



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 ABSTRACTING SERVICE

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1. Chen KH, Li PC, Lin WH, Chien CT, Low BH. Depression by a green tea extract of alcohol-induced oxidative stress and lipogenesis in rat liver. *Biosci Biotechnol Biochem.* 2011;75(9):1668-76. We determined the effects of a green tea extract with 36% alcohol on the blood alcohol content, oxidative stress, lipogenesis, inflammation and liver function of female Wistar rats. Tea alcohol significantly decreased the O, HO and HOCl amounts via catechins and not caffeine. Thirty days of alcohol gavage improved the level of reactive oxygen species (ROS) in the liver, bile and blood, increased the 4-hydroxynonenal-protein adducts, Kupffer cell infiltration and lipid accumulation in the liver, and elevated the plasma alanine aminotransferase level. A western blot analysis showed reduced expression of the oxidative enzymes (CYP2E1 and NADPH oxidase p47phox protein) and lipogenic enzymes (SREBP-1c and fatty acid synthase) in the alcohol-treated liver. Tea alcohol significantly attenuated these elevated parameters. We conclude that the green tea extract in alcohol efficiently reduced the amounts of O, HO and HOCl primarily due to the catechin content, and not caffeine. The developed tea liquor attenuated alcohol-induced oxidative injury and lipogenesis in the liver by the synergetic action of catechins and caffeine.
2. Levine M, Ruha AM, Graeme K, Brooks DE, Canning J, Curry SC. Toxicology in the ICU: part 3: natural toxins. *Chest.* 2011;140(5):1357-70. This is the third article of a three-part series that reviews the care of poisoned patients in the ICU. This article focuses on natural toxins, such as heavy metals and those produced by plants, mushrooms, arthropods, and snakes. The first article discussed the general approach to the patient, including laboratory testing; the second article focused on specific toxic agents, grouped into categories.
3. Abrams DI, Couey P, Shade SB, Kelly ME, Benowitz NL. Cannabinoid-opioid interaction in chronic pain. *Clin Pharmacol Ther.* 2011;90(6):844-51. Cannabinoids and opioids share several pharmacologic properties and may act synergistically. The potential pharmacokinetics and the safety of the combination in humans are unknown. We therefore undertook a study to answer these questions. Twenty-one individuals with chronic pain, on a regimen of twice-daily doses of sustained-release morphine or oxycodone were enrolled in the study and admitted for a 5-day inpatient stay. Participants were asked to inhale vaporized cannabis in the evening of day 1, three times a day on days 2-4, and in the morning of day 5. Blood sampling was performed at 12-h intervals on days 1 and 5. The extent of chronic pain was also assessed daily. Pharmacokinetic investigations revealed no significant change in the area under the plasma concentration-time curves for either morphine or oxycodone after exposure to cannabis. Pain was significantly decreased (average 27%, 95% confidence interval

(CI) 9, 46) after the addition of vaporized cannabis. We therefore concluded that vaporized cannabis augments the analgesic effects of opioids without significantly altering plasma opioid levels. The combination may allow for opioid treatment at lower doses with fewer side effects.

4. Bronstein AC, Spyker DA, Cantilena LR, Green JL, Rumack BH, Dart RC. 2010 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 28th Annual Report. *Clin Toxicol (Phila)*. 2011;49(10):910-41.

Abstract Background: This is the 28th Annual Report of the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS). All US poison centers upload case data automatically with a median time interval of 19.0 [11.9, 40.6] (median [25%, 75%]) minutes, creating a near real-time national exposure and information database and surveillance system. Methodology: We analyzed the case data tabulating specific indices from NPDS. The methodology was similar to that of previous years. Where changes were introduced, the differences are identified. Poison center cases with medical outcomes of death were evaluated by a team of 33 medical and clinical toxicologist reviewers using an ordinal scale of 1 (Undoubtedly responsible) - 6 (Unknown) to determine Relative Contribution to Fatality (RCF) of the exposure to the death. Results: In 2010, 3,952,772 closed encounters were logged by NPDS: 2,384,825, human exposures, 94,823 animal exposures, 1,466,253 information calls, 6537 human confirmed nonexposures, and 334 animal confirmed nonexposures. Total encounters showed a 7.7% decline from 2009 while health care facility calls increased by 2.7%. Human exposures with more serious outcomes (minor, moderate, major or death) increased 4.5% while those with less serious outcomes (all other medical outcome categories) decreased 5.9%. All information calls decreased 12.6% and health care facility (HCF) information calls decreased 13.6%, Drug ID calls decreased 10.9%, and human exposures decreased 3.8%. The top 5 substance classes most frequently involved in all human exposures were analgesics (11.5%), cosmetics/personal care products (7.7%), household cleaning substances (7.3%), sedatives/hypnotics/ antipsychotics (6.0%), and foreign bodies/toys/miscellaneous (4.2%). Analgesic exposures as a class increased the most rapidly by 32.8% over the last decade. The top five most common exposures in children age 5 years or less were cosmetics/personal care products (13.2%), analgesics (9.4%), household cleaning substances (9.2%), foreign bodies/toys/miscellaneous (7.2%), and topical preparations (6.8%). THC homolog and designer amphetamine ("Bath Salts") exposures were identified as emerging public health threats. Drug identification requests comprised 64.3% of all information calls. NPDS documented 1730 human exposures resulting in death with 1146 human fatalities judged related with an RCF of 1-Undoubtedly responsible, 2-Probably responsible, or 3-Contributory. Conclusions: These data support the continued value of poison center expertise and need for specialized medical toxicology information to manage the more severe exposures, despite a decrease in calls involving less severe exposures. Unintentional and intentional exposures continue to be a significant cause of morbidity and mortality in the US. The near real-time, always current status of NPDS represents a national public health resource to collect and monitor US exposure cases and information calls. The continuing mission of NPDS is to provide a nationwide infrastructure for public health surveillance for all types of exposures, public health event identification, resilience response and situational awareness tracking. NPDS is a model system for the nation and global public health.

5. Hill SL, Thomas SH. Clinical toxicology of newer recreational drugs. *Clin Toxicol (Phila)*. 2011;49(8):705-19.

INTRODUCTION: Novel synthetic 'designer' drugs with stimulant, ecstasy-like (entactogenic) and/or hallucinogenic properties have become increasingly popular among recreational drug

users in recent years. The substances used change frequently in response to market trends and legislative controls and it is an important challenge for poisons centres and clinical toxicologists to remain updated on the pharmacological and toxicological effects of these emerging agents. AIMS: To review the available information on newer synthetic stimulant, entactogenic and hallucinogenic drugs, provide a framework for classification of these drugs based on chemical structure and describe their pharmacology and clinical toxicology. METHODS: A comprehensive review of the published literature was performed using PUBMED and Medline databases, together with additional non-peer reviewed information sources, including books, media reports, government publications and internet resources, including drug user web forums. EPIDEMIOLOGY: Novel synthetic stimulant, entactogenic or hallucinogenic designer drugs are increasingly available to users as demonstrated by user surveys, poisons centre calls, activity on internet drug forums, hospital attendance data and mortality data. Some population sub groups such as younger adults who attend dance music clubs are more likely to use these substances. The internet plays an important role in determining the awareness of and availability of these newer drugs of abuse. CLASSIFICATION: Most novel synthetic stimulant, entactogenic or hallucinogenic drugs of abuse can be classified according to chemical structure as piperazines (e.g. benzylpiperazine (BZP), trifluoromethylphenylpiperazine), phenethylamines (e.g. 2C or D-series of ring-substituted amfetamines, benzodifurans, cathinones, aminoindans), tryptamines (e.g. dimethyltryptamine, alpha-methyltryptamine, ethyltryptamine, 5-methoxy-alpha-methyltryptamine) or piperidines and related substances (e.g. desoxyipradrol, diphenylprolinol). Alternatively classification may be based on clinical effects as either primarily stimulant, entactogenic or hallucinogenic, although most drugs have a combination of such effects. CLINICAL TOXICOLOGY: Piperazines, phenethylamines, tryptamines and piperidines have actions at multiple central nervous system (CNS) receptor sites, with patterns of effects varying between agents. Predominantly stimulant drugs (e.g. benzylpiperazine, mephedrone, naphyrone, diphenylprolinol) inhibit monoamine (especially dopamine) reuptake and are characteristically associated with a sympathomimetic toxidrome. Entactogenic drugs (e.g. phenylpiperazines, methylone) provoke central serotonin release, while newer hallucinogens (e.g. 5-methoxy-N,N-diisopropyltryptamine (5-MeO-DiPT), 2,5-dimethoxy-4-bromoamfetamine (DOB)) are serotonin receptor agonists. As a result, serotonergic effects predominate in toxicity. CONCLUSIONS: There are limited reliable data to guide clinicians managing patients with toxicity due to these substances. The harms associated with emerging recreational drugs are not fully documented, although it is clear that they are not without risk. Management of users with acute toxic effects is pragmatic and primarily extrapolated from experience with longer established stimulant or hallucinogenic drugs such as amfetamines, 3,4-methylenedioxy-methamphetamine (MDMA) and lysergic acid diethylamide (LSD).

6. Sumerkan MC, Agirbasli M, Altundag E, Bulur S. Mad-honey intoxication confirmed by pollen analysis. *Clin Toxicol (Phila)*. 2011;49(9):872-3.

CONTEXT: Despite numerous publications showing rhythm disturbance and hypotension caused by mad-honey intoxication, none of the findings are associated with ischemic heart disease. CASE DETAILS: A 48-year-old patient was admitted to emergency service with acute anterior wall myocardial infarction after ingestion of mad-honey. Stent was implanted to the 99% stenosis lesion in the mid-portion of left anterior descending coronary artery. In this case, pollen analysis showed the suspected honey heavily contaminated with *Rhododendron* species pollen. DISCUSSION: Mad-honey intoxication cases often apply to emergency service with similar signs and symptoms of acute coronary syndrome; therefore it may cause acute coronary syndrome to be bypassed. This also shows that in the cases of mad-honey intoxication, suspected honey pollen and/or toxin analysis should be done to confirm the diagnosis of mad-

honey intoxication.

7. Sun TW, Xu QY, Zhang XJ, Wu Q, Liu ZS, Kan QC, et al. Management of thallium poisoning in patients with delayed hospital admission. *Clin Toxicol (Phila)*. 2011.
Objective. To describe the clinical features and management of thallium poisoning in patients with delayed hospital admission. Methods. Fourteen patients (median age 36 years) were admitted 9-19 days after ingesting food poisoned with thallium. Clinical and laboratory data, including blood and urine thallium concentrations, were collected. Patients were treated with oral Prussian blue, a chelating agent sodium dimercaptosulfonate, and hemodialysis. Results. All patients experienced a triad of symptoms of acute gastrointestinal upset, painful combined polyneuropathy, and hair loss after consuming poisoned food. Fatigue and skin pigmentation were observed in all patients. Abnormal liver function tests were found in 6 (42.9%) and delirium and coma were identified in 4 (28.6%). Two weeks after the poisoning, the blood and urine thallium concentration ranged from 219.0 to 1414.4 mug/L (median: 535.3) and 956.5 to 11285.0 mug/L (median: 7460.0), respectively. One patient (7.1%) with a previous history of pulmonary fibrosis died of respiratory failure in hospital. Symptoms were improved and blood or urine thallium levels were normalized in the remaining 13 patients before discharge. After a 6.5 +/- 1-month follow-up, 1 patient (7.1%) developed deep venous thrombosis in the left lower limb. In another patient (7.1%), numbness in the lower limbs remained. Conclusion. Acute thallium poisoning is commonly manifested by gastrointestinal upset, painful polyneuropathy, and significant hair loss. Treatment strategies included Prussian blue and hemodialysis, which were associated with a good outcome in this case series.
8. Fang ZZ, Zhang YY, Wang XL, Cao YF, Huo H, Yang L. Bioactivation of herbal constituents: simple alerts in the complex system. *Expert Opin Drug Metab Toxicol*. 2011;7(8):989-1007.
Introduction: The elucidation of the toxicological mechanisms of herbal medicines is becoming more and more important with the increasing application of herbal medicines, for treatment of various diseases and the promotion of health. Furthermore, it is widely recognized that as herbal components undergo bioactivation, there is a critical need for a greater understanding of herbal toxicity induction. Areas covered: This article summarizes the current understanding of structural alerts present in herbal remedies as well as the herbs' and individuals' factors, complicating the interpretation of herbal toxicity via bioactivation. Medline (by means of PubMed up to July 2010) has been searched using proper relevant terms. The reader is provided with reported examples of herbal bioactivation based on toxicophores, which are summarized in an extended list. The article also discusses the factors which influence the herbal bioactivation study, including herbal complexity, competitive detoxification metabolism pathways as well as the individual and species difference of drug metabolizing enzymes and intestinal factors. Expert opinion: The early evaluation of the bioactivation potential of herbal components is helpful for providing alerts of herbal toxicity. However, the potential toxic effects should be considered in the context of the complex systems of herbs and the individual patient.
9. Awodele O, Oreagba IA, Odoma S, Teixeira da Silva JA, Osunkalu VO. Toxicological evaluation of the aqueous leaf extract of *Moringa oleifera* Lam. (Moringaceae). *J Ethnopharmacol*. 2012;139(2):330-6.
ETHNOPHARMACOLOGICAL RELEVANCE: The rapid increase in consumption of herbal remedies worldwide has been stimulated by several factors, including the notion that all herbal products are safe and effective. However, over the past decade, several news-catching episodes in developed communities indicated adverse effects, sometimes life-threatening,

allegedly arising as a consequence to taking herbal products or traditional medicines from various ethnic groups. Despite the popular use of *Moringa oleifera* for treating various disorders, there is limited or no scientific data available regarding safety aspects of this remedy, nor are there any documented toxicological studies that can be used to ascertain the safety index of its herbal preparation. Therefore, this present study aimed to carry out extensive toxicological evaluation of the aqueous leaf extract of *Moringa oleifera*. **MATERIALS AND METHODS:** In an acute toxicity test, male Wistar albino mice were orally administered an aqueous extract up to 6400mg/kg and intraperitoneally up to 2000mg/kg. A sub-chronic toxicity test was performed by daily administration with the extract at 250, 500 and 1500mg/kg orally for 60 days. Control rats received distilled water. Sperm quality was analyzed, haematological and biochemical (liver enzymes, urea and creatinine) parameters were determined and a histopathological examination was carried out. **RESULTS:** The LD(50) was estimated to be 1585mg/kg. The extract did not elicit any significant difference ($P \geq 0.05$) in sperm quality, haematological and biochemical parameters in the treated rats compared to the control. Moreover, there was no significant difference in weight gain of the control and treated animals although there was a dose-dependent reduction in food consumption of the animals treated with 250 to 1500mg/kg extract. **CONCLUSIONS:** Results obtained in this study suggest that the aqueous leaf extract of *Moringa oleifera* is relatively safe when administered orally.

10. Bussmann RW, Malca G, Glenn A, Sharon D, Nilsen B, Parris B, et al. Toxicity of medicinal plants used in traditional medicine in Northern Peru. *J Ethnopharmacol.* 2011;137(1):121-40. **ETHNOPHARMACOLOGICAL RELEVANCE:** The plant species reported here are traditionally used in Northern Peru for a wide range of illnesses. Most remedies are prepared as ethanol or aqueous extracts and then ingested. The aim of this study was to evaluate the potential toxicity of these extracts. **MATERIALS AND METHODS:** The toxicity of ethanolic and water extracts of 341 plant species was determined using a brine-shrimp assay. **RESULTS:** Overall 24% of the species in water extract and 76% of the species in alcoholic extract showed elevated toxicity levels to brine-shrimp. Although in most cases multiple extracts of the same species showed very similar toxicity values, in some cases the toxicity of different extracts of the same species varied from non-toxic to highly toxic. **CONCLUSIONS:** Traditional preparation methods take different toxicity levels in aqueous and ethanol extracts into account when choosing the appropriate solvent for the preparation of a remedy.
11. Gunturu KS, Nagarajan P, McPhedran P, Goodman TR, Hodsdon ME, Strout MP. Ayurvedic herbal medicine and lead poisoning. *J Hematol Oncol.* 2011;4(1):51. **ABSTRACT:** Although the majority of published cases of lead poisoning come from occupational exposures, some traditional remedies may also contain toxic amounts of lead. Ayurveda is a system of traditional medicine that is native to India and is used in many parts of world as an alternative to standard treatment regimens. Here, we report the case of a 58-year-old woman who presented with abdominal pain, anemia, liver function abnormalities, and an elevated blood lead level. The patient was found to have been taking the Ayurvedic medicine Jamburulin prior to presentation. Chemical analysis of the medication showed high levels of lead. Following treatment with an oral chelating agent, the patient's symptoms resolved and laboratory abnormalities normalized. This case highlights the need for increased awareness that some Ayurvedic medicines may contain potentially harmful levels of heavy metals and people who use them are at risk of developing associated toxicities.
12. Hansen CK, Kashani J, Ruck B, Marcus S. Analysis and Validation of Putative Substances

Involved in Fatal Poisonings. *J Med Toxicol.* 2011.

Each year, poison control centers throughout the United States respond to over 4 million calls for help in treating individuals exposed to toxic substances. Although most cases develop no or minimal clinical effects, a small proportion of patients who receive medical care for overdoses with poison center consultation expire. When such cases are investigated by a medical examiner, the postmortem toxicology results may show substances other than those considered in the consultation with the poison center. We sought to determine the characteristics of discordance in fatal cases between the toxic substances reported to a regional poison control center and postmortem toxicology results. We conducted a retrospective study of the New Jersey regional poison control center records of all fatal cases between the years 1986 and 2006. Substances reported as putative agents to the poison center were compared to the postmortem toxicology results obtained by the medical examiner. The frequencies and characteristics surrounding discordance were examined. Of the 708 fatal cases reported to our poison center within the study period, complete postmortem toxicological evaluations were available for 206 (29.0%). Comparison of putative agents between information obtained by history and at postmortem evaluation showed discordance in 41 (19.9%). In a substantial number of fatal cases receiving poison center consultation, substances were found at the time of postmortem examination that were not considered in the poison center consultation. The reasons for this discordance may include a lack of thorough history-taking or a cognitive bias to the substances initially reported.

13. Gasparetto JC, Martins CA, Hayashi SS, Otuky MF, Pontarolo R. Ethnobotanical and scientific aspects of *Malva sylvestris* L.: a millennial herbal medicine. *J Pharm Pharmacol.* 2012;64(2):172-89.

Objectives *Malva sylvestris* L., known as common mallow, is native to Europe, North Africa and Asia. In the Mediterranean region, this species has a long history of use as food, and due to its therapeutic relevance, some parts of this plant have been employed in traditional and ethnoveterinary medicines. The leaves in particular have been reported to have potent anti-inflammatory, antioxidant, anti-complementary, anticancer and skin tissue integrity activity. Additionally, an anti-ulcerogenic effect was recently proven, demonstrating that the aqueous extract was more effective than cimetidine, a potent medicine used to treat gastric ulcers. Due to its wide use and medicinal importance, many studies have been conducted; however, the information in the literature is very extensive and disseminated, making it difficult to use. Key findings A complete review involving the ethnobotanical and scientific aspects of *M. sylvestris* has been made. The research has provided evidence that *M. sylvestris* has potential use as a medicinal plant and has highlighted a need for more studies involving clinical and toxicological aspects of its use. Summary This review can contribute to the field with its historical context, and by describing the progress made, new ideas for researchers can arise.

14. Broides A, Sofer S, Lazar I. Contact dermatitis with severe scalp swelling and upper airway compromise due to black henna hair dye. *Pediatr Emerg Care.* 2011;27(8):745-6.

Temporary tattooing with black henna is known to cause contact dermatitis; however, this adverse effect is not considered to be life threatening. We report a female adolescent who used black henna as a hair dye and developed severe contact dermatitis with scalp, facial, and neck swelling causing hoarseness and stridor. A flexible bronchoscopy showed a normal epiglottis, and the patient was intubated, ventilated, and eventually recovered. We conclude that the use of black henna hair dye in sensitized patients can be life threatening.

15. Gilmour J, Harrison C, Asadi L, Cohen MH, Vohra S. Natural health product-drug interactions: evolving responsibilities to take complementary and alternative medicine into account. *Pediatrics*. 2011;128 Suppl 4:S155-60.
Natural health products (NHPs) (known as dietary supplements in the United States) are a popular form of self-care, yet many patients do not disclose their use to clinicians. NHP-drug interactions are known to occur and can harm patients and affect the efficacy of conventional treatment. Using the example of an HIV-positive adolescent who had been responding well to antiretroviral therapy but then experienced a sudden unexplained deterioration in her condition, we review (1) clinicians' obligation to inquire about complementary and alternative medicine (CAM) use when assessing, treating, and monitoring patients, (2) how clinicians' duty to warn about risks associated with treatment has evolved and expanded, and (3) patients' and parents' responsibility to disclose CAM use. It also addresses the responsibility of hospitals and health facilities to ensure that the reality of widespread CAM/NHP use is taken into account in patient care to effectively protect patients from harm.
16. Mao QQ, Ip SP, Xian YF, Hu Z, Che CT. Anti-depressant-like effect of peony: a mini-review. *Pharm Biol*. 2012;50(1):72-7.
Context: Depression is a common psychiatric disorder, yet the clinical efficacy of antidepressant therapies is unsatisfactory. Thus, the search for new anti-depressants continues, and natural products remain a promising source of new therapeutic agents. The root part of *Paeonia lactiflora* Pall. (Ranunculaceae), known as peony, is often used in Chinese herbal prescriptions for the treatment of depression-like disorders. Objectives: The objective of this review is to provide scientific evidence to support further research on peony as a potential anti-depressant drug. Methods: This review summarizes the results obtained in our laboratory, together with other literature data obtained through a comprehensive search in databases including PubMed, ScienceDirect, Scirus, and Web of Science. Results: The peony extract is active in the mouse forced swim test and tail suspension test, and it produces anti-depressant effects in chronic unpredictable mild stress-induced depression model in mice and rats. The anti-depressant mechanisms of peony are likely mediated by the inhibition of monoamine oxidase activity, neuro-protection, modulation of the function of hypothalamic-pituitary-adrenal axis, inhibition of oxidative stress, and the up-regulation of neurotrophins. Conclusions: Peony is used clinically to treat depression-like symptoms in Chinese medicine, and it has been shown to possess anti-depressant property in a battery of test models using laboratory animals. Its effect is likely mediated by multiple targets. Further studies are warranted to delineate the molecular mechanisms of action, determine the pharmacokinetics, establish the toxicological profile, and assess the potentials of peony in clinical applications. Identification of the clinically active ingredient(s) is also warranted.
17. Lee MY, Seo CS, Shin IS, Ha H, Kim JH, Cho JW, et al. Toxicological evaluation of Gumiganghwaltang aqueous extract in Crl:CD (SD) rats: 13weeks oral gavage studies. *Regul Toxicol Pharmacol*. 2011.
Gumiganghwaltang is a traditional oriental herbal medicine that has been commonly used to treat colds and inflammatory diseases. Aqueous extract of Gumiganghwaltang (GMGHT) was administered daily by oral gavage to male and female rats for 13weeks. A dose of 2000mg/kg/day was selected as a maximum, and doses of 1000 and 500mg/kg/day were determined as medium and low doses, respectively. No treatment-related clinical signs or mortality were observed in the treatment group. We observed no clear treatment-related effects with regard to body weight, food consumption, ophthalmology, hematology, or urinalysis data. The serum biochemistry values for sodium and chloride in the treated male and female groups

(1000mg/kg/day) were lower than in those treated with the vehicle control. However, these changes lacked dose dependence, and no abnormalities were found in corresponding pathological findings. Our results indicated that the no-observed-adverse-effect-level (NOAEL) for GMGHT was determined to be a dietary dose of over 2000mg/kg/day for both sexes under the present experimental conditions.

18. Harris ES, Cao S, Littlefield BA, Craycroft JA, Scholten R, Kaptchuk T, et al. Heavy metal and pesticide content in commonly prescribed individual raw Chinese Herbal Medicines. *Sci Total Environ.* 2011;409(20):4297-305.
Heavy metal and pesticide contamination has previously been reported in Chinese Herbal Medicines (CHMs), in some cases at potentially toxic levels. This study was conducted to determine general patterns and toxicological significance of heavy metal and pesticide contamination in a broad sample of raw CHMs. Three-hundred-thirty-four samples representing 126 species of CHMs were collected throughout China and examined for arsenic, cadmium, chromium, lead, and mercury. Of the total, 294 samples representing 112 species were also tested for 162 pesticides. At least 1 metal was detected in all 334 samples (100%) and 115 samples (34%) had detectable levels of all metals. Forty-two different pesticides were detected in 108 samples (36.7%), with 1 to 9 pesticides per sample. Contaminant levels were compared to toxicological reference values in the context of different exposure scenarios. According to a likely scenario of CHM consumption, only 3 samples (1%) with heavy metals and 14 samples (5%) with pesticides were found with concentrations that could contribute to elevated background levels of contaminant exposure. According to the most conservative scenario of CHM consumption, 231 samples (69%) with heavy metals and 81 samples (28%) with pesticides had contaminants that could contribute to elevated levels of exposure. Wild collected plants had higher contaminant levels than cultivated samples. Cadmium, chromium, lead, and chlorpyrifos contamination showed weak correlations with geographic location. Based on our assumptions of the likely mode of consumption of raw CHMs, the vast majority (95%) of the 334 samples in this study contained levels of heavy metals or pesticides that would be of negligible concern. However, given the number of samples with detectable contaminants and the range between the more likely and more conservative scenarios of contaminant exposure, more research and monitoring of heavy metals (especially cadmium and chromium) and pesticide residues (especially chlorpyrifos) in raw CHMs are advised.
19. Bark KM, Sun YW, Yoon TJ, Kim TH. Phototoxicity of oriental medicinal plants: measurement and possible applications. *Skinmed.* 2011;9(5):294-300; quiz 300.
Phototoxicity can be either harmful and induce adverse skin reactions or beneficial and be used therapeutically as in psoralen and UV-A or photodynamic therapy. Hundreds of medicinal plants are widely used in Asia and Western countries in oriental medicine, yet the phototoxicity of oriental medicinal plants is an understudied area. In this contribution, the authors discuss some methods used to measure the phototoxicity of plants and give an overview of the results of their previous and ongoing studies into the phototoxicity of medicinal plants. The authors argue that because they found that more than a quarter of oriental medicinal plants can be phototoxic, such research is helpful for dermatologists and that active phototoxic components extracted from oriental medicinal plants may be used therapeutically.
20. Hu X, Primack BA, Barnett TE, Cook RL. College students and use of K2: an emerging drug of abuse in young persons. *Subst Abuse Treat Prev Policy.* 2011;6:16.
BACKGROUND: K2 or "spice" has emerged as a popular legal alternative to marijuana among adolescents and young adults. However, no data has been published assessing prevalence of and

associations with ever K2 use in any population. This study's aims were to examine prevalence of ever K2 use among a sample of college students, to determine characteristics of persons who use K2, and to assess the association between K2 and other drug use. FINDINGS: Ever use of K2 was reported by 69 (8%) of the sample of 852 college students. Response rate was 36%. Bivariate and multivariate analyses assessed whether sociodemographic characteristics and other drug use were associated with ever use of K2. Ever use of K2 was reported by 69 (8%) of the sample. Among these 69 individuals, 61 (88%) had used a cigarette and 25 (36%) had used a hookah to smoke K2. In multivariate analyses, K2 use was more common in males (vs. females, adjusted Odds Ratio (aOR)=2.0, 95% Confidence Interval (CI)=1.2-3.5, p=0.01) and 1st or 2nd year college students (vs. 3rd year or above, aOR=2.4, 95% CI=1.2-5.0, p=0.02). CONCLUSIONS: Ever use of K2 in this sample was higher than ever use of many other drugs of abuse that are commonly monitored in adolescents and young adults. Although DEA had banned five synthetic cannabinoids recently, clinicians and public health officials concerned with substance abuse in youth should be aware of and monitor the use of this drug in college students over time.

21. Porter A, Phillips G, Smith L, Erwin-Cohen R, Tammariello R, Hale M, et al. Evaluation of a ricin vaccine candidate (RVEc) for human toxicity using an in vitro vascular leak assay. *Toxicol.* 2011;58(1):68-75.

To protect against ricin intoxication, a genetically derived ricin A chain vaccine candidate (RVEc) was developed lacking the toxic N-glycosidase activity (Olson et al., 2004). The vaccine protects animals against an aerosolized ricin holotoxin (RT) challenge (Carra et al., 2007). In the current study, the RVEc vaccine was evaluated for its interaction and effect on human endothelial cells. RVEc was tested in an in vitro cellular-based bioassay, consisting of primary human endothelial cells cultured on collagen-coated inserts, to which concentrations of the vaccine candidate (0.6, 2, 2.5 or 9 μM) were added. RVEc showed no signs of adverse activity on the cells (e.g., cytotoxicity activity) as measured by changes in trans-endothelial electrical resistance (TEER). In contrast, ricin toxin (RT) cytotoxicity was observed at all concentrations tested. Under light microscopy, no cytotoxicity was visible at 24h with 0.6 or 9 μM of RVEc. However, cytotoxicity was observed for RT and to a lesser degree for RTA. Flow cytometric analysis showed binding of RT, slight binding of RTA, and no binding of the RVEc vaccine to endothelial cells. The presence of RTB as a contaminant contributing to the cytotoxicity in the RTA preparation was ruled out by a RTB-specific ELISA. In addition, RTA at 9 μM produced a cytotoxic activity that could not be explained exclusively by the presence of azide in the RTA buffer. In the current study, the model demonstrated no discernable adverse events of the RVEc vaccine on human endothelial cells, when compared to the toxicity caused by holotoxin or native RTA preparations.