



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.

American Academy of Clinical Toxicology Herbs & Dietary Supplements Special Interest Group ABSTRACTING SERVICE

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1. Reuter J, Merfort I, Schempp CM. Botanicals in dermatology: an evidence-based review. *Am J Clin Dermatol*. 2010;11(4):247-67. Botanical extracts and single compounds are increasingly used in cosmetics but also in over-the-counter drugs and food supplements. The focus of the present review is on controlled clinical trials with botanicals in the treatment of acne, inflammatory skin diseases, skin infections, UV-induced skin damage, skin cancer, alopecia, vitiligo, and wounds. Studies with botanical cosmetics and drugs are discussed, as well as studies with botanical food supplements. Experimental research on botanicals was considered to a limited extent when it seemed promising for clinical use in the near future. In acne therapy, Mahonia, tea tree oil, and *Saccharomyces* may have the potential to become standard treatments. Mahonia, Hypericum, Glycyrrhiza and some traditional Chinese medicines appear promising for atopic dermatitis. Some plant-derived substances like dithranol and methoxsalen (8-methoxypsoralen) [in combination with UVA] are already accepted as standard treatments in psoriasis; Mahonia and Capsicum (capsaicin) are the next candidates suggested by present evidence. Oral administration and topical application of antioxidant plant extracts (green and black tea, carotenoids, coffee, and many flavonoids from fruits and vegetables) can protect skin from UV-induced erythema, early aging, and irradiation-induced cancer. Hair loss and vitiligo are also traditional fields of application for botanicals. According to the number and quality of clinical trials with botanicals, the best evidence exists for the treatment of inflammatory skin diseases, i.e. atopic dermatitis and psoriasis. However, many more controlled clinical studies are needed to determine the efficacy and risks of plant-derived products in dermatology. Safety aspects, especially related to sensitization and photodermatitis, have to be taken into account. Therefore, clinicians should not only be informed of the beneficial

effects but also the specific adverse effects of botanicals used for dermatologic disorders and cosmetic purposes.

2. Fong TL, Klontz KC, Canas-Coto A, Casper SJ, Durazo FA, Davern TJ, 2nd, et al. Hepatotoxicity due to hydroxycut: a case series. *Am J Gastroenterol.* 2010;105(7):1561-6.
OBJECTIVES: Muscletech Hydroxycut (Iovate Health Sciences Research, Oakville, Ontario, Canada) was a popular weight-loss supplement that was recalled by the manufacturer in May 2009 on the basis of reports of hepatotoxicity associated with this supplement. We sought to characterize the clinical presentation of Hydroxycut-associated liver injury and to adjudicate these cases for causal association with Hydroxycut. METHODS: We assessed the causality and grading of severity of liver injury using methodology developed by the Drug-Induced Liver Injury Network (DILIN) study. RESULTS: Eight patients who developed liver injury after taking Hydroxycut treated at different medical centers were identified. All were hospitalized, and three of eight patients required liver transplantation. Nine other cases with adequate clinical information were obtained from the FDA MedWatch database, including one fatal case of acute liver failure. Usual symptoms were jaundice, fatigue, nausea, vomiting, and abdominal pain. Most patients exhibited a hepatocellular pattern of injury. Adjudication for causality revealed eight cases as definite, five highly likely, two probable, and two were considered to be possible. CONCLUSIONS: Hydroxycut has been clearly implicated as a cause for severe liver injury that may lead to acute liver failure and death. Weight-loss supplements represent a class of dietary supplements that should be regarded as capable of causing severe hepatic toxicity when the usual causes of identified liver injury cannot be otherwise elucidated.
3. Chia JS, Du JL, Hsu WB, Sun A, Chiang CP, Wang WB. Inhibition of metastasis, angiogenesis, and tumor growth by Chinese herbal cocktail Tien-Hsien Liquid. *BMC Cancer.* 2010;10:175.
BACKGROUND: Advanced cancer is a multifactorial disease that demands treatments targeting multiple cellular pathways. Chinese herbal cocktail which contains various phytochemicals may target multiple dys-regulated pathways in cancer cells and thus may provide an alternative/complementary way to treat cancers. Previously we reported that the Chinese herbal cocktail Tien-Hsien Liquid (THL) can specifically induce apoptosis in various cancer cells and have immunomodulating activity. In this study, we further evaluated the anti-metastatic, anti-angiogenic and anti-tumor activities of THL with a series of in vitro and in vivo experiments. METHODS: The migration and

invasion of cancer cells and endothelial cells was determined by Boyden chamber transwell assays. The effect of THL on pulmonary metastasis was done by injecting CT-26 colon cancer cells intravenously to syngenic mice. The in vitro and in vivo microvessel formation was determined by the tube formation assay and the Matrigel plug assay, respectively. The in vivo anti-tumor effect of THL was determined by a human MDA-MB-231 breast cancer xenograft model. The expression of metalloproteinase (MMP)-2, MMP-9, and urokinase plasminogen activator (uPA) was measured by gelatin zymography. The expression of HIF-1alpha and the phosphorylation of ERK1/2 were determined by Western blot. RESULTS: THL inhibited the migration and invasion ability of various cancer cells in vitro, decreased the secretion of MMP-2, MMP-9, and uPA and the activity of ERK1/2 in cancer cells, and suppressed pulmonary metastasis of CT-26 cancer cells in syngenic mice. Moreover, THL inhibited the migration, invasion, and tube formation of endothelial cells in vitro, decreased the secretion of MMP-2 and uPA in endothelial cells, and suppressed neovascularization in Matrigel plugs in mice. Besides its inhibitory effect on endothelial cells, THL inhibited hypoxia-induced HIF-1alpha and vascular endothelial growth factor-A expression in cancer cells. Finally, our results show that THL inhibited the growth of human MDA-MB-231 breast cancer xenografts in NOD-SCID mice. This suppression of tumor growth was associated with decreased microvessel formation and increased apoptosis caused by THL. CONCLUSION: Our data demonstrate that THL had broad-spectra anti-cancer activities and merits further evaluation for its use in cancer therapy.

4. Zeng ZP, Jiang JG. Analysis of the adverse reactions induced by natural product-derived drugs. *Br J Pharmacol*. 2010;159(7):1374-91. Compared with the therapeutic effects of established medicinal drugs, it is often considered that natural product-derived drugs are of a more benign nature in side-effects, which has made natural medicines become a popular form of therapy. Traditional Chinese medicine (TCM) is generally considered as being natural and harmless. TCM has been paid much more attention than before and widely used for the treatment nowadays. However, with the increasing cases of adverse drug reactions (ADRs), the ADRs induced by TCM are becoming more widely recognized. Some ADRs are sometimes even life-threatening. This article reviews literatures on ADRs induced by TCM which was published in the past 10 years. A total of 3122 cases including complete data are selected for the present analysis. From the data of the 3122 cases, statistics is carried out to the distribution of administration routes and time of the occurrence of ADRs, the

prognosis of ADRs, sex and age factors, types and clinical symptoms of ADRs, and drugs involved in ADRs. In addition, occurrence and influencing factors of TCM-induced diseases are also analysed, which includes spices confusion, processing drugs improperly, toxic components, long-term medication, improper concerted application, interaction of TCM and Western medicine. It is concluded that the efficacy and toxicity of TCM, often using the compound prescription involving various plants and animals, resulted from a variety of chemical constituents, which lead to a comprehensive response in the human body. The 'toxicity' of TCM should be correctly recognized and reasonably utilized.

5. Balakumar P, Kaur J. Arsenic exposure and cardiovascular disorders: an overview. *Cardiovasc Toxicol.* 2009;9(4):169-76.
The incidence of arsenic toxicity has been observed in various countries including Taiwan, Bangladesh, India, Argentina, Australia, Chile, China, Hungary, Peru, Thailand, Mexico and United States of America. Arsenic is a ubiquitous element present in drinking water, and its exposure is associated with various cardiovascular disorders. Arsenic exposure plays a key role in the pathogenesis of vascular endothelial dysfunction as it inactivates endothelial nitric oxide synthase, leading to reduction in the generation and bioavailability of nitric oxide. In addition, the chronic arsenic exposure induces high oxidative stress, which may affect the structure and function of cardiovascular system. Further, the arsenic exposure has been noted to induce atherosclerosis by increasing the platelet aggregation and reducing fibrinolysis. Moreover, arsenic exposure may cause arrhythmia by increasing the QT interval and accelerating the cellular calcium overload. The chronic exposure to arsenic upregulates the expression of tumor necrosis factor- α , interleukin-1, vascular cell adhesion molecule and vascular endothelial growth factor to induce cardiovascular pathogenesis. The present review critically discussed the detrimental role of arsenic in the cardiovascular system.
6. Rentsch KM. Review: Laboratory diagnostics in acute poisoning: critical overview. *Clin Chem Lab Med.* 2010.
Abstract Laboratory diagnostics play an important role in the treatment of patients with acute poisoning. The classical clinical chemistry and hematology tests help initiate supportive treatment, and specialized methods enable elucidation of the poisons involved. In this context, two different analytical approaches are used: the direct quantification of a potentially involved compound or screening procedures looking either for a distinct drug class or a wide variety of

different compounds. The most common tests are immunoassays, which have the advantage of being fast and highly automated. These assays are available for the substances which are often involved in intoxications. The other analytical technique which is widely used is hyphenated chromatography consisting of either high-performance liquid chromatography or gas chromatography as chromatographic systems and detection with a diode-array or mass spectrometer. Whereas gas chromatography mass spectrometry screening procedures have been known for a long time, liquid chromatography mass spectrometry screening methods are now developed by different research groups and still need to prove their reliability. In this review, the different analytical technologies and their application will be discussed. Clin Chem Lab Med 2010;48.

7. Holst L, Haavik S, Nordeng H. Raspberry leaf--should it be recommended to pregnant women? *Complement Ther Clin Pract.* 2009;15(4):204-8.

This review evaluates the safety and efficacy of raspberry leaf (*Rubus idaeus*) in pregnancy. The electronic databases PubMed, ISI Web of Science, AMED, EMBASE, Natural Medicines Comprehensive Database and Cochrane Library were searched. Altogether 12 original publications with focus on safety or efficacy during pregnancy, pharmacology and in vitro tests explaining mode of action or constituents in *Rubus idaeus* were reviewed. Limited documentation exists and part of it is 50 years old or older. Only the latest animal study indicates an increased risk for the unborn child; however, all the studies are small and cannot rule out negative effects on pregnancy outcome. The efficacy of raspberry leaf is not convincingly documented. The use of raspberry leaf in pregnancy is a traditional herbal therapy and is recommended by some midwives. Due to the lack of evidence for safety and efficacy such recommendations are questionable. Suggestions for future work are given.

8. Holst L, Wright D, Nordeng H, Haavik S. Use of herbal preparations during pregnancy: focus group discussion among expectant mothers attending a hospital antenatal clinic in Norwich, UK. *Complement Ther Clin Pract.* 2009;15(4):225-9.

BACKGROUND: The extent of herbal medicine use in pregnancy has been widely researched throughout the world but little research has been published about the motivations for this use. METHODS: Focus group discussion. Women who participated in a survey at an antenatal clinic were asked to participate in a focus group discussion to elaborate further on some of the results from the survey. Six women

participated. RESULTS: The major themes identified were: the "underground" nature of taking herbal remedies, reliance on family and friends for information, perceived safety of herbal remedies whilst acknowledging the lack of trial evidence and a desire for the NHS to be more open minded. CONCLUSION: Herbal medicines are pharmacologically active and pregnant women frequently take these without informing their pregnancy care provider. If doctors want to obtain a full medical picture which includes herb use then non-judgemental responses to such behaviour is required.

9. Dangerous supplements: what you don't know about these 12 ingredients could hurt you. *Consum Rep.* 2010;75(9):16-20.
10. Nakae H. Blood purification for intoxication. *Contrib Nephrol.* 2010;166:93-9.

Blood purification is administered in cases of acute intoxication when the substance causing the intoxication is to be eliminated or when the substance leads to a case of organ dysfunction, such as in renal or hepatic failure. The causative substances cover a wide range, from medical drugs or agrichemicals to natural poisons (such as poisonous mushrooms). In removing these substances, gastric lavage, activated carbon administration, laxative administration or enema cleaning are the preferred methods, and blood purification is not routinely conducted. However, when the causative substance is unknown or when there are several causative substances, it is not easy to immediately grasp the disposition of the patient and so judge whether or not blood purification should be performed. In such cases, blood purification must be conducted in a timely manner and in accordance with the crisis management principle of 'prepare for the worst'. In general, substances whose molecular weight is within the removal spectrum, having a small distribution volume and a low protein-binding rate, are easier to remove. For substances with high protein-binding rates, albumin dialysis (MARS and Prometheus) is performed in order to remove albumin-binding substances. Since MARS and Prometheus have not been introduced in Japan, plasma diafiltration, employing selective plasma filtration with dialysis, is a practical alternative.
11. Parker AJ, Lee JB, Redman J, Jolliffe L. Strychnine poisoning: gone but not forgotten. *Emerg Med J.* 2010.

Strychnine was used as a pesticide until 1968 and a rodenticide until 2006 when its sale was banned throughout the EU and all supplies recalled. A case of strychnine poisoning seen in a UK emergency department in 2009 is reported to remind clinicians of the features

and management of this increasingly rare presentation. Prompt recognition and early intensive supportive therapy can result in a favourable outcome.

12. Carvalho CM, Lu J, Zhang X, Arner ES, Holmgren A. Effects of selenite and chelating agents on mammalian thioredoxin reductase inhibited by mercury: implications for treatment of mercury poisoning. *FASEB J.* 2010.
Mercury toxicity is a highly interesting topic in biomedicine due to the severe endpoints and treatment limitations. Selenite serves as an antagonist of mercury toxicity, but the molecular mechanism of detoxification is not clear. Inhibition of the selenoenzyme thioredoxin reductase (TrxR) is a suggested mechanism of toxicity. Here, we demonstrated enhanced inhibition of activity by inorganic and organic mercury compounds in NADPH-reduced TrxR, consistent with binding of mercury also to the active site selenolthiol. On treatment with 5 μ M selenite and NADPH, TrxR inactivated by HgCl₂ displayed almost full recovery of activity. Structural analysis indicated that mercury was complexed with TrxR, but enzyme-generated selenide removed mercury as mercury selenide, regenerating the active site selenocysteine and cysteine residues required for activity. The antagonistic effects on TrxR inhibition were extended to endogenous antioxidants, such as GSH, and clinically used exogenous chelating agents BAL, DMPS, DMSA, and alpha-lipoic acid. Consistent with the in vitro results, recovery of TrxR activity and cell viability by selenite was observed in HgCl₂-treated HEK 293 cells. These results stress the role of TrxR as a target of mercurials and provide the mechanism of selenite as a detoxification agent for mercury poisoning.-Carvalho, C. M. L., Lu, J., Zhang, X., Arner, E. S. J., Holmgren, A. Effects of selenite and chelating agents on mammalian thioredoxin reductase inhibited by mercury: implications for treatment of mercury poisoning.
13. Vardar R, Gunsar F, Ersoz G, Akarca US, Karasu Z. Efficacy of fractionated plasma separation and adsorption system (Prometheus) for treatment of liver failure due to mushroom poisoning. *Hepatogastroenterology.* 2010;57(99-100):573-7.
BACKGROUND/AIMS: Consuming wild mushrooms is an ordinary habit in late summer and autumn in our region. Every year, several cases of hepatic toxicity secondary to mushroom poisoning are observed because of poor identification of the mushrooms. Unfortunately some of them are fatal. Prometheus system is a newly developed extracorporeal liver support device for fractionated plasma separation and adsorption (FPSA) that enables removal of albumin-bound and

water-soluble toxins. Therefore, it may be a promising treatment option for patients with liver failure due to mushroom poisoning. **METHODOLOGY:** We studied 8 patients with mushroom poisoning. All patients underwent 1 to 4 consecutive FPSA (Prometheus)-system in addition to medical and supportive treatment such as fluid replacement, Penicillin G, N-acetylcysteine (NAC) and silymarin. A variety of clinical and biochemical parameters were assessed. **RESULTS:** We had improvement of the biochemical parameters after first treatment with FPSA-system. Seven of 8 patients survived and were discharged to resume an independent life. One patient who had grade III encephalopathy when admitted to hospital died. No major adverse events were observed during the application of this therapy modality. **CONCLUSIONS:** FPSA-system may be a safe and effective treatment option for patient with mushroom poisoning. Early hospitalization is essential in order to be successful. Controlled studies are needed to evaluate the efficacy of this new treatment choice on survival of patients with acute liver failure (ALF) due to mushroom poisoning.

14. Batista-Navarro RT, Bandojo DA, Gatapia MA, Santos RN, Marcelo AB, Panganiban LC, et al. ESP: an expert system for poisoning diagnosis and management. *Inform Health Soc Care*. 2010;35(2):53-63. We describe a clinical decision support system (CDSS) designed to provide timely information germane to poisoning. The CDSS aids medical decision making through recommendations to clinicians for immediate evaluation. The system is implemented as a rule-based expert system with two major components: the knowledge base and the inference engine. The knowledge base serves as the database which contains relevant poisoning information and rules that are used by the inference engine in making decisions. This expert system accepts signs and symptoms observed from a patient as input and presents a list of possible poisoning types with the corresponding management procedures which may be considered in making the final diagnosis. A knowledge acquisition tool (KAT) that allows toxicological experts to update the knowledge base was also developed. This article describes the architecture of the fully featured system, the design of the CDSS and the KAT as web applications, the utilisation of the inferencing mechanism of C Language Integrated Production System (CLIPS), which is an expert system shell that helps the system in decision-making tasks, the methods used as well as problems encountered. We also present the results obtained after testing the system and propose some recommendations for future work.

15. Johnston BD. Harm reduction for unintentional poisoning. *Inj Prev.* 2010;16(4):217-8.
16. Buettner C, Mukamal KJ, Gardiner P, Davis RB, Phillips RS, Mittleman MA. Herbal supplement use and blood lead levels of United States adults. *J Gen Intern Med.* 2009;24(11):1175-82.
BACKGROUND: Some herbal supplements may contain lead. OBJECTIVE: To examine whether use of specific herbal dietary supplements during the last 30 days is associated with blood lead levels in US men and women. DESIGN: Cross-sectional analysis. STUDY POPULATION: NHANES participants from 1999-2004, a representative sample of the civilian non-institutionalized US population. MEASUREMENTS: Lead was measured in blood. Associations between lead and self-reported supplement use were estimated using multivariable regression weighted to account for NHANES sampling. Herbal supplements investigated were those previously reported to contain high heavy metal content: Ayurvedic or traditional Chinese medicine herbs, echinacea, ginkgo, ginseng, St. John's wort, and "other" herbs (specifically, kava, valerian, black cohosh, bee pollen, and nettle). MAIN RESULTS: Among 6,712 women > or =20 years, those using herbal supplements had lead levels that were 10% higher than non-users (95% CI 3%-17%, p = 0.005). Women using Ayurvedic or traditional Chinese medicine herbs, St. John's wort, and "other" herbs had lead levels 24% (95% CI 5%-45%, p = 0.01), 23% (95% CI 4%-46%), p = 0.02), and 21% (95% CI 2%-44%, p = 0.03) higher, respectively, than non-users. No significant associations were observed between herb use and lead levels among men (n = 6,095). Among reproductive-aged women (16-45 years), herbal supplement users had lead levels 20% higher than non-users (95% CI 5%-34%, p = 0.008). In contrast, garlic and other dietary supplements were not associated with higher lead levels. CONCLUSION: Use of specific herbal supplements is associated with higher blood lead levels among women. Our data suggest testing guidelines for herbal supplements and regulations limiting lead in supplements are needed.
17. Jaramillo JE, Marchbanks B, Willis B, Forrester MB. Evaluation of completeness of selected poison control center data fields. *J Med Syst.* 2010;34(4):499-507.
Poison control center data are used in research and surveillance. Due to the large volume of information, these efforts are dependent on data being recorded in machine readable format. However, poison center records include non-machine readable text fields and machine readable coded fields, some of which are duplicative. Duplicating this

data increases the chance of inaccurate/incomplete coding. For surveillance efforts to be effective, coding should be complete and accurate. Investigators identified a convenience sample of 964 records and reviewed the substance code determining if it matched its text field. They also reviewed the coded clinical effects and treatments determining if they matched the notes text field. The substance code matched its text field for 91.4% of the substances. The clinical effects and treatments codes matched their text field for 72.6% and 82.4% of occurrences respectively. This under-reporting of clinical effects and treatments has surveillance and public health implications.

18. Chaubey SK, Sangla KS, Suthaharan EN, Tan YM. Severe hypoglycaemia associated with ingesting counterfeit medication. *Med J Aust.* 2010;192(12):716-7.
Cross-border importation of traditional and prescription medications is common, and many of these drugs are not approved by the Australian Therapeutic Goods Administration. Furthermore, counterfeit versions of prescription medications are also available (eg, weight-loss medications, anabolic steroids, and medications to enhance sexual performance). We describe a 54-year-old man with the first Australian case of severe hypoglycaemia induced by imported, laboratory-confirmed counterfeit Cialis. This serves to remind medical practitioners that counterfeit medication may be the cause of severe hypoglycaemia (or other unexplained illness).
19. Riaz A, Khan RA, Ahmed S, Afroz S. Assessment of acute toxicity and reproductive capability of a herbal combination. *Pak J Pharm Sci.* 2010;23(3):291-4.
The drug under investigation is a herbal combination of *Withania somnifera*, *Tribulus terrestris*, *Mucuna Pruriens* and *Argyreia speciosa* which has been used for several years of its bio-stimulating, revitalizing and fertility enhancing effects. Present preclinical study is specifically designed to assess the safety and efficacy of the product. The result of acute oral toxicity reveals that product is safe up to the dose of 5000 mg/kg. The effects of study related to reproductive capability of drug on both sex reveals increase in reproduction rate up to two generations i.e. F(0) and F(1).
20. Al Momen A. Thrombocytosis secondary to chronic lead poisoning. *Platelets.* 2010;21(4):297-9.
We report a case of total hyperpigmentation of the skin, severe itching, muscle weakness and thrombocytosis. Laboratory investigation showed white blood cell (WBC) $8.2 \times 10(6)/L$, Hb 125 g/L, platelets

1221 x 10⁶/L and urinary lead after DMSA mobilization test 2684 mcg/g creatinine (normal <5). Chelation therapy with DMSA resulted in complete recovery of the hyperpigmentation, itching and thrombocytosis. Lead poisoning should be considered in the differential diagnosis of obscured thrombocytosis.

21. Kapur N, Clements C, Bateman N, Foex B, Mackway-Jones K, Hawton K, et al. Self-poisoning suicide deaths in England: could improved medical management contribute to suicide prevention? *QJM*. 2010.
BACKGROUND: Suicide by self-poisoning is a major cause of death worldwide. Few studies have investigated the medical management of fatal self-poisoning. AIM: To describe the characteristics and management of a national sample of individuals who died by intentional self-poisoning in hospital and assess the quality of care that they received. DESIGN: National population-based descriptive study and confidential inquiry. METHODS: Adults (aged ≥16 years) who had died by self-poisoning in English hospitals in 2005 and received a coroner's verdict of suicide or undetermined death at inquest were included. Socio-demographic and clinical data were collected through detailed questionnaires sent to clinicians at the treating hospitals. A panel of three expert assessors rated each case with respect to quality of care and likely contribution to the fatal outcome. RESULTS: We obtained information on 121 cases (response rate for questionnaires 77%). Expert assessors rated 41/104 cases [39% (95% CI 30-49%)] as having received inadequate care; in the majority (38/41-93%) of these, this poor care was felt to have potentially contributed to the patient's death. The most common reason for a rating of inadequate care was poor airway management (recorded in over half of inadequate care cases). In three cases, the receipt of inadequate care was associated with the presence of some form of advance directive. CONCLUSION: In as many as 39% of in-hospital self-poisoning fatalities, the care received may be in some way sub-optimal. The challenge for clinical services is to ensure that optimal management strategies are implemented in practice.
22. Vickery M. Plant poisons: their occurrence, biochemistry and physiological properties. *Sci Prog*. 2010;93(Pt 2):181-221.
Plants produce poisons as a defence against predators. Many of these substances are biosynthesised from non-protein amino acids by biosynthetic pathways which have been deduced from the results of isotopic tracer analysis. These secondary metabolites have been used by humans over thousands of years, both as drugs and as agents to kill animals and commit homicide.

23. Wargo KA, Allman E, Ibrahim F. A possible case of saw palmetto-induced pancreatitis. *South Med J.* 2010;103(7):683-5.
A 65-year-old male with a history of diabetes, hypertension, hyperlipidemia, gout, Barrett esophagitis, and chronic gastritis developed acute pancreatitis after taking one week of the herbal medicine, saw palmetto, for symptoms related to benign prostatic hyperplasia (BPH). Ultrasound and computed tomography ruled out cholelithiasis and obstruction, triglycerides were normal, and he had no recent infection or trauma. He had a history of occasional alcohol consumption, though there was no recent increased intake. The most likely cause of pancreatitis in this case was saw palmetto. Saw palmetto (*Serenoa repens*) is an herbal medication used primarily in the treatment of symptoms related to BPH. It has a high content of fatty acids and phytosterols which are thought to exert their effects by inhibiting the enzyme 5-alpha-reductase, thereby preventing the conversion of testosterone into dihydrotestosterone (DHT). It has been postulated that saw palmetto directly stimulates estrogenic receptors and inhibits progesterone receptors in the prostate tissue. A previous report implicated the estrogen/antiandrogen properties of saw palmetto as inducing hepatotoxicity in a patient. Additionally, it has also been postulated that stimulation of the estrogenic receptors may lead to increased triglyceride levels or induction of a hypercoagulable state that leads to pancreatic necrosis. Finally, inhibition of cyclooxygenase, a property of saw palmetto, may be linked to acute pancreatitis. Acute pancreatitis, a serious and sometimes fatal disorder may occur secondary to medications. Although the mechanism is not fully known, this is the second case of acute pancreatitis that has been documented secondary to the herbal medication saw palmetto. It is important for clinicians to obtain detailed medication histories, including over-the-counter and herbal medications, in order to prevent further complications from occurring.
24. Vardakou I, Pistos C, Spiliopoulou C. Spice drugs as a new trend: mode of action, identification and legislation. *Toxicol Lett.* 2010;197(3):157-62.
The present review highlights the existing monitoring and legislation status of synthetic cannabinoids in "Spice" products and alert research community about the identification and risk assessment problems of these compounds. Available data were collected by various literature search engines. All valuable information about psychoactive properties, safety profile, clinical data and detection problems for synthetic cannabinoids and their use as "herbal highs" were managed to spot and

summarise. "Spice" contains synthetic cannabinoids that bind to cannabinoid-like receptors and they are stronger than natural cannabis. Chronic abuse of "Spice" has linked with signs of addiction syndrome and withdrawal symptoms similar to syndromes observed in cannabis abuse. These cannabinoids can be considered as new products to be added to the list of "designer drugs". Although it remains unclear where and how the actual production of the herbal mixtures takes place, it is evident that producers are purposely risk the health of consumers to skim high profits. Only recently a number of countries in Europe, as well as in US and Canada banned the use of these substances. The difficulty in identification of related compounds leads to the necessity for the availability of reference standards in order to aid toxicological analyses.

25. Vitalone A, Catalani A, Cinque C, Fattori V, Matteucci P, Zuena AR, et al. Long-term effects of developmental exposure to low doses of PCB 126 and methylmercury. *Toxicol Lett.* 2010;197(1):38-45. Methylmercury (MeHg) and polychlorinated biphenyls (PCBs) are food contaminants often found in fish. Experimental and epidemiological studies indicate that both PCBs and MeHg are developmental neurotoxicants, and some reports suggest that they may cause additive and/or synergistic neurotoxicity. We had previously investigated the effects of exposure to low doses of MeHg (0.5 mg/kg/day in drinking water) and PCB 126 (100 ng/kg/day in food) alone or in combination, from gestational day 7 to post-partum day 21, on neurobehavioral development in Wistar rats. The main finding was hyperactivity in male rats exposed to PCB 126, and in female animals exposed to PCB 126+MeHg at 4 months of age (Vitalone et al., 2008). Since effects caused by developmental exposure may be exacerbated as the animal ages, aim of the present study was to investigate behavioral effects of the same developmental exposure to PCB 126 and/or MeHg up to the age of 20 months. Results indicate that aging did not enhance the behavioral effects of early exposures; however, behavioral alterations found in the first months of life in male rats exposed to PCB 126, or in female rats exposed to PCB 126+MeHg, were persistent. Furthermore, an additional effect (increased body weight) was unmasked in adulthood in male rats exposed to PCB 126. These results indicate that developmental exposure to a low, environmentally relevant dose of PCB 126 causes long-lasting hyperactivity in male rats, and a significant increase in body weight.