

Synthetic Cannabinoids

Spice, K2, Newport, AK 47, Scooby Snax, Bahama Breeze, Bizarro, legal high... these are a few of the many street names for synthetic cannabinoids, commonly called synthetic marijuana. Scientists and the pharmaceutical industry originally synthesized these compounds for research purposes. By the mid to late 2000s, these chemicals began to be used recreationally. Numerous compounds exist and they continue to change, making it difficult to legislate against them. While some have been made schedule I by the DEA, others are currently legal.

Synthetic cannabinoids are manufactured in a laboratory with most originating from China and Southeast Asia. The synthesized substances are applied to inert plant matter, often as an uneven mixture of multiple compounds. They can be found for sale as "herbal incense" or "potpourri" in colorful pouches in gas stations, convenience stores, and on the internet. The main route of exposure is inhalation by smoking and there are now liquid forms for use in e-cigarettes.

The pharmacology of synthetic cannabinoids is not fully characterized. The synthetic cannabinoid compounds that have been studied have nonselective affinity for and agonist action at cannabinoid receptors CB1 and CB2. This is similar to delta-9-tetrahydrocannabinol (THC), the psychoactive cannabinoid in cannabis plants. However, there are important differences. THC is a partial agonist at CB1 whereas synthetic cannabinoids are full agonists. They are also thought to have multiple times the receptor affinity and longer half-lives compared to THC. The CB1 receptor is predominant throughout the CNS and causes the majority of psychoactive effects of synthetic cannabinoids. CB1 receptors are located presynaptically on both glutamatergic and GABAergic synapses, suggesting a role in modulating these neurotransmitters. GABA inhibition may explain some excitatory effects. CB2 receptors predominate peripherally and are thought to have anti-inflammatory, immune modulating, analgesic, and anti-emetic effects.

The use of synthetic cannabinoids is a growing problem. A 2014 Monitoring the Future survey of middle and high school students ranked it the 3rd most prevalent drug used after marijuana and amphetamines. Most users are in their teens and 20's, and over 70% are male. From Jan 1, 2015 through May 27, 2015, the Maryland Poison Center (MPC) received 96 calls about synthetic cannabinoid exposures, passing 2014's total of 90 cases. This surge is similar throughout the nation. In 2015 through May 27th, there were 3548 cases reported to U.S. poison centers, while in all of 2014 there were 3682 cases.

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Did you know?

All Synthetic cannabinoid exposures should be reported to a local poison control center.

Poison centers are closely monitoring synthetic cannabinoid trends along with public health officials. This collected data is being used to update emergency providers on the latest effects and management recommendations. Reporting synthetic cannabinoid exposures enables officials to characterize the toxicity of these compounds and pass laws against them.



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A 2010 review of national poison center data listed the most common clinical effects with synthetic cannabinoid exposures as tachycardia (40%), agitation/irritability (23.4%), vomiting (15.3%), drowsiness/lethargy (13.5%), confusion (12%), and nausea (10%) (*Ann Emerg Med* 2010;60:435-8). Seizure was the most common life threatening effect but most cases had only minimal symptoms. Mydriasis, psychosis, rhabdomyolysis, ischemic stroke, myocardial infarction, and acute kidney injury have also occurred.

Over the last two months, poison centers have reported more cases and more diverse and serious adverse effects. The clinical picture appears different: CNS depression or agitation, bradycardia, and respiratory depression requiring intubation. Some patients have presented in cardiac arrest. There have been 58 cases with moderate or major effects reported to MPC thus far in 2015, up from 39 in all of 2014.

New types of compounds may be to blame. Indazole carboxamine (INACA) compounds are frequently being isolated in synthetic cannabinoid seizures by law enforcement agencies. These include MAB/AB CHMINACA and FUBI-NACA. Other isolates obtained recently from police analysis include FUB-PB-22 and XLR 11. Adulterants may also play a role because other psychoactive drugs such as PCP have been identified in synthetic cannabinoid products.

Synthetic cannabinoids cannot be detected on standard urine drug screens; they do not test positive for THC. Management remains supportive with benzodiazepines administered for agitation and seizures. Intubation may be needed if the patient has significant CNS depression and/or respiratory depression. Antipsychotics should be avoided due to their adverse effects, including the potential for lowering seizure threshold. Ketamine administration by prehospital providers has been used effectively and safely to provide sedation in synthetic cannabinoid exposures (*Clin Toxicol* 2015;53:365).

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