consequence of eating mushrooms has been reported repeatedly after ingestion of webcaps of the Cortinarius orellanus group. But mushrooms of the genus Amanita can also cause renal failure: Amanita smithiana (North America) and Amanita proxima (Mediterranean area). Here, we discuss poisonings caused by other white amanitas. A German and-independently-two Portuguese patients reported the ingestion of completely white mushrooms with ring. Similar to intoxications with A. smithiana or A. proxima, the clinical picture was characterized by nausea and vomiting 10-12 h after ingestion, severe acute renal failure and mild hepatitis. Renal biopsy showed acute interstitial nephritis and tubular necrosis. Two patients were given temporary haemodialysis. All have fully recovered their renal function. Poisonings caused by mushrooms containing the toxin of A. smithiana were suspected. We tested 20 Amanita species for the presence of this toxin.METHODS: Thin layer chromatography was applied to detect A. smithiana nephrotoxin in herbarium specimens using authentic material of A. smithiana as reference.RESULTS: A. smithiana toxin could be detected in Amanita boudieri, Amanita gracilior and in Amanita echinocephala. A. boudieri was collected by the Portuguese patients. A. echinocephala is the only nephrotoxic Amanita growing North of the Alps and is suspected to be the cause of renal failure in the German patient. No A. smithiana toxin was detectable in the nephrotoxic A. proxima.CONCLUSIONS: A. boudieri, A. gracilior and A. echinocephala are nephrotoxic. These intoxications are clinically similar to that of A. smithiana, with acute reversible renal failure and mild hepatitis but are different in their clinical picture from Orellanus syndrome characterized by a delayed onset of severe and often irreversible renal failure.
18. Shi DH, Liu YW, Liu WW, Gu ZF. Inhibition of urease by extracts derived from 15 Chinese medicinal herbs. *Pharm Biol*. 2011;49(7):752-5
CONTEXT: Helicobacter pylori is a major causative factor in gastritis-like disorders, and urease plays a key role in Helicobacter pylori colonizing and persisting in the mucous layer of the human stomach. In China, a variety of Chinese medicinal herbs have been prescribed to attenuate or eradicate gastritis-like disorders. However, little is known about the urease inhibition of Chinese medicinal herbs. OBJECTIVE: The present study was conducted to investigate the urease inhibition activities of the ethanol and water extracts of 15 Chinese medicinal herbs. MATERIALS AND METHODS: The ethanol and water extracts derived from 15 medicinal herbs, traditionally used for the treatment of gastritis-like disorders in China, were tested for urease-inhibition activity using the phenol red method. RESULTS: Screened at 10 microg/mL, 14 ethanol extracts and 10 water extracts showed urease inhibition. The ethanol extracts of Magnolia officinalis Rehd. et Wils. (Magnoliaceae) and Cassia obtusifolia L. (Leguminosae) possessed inhibition rates higher than 50% with IC values of 6.5 and 12.3 microg/mL, respectively. After fractionating successively, the petroleum ether fraction of the ethanol extracts of Magnolia officinalis showed the best activity with 90.8% urease inhibition at a concentration of 10 microg/mL. The bioautography of the petroleum ether fraction indicated the existence of the urease inhibitors in the herb. DISCUSSION AND CONCLUSION: The

present results indicated that some Chinese medicinal herbs might treat gastritis-like disorders via the inhibition of *Helicobacter pylori* urease and the further possibility for discovering useful novel urease inhibitors from the Chinese medicinal herbs.

19. Teschke R, Schmidt-Taenzer W, Wolff A. Spontaneous reports of assumed herbal hepatotoxicity by black cohosh: is the liver-unspecific Naranjo scale precise enough to ascertain causality? *Pharmacoepidemiol Drug Saf.* 2011;20(6):567-82
PURPOSE: Causality assessment of cases with herbal hepatotoxicity represents a major regulatory challenge and included, in the past, the application of a diagnostic algorithm consisting of causality evaluation methods with either liver-specific or liver-unspecific characteristics. To evaluate various causality assessing methods in cases with suspected herbal hepatotoxicity, two different scales were now used for reasons of comparison. METHODS: We used the liver-specific scale of the updated Council for International Organizations of Medical Sciences (CIOMS) as well as the Naranjo scale that is not organ specific and therefore not liver specific. Both scales were applied to 22 cases of spontaneous reports with initially assumed herbal hepatotoxicity caused by black cohosh, used for menopausal symptoms. RESULTS: The analysis shows that causality was either unlikely (n = 6) or excluded (n = 16), using the updated CIOMS scale. There were various confounding variables: pre-existing liver diseases (n = 6) including genuine autoimmune hepatitis or alcoholic or cardiac hepatopathy; hepatotoxicity induced by interferon or fluoxetine (n = 2); marginally increased serum activities of alanine aminotransferase (n = 2) or gamma-glutamyltranspeptidase (n = 2) of unassessable causality; a mixed group consisting of unassessable cases (n = 6) and cases with questionable, poorly documented hepato-biliary diseases (n = 3); and rosuvastatin-induced rhabdomyolysis (n = 1). These confounding factors were not recognized by the Naranjo scale. CONCLUSIONS: Structured hepatotoxicity-specific causality assessment methods such as the updated CIOMS scale are the preferred tools for causality assessment of assumed herbal hepatotoxicity and should replace the liver-unspecific Naranjo scale. Applying the updated CIOMS scale to cases with initially assumed hepatotoxicity by BC, causality was now found either unlikely or excluded.

20. Lu YF, Wu Q, Liang SX, Miao JW, Shi JS, Liu J. Evaluation of hepatotoxicity potential of cinnabar-containing An-Gong-Niu-Huang Wan, a patent traditional Chinese medicine. *Regul Toxicol Pharmacol.* 2011;60(2):206-11
An-Gong-Niu-Huang Wan (AGNH) is a patent traditional Chinese medicine for brain disorders. It contains 10% cinnabar (HgS). Hg is known to produce toxicity to the kidney, brain and liver. Is AGNH safe? Liver is a major organ for drug metabolism, whether the long-term use of AGNH would affect hepatic P450 enzymes is unknown. To address these concerns, mice were given orally cinnabar (300mg/kg), cinnabar-containing AGNH daily for 44days, and liver toxicity was examined and compared with that of methylmercury (MeHg, 2.6mg/kg) and mercuric chloride (HgCl₂, 32mg/kg). Serum aminotransferases were increased by MeHg and HgCl₂ only. Histopathology showed more severe liver damage in MeHg- and HgCl₂-treated mice than in the cinnabar and AGNH groups. Accumulation of Hg in MeHg- and HgCl₂-treated mice was 96- and 71-fold higher than controls, respectively, but was only 2-fold after cinnabar and AGNH administration. Expressions of metallothionein-1 and heme oxygenase-1, biomarkers for Hg toxicity, were increased by MeHg and HgCl₂, but were not altered in cinnabar- and AGNH-treated mice. Expression of hepatic cytochrome P450 genes, such as Cyp1a1, Cyp1b1 and Cyp4a10 was increased only after MeHg and HgCl₂, and the expressions of Cyp3a1 and Cyp3a25 were increased by all treatments, indicating the potential Hg-drug interactions after long-term use of cinnabar-containing traditional medicines. Taken together,

the results demonstrate that AGNH is much less hepatotoxic than common mercurials, and that the use of total Hg content to evaluate the toxicity of cinnabar-containing traditional Chinese medicines appears to be inappropriate.

21. Sondergaard TE, Hansen FT, Purup S, Nielsen AK, Bonfeld-Jorgensen EC, Giese H, et al. Fusarin C acts like an estrogenic agonist and stimulates breast cancer cells in vitro. *Toxicol Lett.* 2011;205(2):116-21
Fusarin C is a mycotoxin produced by several *Fusarium* species and has been associated with esophageal cancer due to its carcinogenic effects. Here, we report that fusarin C stimulates growth of the breast cancer cell line MCF-7. This suggests that fusarin C can act as an estrogenic agonist and should be classified as a mycoestrogen. MCF-7 cells were stimulated in the range between 0.1 and 20µM and inhibited when the concentration exceeded 50µM. The toxicity of fusarin C is comparable to other mycoestrogens such as zearalenone, but the chemical structure of fusarin C is very different from other known estrogen agonists. Furthermore, the toxicity of fusarin C was tested in five additional human cell lines Caco 2, U266, PC3, MDA-MB-231 and MCF-10a which were all inhibited when the concentration of fusarin C exceeded 10µM. To the best of our knowledge this is the first report on the mycoestrogenic properties of fusarin C.