# ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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**The Maryland Poison Center's Monthly Update: News, Advances, Information**


## Synthetic Cannabinoids: An Undetectable and Uncomfortable High

*A 26-year-old male presented to the emergency department 4 hours after smoking K2. He was uncooperative, agitated, and running around in circles. Vital signs included a heart rate of 123 bpm, blood pressure of 116/67 mmHg, respiratory rate of 20 breaths/minute; he was diaphoretic and had dilated pupils. After administration of 5 mg midazolam, 5 mg haloperidol, 50 mg diphenhydramine, and 3 mg of lorazepam, he calmed down and vital signs returned to normal. He was discharged 7 hours after presentation.*

Synthetic cannabinoids (SCs) are old news; 1940's old. In the early 1940's, Roger Adams was modifying side chains of 9-delta-tetrahydrocannabinol (THC) and studying the potency in animals. Interest in modified THC molecules for medical purposes continued with the use of nabilone in the 1970's. Fast forward to 1993, when researcher John W. Huffman synthesized and published the formula for JWH-018, a fully synthetic cannabinoid. Abuse began in Europe in the mid-2000's with the first US customs seizure in 2008. Calls to U.S. poison centers concerning SC's peaked in 2015, with 7,779 calls that year.

Although often called "synthetic marijuana", today's SCs are structurally dissimilar from THC. There are hundreds of fully synthetic molecules that are manufactured in labs and new chemicals are being synthesized all the time. They are sprayed onto inert plant material to be smoked, or sold as a liquid for use in e-cigarettes . *In vitro* potency experiments of SCs tested from 2010 to 2016 suggested that many of the SCs are ~50 to 100 times more potent than THC. Most are considered full agonists at the cannabinoid receptor 1 (CB1), whereas THC is considered a partial agonist *(NEJM 2017;376:235-42).* In a study published in 2016, 11 different chemicals were detected over an 8 month time-frame, and all of the paraphernalia tested positive for more than one SC *(MMWR 2016;65:1108-11).*

Low cost (~ $1/joint) and lack of detection on typical urine toxicology screening are attractive to many users. Common users of SCs are military personnel, the homeless population, those who undergo frequent drug testing (e.g. commercial drivers), and high-school students. Periodic outbreaks of severe cases of intoxication due to SC's have been reported across the country in major urban centers *(NEJM 2017;376:235-42*). At least 27 deaths have been reported in the U.S., including Maryland *(Clin Toxicol 2016;54:1-13; NEJM 2015;373:103-7).* Patients present to the emergency department more often for synthetic cannabinoids than natural THC. A recent study reported that 10.1% of ambulance transports were due to SC intoxication during an 8-month period *(MMWR 2016;65:1108-11).*

Multiple clinical effects have been reported following the use of SCs including nausea, vomiting, agitation, tachycardia, bradycardia, hypertension, hypotension, seizures, acute kidney injury, lethargy, tachypnea, new onset psychosis, and myocardial infarction. Very few published case series and case reports confirmed exposure by lab testing; therefore, it is difficult to identify what effects were attributable to the reported exposure or to other factors.

Management consists of treating specific symptoms including airway and blood pressure support, antiemetics for nausea and vomiting, and benzodiazepines for agitation. Typical urine toxicology screening will not detect SCs.


## Did you know?

**"Not for human consumption" on a synthetic cannabinoid product label is an attempt to protect retailers and distributors from legal action.**

Synthetic cannabinoids are often packaged in colorful foil pouches or bottles, usually labeled as herbal potpourri or herbal incense as a disguise. Most packages state that the product is "not for human consumption" to avoid prosecution. However, this does not circumvent legal action if the product contains a scheduled drug or if the prosecution can prove that human consumption is intended.


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