



UtoXUpdate

UPCC A PUBLICATION OF THE UTAH POISON CONTROL CENTER FOR HEALTH PROFESSIONALS

An Overview of Herbal Ecstasy and Other Stimulants

Case Report

A 21 year old man was brought to the emergency department (ED) two hours after the ingestion of four capsules of herbal "ecstasy", (kola nut, nutmeg, and ginseng). He also consumed ethanol and smoked one marijuana cigarette. His symptoms began approximately 30 minutes after the ingestion and included bitemporal headache (severity 9/10), nausea and vomiting, dyspnea, diaphoresis, and dizziness. He vomited seven times. He denied chest pain or palpitations. His vital signs taken by the paramedics were: blood pressure 220/120 mm Hg, heart rate 120 beats per minute (bpm), and respiratory rate 20 breaths/minute. The patient had no previous family history of hypertension.

Upon arrival at the ED, the patient was drowsy but was oriented and conversant. His initial vital signs were: blood pressure 190/116 mm Hg, pulse 90 bpm, respiratory rate 16 breaths/minute, temperature 36.6 °C. His pupils and fundi were normal. The rest of the physical exam was unremarkable. A normal saline infusion was started, and the patient was placed on a cardiac monitor. Supplemental oxygen (7 L/min) was also administered. Laboratory tests (including CBC, electrolytes, LFT's) were within normal limits except for a potassium of 3.2 mmol/L. The urine toxicology screen was positive for ephedrine, pseudoephedrine, cannabinoid metabolites, and traces of opiate and caffeine. An ECG performed shortly after arrival showed sinus rhythm with frequent multifocal ventricular ectopic beats and probable left ventricular hypertrophy. His blood pressure was as high as 210/140 mm Hg. The patient was started on nitroprusside and lidocaine infusions. Nitroprusside was discontinued after five hours. At that time, the patient's blood pressure was 155/85 mm Hg. The patient was admitted for observation, had no further symptoms and was discharged the following day with a blood pressure of 110/80 mm Hg.¹

Introduction

The term "ecstasy" was originally used to describe methylenedioxymeth-amphetamine (MDMA). Recently the use of the term "ecstasy" has expanded. "Herbal ecstasy" is most often used to describe products with Ma Huang (ephedra), "liquid ecstasy" implies GHB, and "OTC ecstasy" contains dextromethorphan

Herbal stimulants, such as "herbal ecstasy", have gained recent popularity among high school and college students as "safer" alternatives to illicit street drugs. These drugs are sold under names such as "Cloud 9", "Ultimate Xphoria", "Up Your Gas" and "Ripped Fuel", and contain common ingredients with sympathomimetic properties (see table 1). Many of these drug combination products are marketed as diet or energy aids and some boast that ingesting these herbs results in euphoric experiences, increased sexual sensations, and heightened awareness.^{2,3} Several food supplements also contain other herbs such as kola nut and guarana, which are natural sources of caffeine.⁴ In 1996 the FDA warned consumers not to purchase or consume ephedrine containing dietary supplements that often portray the products as apparent alternatives to illicit street drugs such as "ecstasy" because the products pose significant health risks to consumers.⁵

Herbal "ecstasy", a particularly popular stimulant, will be focus of this discussion.

Herbal Ecstasy

Herbal "ecstasy" has been used to describe specific products but is also used as a generic term. It is becoming increasingly popular at raves because of the product's promotion as a safe alternative to the illicit drug "ecstasy" (MDMA). Its main ingredients include caffeine and ephedrine, which claim to increase energy, inner visions, sexual sensations, and cosmic consciousness.¹¹ It is analogous to street speed of the 1980's as "a natural alternative." Historically, the ephedra preparations were used by the Chinese for the management of bronchial disorders. Ephedra has also been used in Asian medicine for the treatment of headache, fever, flu, chills, colds, and nasal congestion.¹¹ Today, it has continued its utility in the treatment of cold symptoms and more recently has been used in combinations with caffeine and other stimulants, including herbal "ecstasy". In 1997, the Federal Trade Commission filed suit against a California company, alleging

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false claims made about herbal "ecstasy's" safety and failing to "disclose health and safety risks of using the product." The company agreed to warn consumers about the safety risks of taking the product and refrain from promoting herbal "ecstasy" for its mind-altering effect. The FDA has compiled hundreds of injury reports associated with ephedra-containing substances, including herbal "ecstasy". The FDA has also published a proposed rule that would limit serving size and require warning in labeling for all ephedrine supplements.¹² Many countries and states have also banned or restricted the marketing of products like "ecstasy". However, it can still be purchased over the counter in drug stores, and other specialty shops around the country, at a cost of approximately \$3.00 per pill.¹³

Pharmacology

Ephedrine is structurally similar to epinephrine, stimulating both alpha and beta-adrenergic receptors. It can be administered orally, parenterally, or topically. Therapeutic doses result in cardiac stimulation, elevated systolic/diastolic blood pressure, respiratory bronchodilation, and relaxation of GI smooth muscle tone.¹⁴ Ephedrine is rapidly and completely absorbed after oral administration and is almost completely excreted in the urine as unchanged drug.¹

Caffeine is the most potent CNS stimulant of the methylxanthines. It stimulates the cerebral cortex and medullary centers, dilates peripheral and coronary vessels, constricts cerebral blood vessels, stimulates skeletal muscle, exerts a positive inotropic and chronotropic effect on the myocardium, and induces diuresis by decreasing tubular reabsorption.^{14,15} Caffeine is rapidly and completely absorbed from the GI tract, with peak plasma concentrations occurring approximately 0.5 hours after ingestion. It is extensively metabolized in the liver via cytochrome P.450 enzymes.¹⁵

Toxicology

Adverse effects from ephedrine can be variable, and are not always dose related. Toxicity is usually manifest by overstimulation of the adrenergic system, including CNS and cardiovascular stimulant effects. CNS effects include insomnia, headache, restlessness, anxiety, psychosis, and seizures. Its major cardiovascular toxicities consist of tachydysrhythmias and hypertension. Other toxic symptoms may include coronary spasm, convulsions, respiratory depression, coma, and death. Patients may also be at an increased risk for rhabdomyolysis.¹⁶

In a 1993-1995 review by the Texas Department of Health, ephedrine had been associated with over 500 cases of adverse effects and eight fatalities. Reports included stroke, myocardial infarction, chest pain, seizures, insomnia, nausea, vomiting, fatigue, and dizziness. Seven of the eight reported fatalities were attributed to myocardial infarction or a cerebrovascular accident.¹⁶ Three cases of ephedrine-related stroke were reported by Bruno et al¹⁷. One case involved ephedrine-related ischemic stroke and the other two involved intracranial hemorrhage. The suggested mechanism of ischemic and hemorrhagic stroke is vasculitis and vasoconstriction in the former and the induction of acute arterial hypertension, resulting in the rupture of cerebral vascular abnormalities in the later.¹⁷

Caffeine also primarily exerts its toxic effects via the CNS and cardiovascular system. CNS toxicity is manifested by anxiety, agitation, psychosis, confusion, and seizures. Cardiovascular toxicity includes sinus tachycardia and ventricular dysrhythmias. It is important to note that in herbal ecstasy preparation, where ephedra is also present, these effects may be additive.¹

Treatment

Decontamination may be helpful in an acute overdose within a certain time frame. If presentation is early (< one hour), activated charcoal may be administered to prevent further drug absorption. Initial management of ephedra-induced toxicity is mainly supportive care. Agitation, tachycardia, hypertension and seizures should be treated with benzodiazepines. Refractory hypertension is treated with vasodilators such as nitroprusside or phentolamine. Ventricular tachydysrhythmias are treated with lidocaine. In theory, acidification should increase ephedrine secretion, therefore enhancing its elimination. However, this is potentially dangerous because it can cause dysrhythmias and facilitate the precipitation of myoglobin in the renal tubules, leading to acute renal failure.^{1,3,14}

Summary

There has been an increased interest in herbal preparations and natural supplements in recent years. These preparations are often perceived by the public as being healthy and harmless because of their "natural" sources. This concept has spread to the streets, where illicit drug users are commonly abusing

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Table 1. Common Herbal Stimulants⁶⁻¹⁰

Name	Stimulant Ingredients	Pharmacology
Kola nut	Main alkaloid: caffeine (0.6 - 3.7%), also theobromine, theophylline.	Competitive inhibitor of phosphodiesterase, the enzyme responsible for the inactivation of cyclic3, 5-adenosine
Guarana	Main alkaloid: caffeine (3.6 - 5.8%), small amount of theobromine, theophylline.	See above
Ma Huang	Main alkaloids: ephedrine, pseudoephedrine, some norephedrine, norpseudoephedrine.	Ephedrine: stimulates alpha and beta-adrenergic receptors. Pseudoephedrine: stimulates alpha and beta receptors of vascular smooth muscle.
Khat	Main alkaloid: cathinone (alpha-aminoprophenone), some cathine (d-morpseudoephedrine).	Cathinone: similar to amphetamine, stimulating dopamine and serotonin release. Cathine: see pseudoephedrine
Dong Quai	Coumarin stimulant: osthol	Possible inhibition of phosphodiesterase activity.
Ginseng	Ginsenoside stimulant: Rg 1	Mechanism of action not well characterized, possible modulation of dopaminergic activity.
Schisandra	Schisandra fruit	Nervous system stimulant, increasing reflex responses and improves mental alertness. MOA not well documented.

readily accessible and even legal herbal-origin substances, such as herbal ecstasy, to achieve intoxication. Unfortunately, these substances are not safe. Both ephedrine and caffeine have significant cardiovascular and CNS toxic effects when taken in large quantities.

Kristine Hanson, PharmD candidate

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UPCC In the News

The UPCC is proud to announce that its 1999 Annual Report is available. This report includes highlights of the over 50,000 calls the UPCC received in 1999. This represents a 5% increase in call volume at a time when there was a nearly 2% decrease in calls to poison centers nationwide. It was our first full year of stable funding, our national accreditation was extended for an additional five years, and Dr. Caravati was granted Medical Toxicology Subspecialty Certification. If you would like a copy of the 1999 Annual report, email us at barbara.crouch@hsc.utah.edu, or call our administrative office at (801) 581-7504.

Seven members of the UPCC staff attended the North American Congress of Clinical Toxicology held September 15-18th. Five posters were presented involving UPCC staff:

- **Caravati EM, Grover J.** Arsine Poisoning from Recycling of Computer Chips
- **Stomness J, Crouch BI, Caravati EM.** Lead Exposures from Indoor Firing Ranges.
- **Anderson BD, Crouch BI.** Comparison of APAP Outcomes and Management Guidelines Between Two Regional Poison Centers.
- **Grover J, Caravati EM.** Oral Overdose of N-Acetylcysteine in an Infant.
- **Hopkins U, Shepherd G, Klein-Schwartz W, Gorman S, Crouch B.** Multicenter Case Series of Gabapentin Exposures.

Phenylpropanolamine

The issue of the safety of phenylpropanolamine (PPA) has once again surfaced. The FDA has recently issued a public health warning on PPA and has requested that all drug companies discontinue marketing products containing PPA. In the early 1980's numerous articles appeared in the medical literature debating the safety of phenylpropanolamine.^{1,2} A study involving medical students in Australia showed a significant rise in diastolic blood pressure following the ingestion of a single dose of a PPA containing product.³ Today, the FDA is taking steps to remove PPA from all drug products following a recently issued report from Yale University entitled "Phenylpropanolamine & Risk of Hemorrhagic Stroke".⁴ Taking PPA has been associated with an increased risk of hemorrhagic stroke, particularly in women. Since there are safer decongestants available OTC, the risks of using PPA outweigh any benefit.

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M-44 Sodium Cyanide Device

The United States Department of Agriculture, Animal and Plant Health Inspection Service, Bureau of Wildlife Services would like us to remind you that the M-44 sodium cyanide device is used in Utah. The device is tubular and is placed in the ground with 1.5 inches sticking out of the ground baited with meat. This device is used in specific situations to control coyotes, redfox, gray fox and wild dogs. The purpose of the device is to protect livestock, poultry, endangered species and to prevent the spread of disease. Although this device is primarily used on private lands, it may also be used on federal land in any county in the state. Areas where it is used are marked with signs. While human exposure to this device would be extremely unlikely, it is important to know that this device contains 91% sodium cyanide. Please report any exposure to this device to the Utah Poison Control Center at (801) 581-7504 or (800) 456-7707. We thank you in advance for your assistance.

Public Education Materials

If you would like to provide your patients with poison prevention public education materials including: brochures, telephone stickers, emergency action cards, quarterly public newsletters and more, call for a complete list and order form. (801) 581-7504.

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