Chris Chase, MD / Edited by: Larissa Velez, MD

Synthetic Cannabinoids

Emergency departments have seen a rise in the use of synthetic cannabinoids over the past few years. There are many misconceptions about these news drugs and their effects. Synthetic cannabinoids are essentially **herbal plant materials that are sprayed with synthetic analogues of THC** (tetrahydrocannabinol), the primary chemical responsible for marijuana's psychological effects. They are smoked like marijuana or can be made into a tea and ingested. These drugs act on cannabinoid receptors (**CB1 and CB2**) and can produce similar psychogenic effects as marijuana. The CB1 receptors are primarily found in the CNS and are the focus of these effects. Synthetic cannabinoids act as **full agonists** at these receptors, while THC acts as a partial agonist. This results in a much higher potency (estimated 5-45x more potent than THC) and unpredictable effects than those seen with cannabis use.

In the mid-90s Dr. John W Huffman, an organic chemistry professor at Clemson University, researched cannabinoid receptors for potential medical applications, and synthesized over 450 analogs of cannabinoids. The chemicals were named after his initials (JWH). His primary analog was named **JWH-018**. Dr. Huffman stated, "JWH-018 can be made by a halfway decent undergraduate chemistry major in three steps using commercially available materials". He also added, "These things are dangerous – anyone who uses them is playing Russian roulette. They have profound psychological effects. We never intended them for human consumption." Unfortunately, this is what happened. In 2004, "Spice" was manufactured in Europe (thought to be recreating Huffman's research). It gained popularity over the next few years and soon competing brands emerged, such as K2. **By 2009, these synthetic drugs began to gain popularity in the US**.

Illicit drug laboratories have manufactured **over 50 known synthetics** including Spice, K2, Yucatan Fire, Sence, Chill X, Genie, and Black Mamba. These synthetic cannabinoids are packaged in 1-3 gram colorful bags and marketed as **"incense"**. They were sold legally in smoke shops and gas stations and could be readily found over the Internet. Each bag had a warning label stating they were "not meant for human consumption" allowing these manufacturers to evade the legal system. Each different analog has a **slightly altered chemical structure which accounts for unpredictable side effects and allow for difficult identification and regulation by the DEA**.

The use of synthetic cannabinoids has been increasing. Seven thousand patient cases are reported to US poison control centers annually and it is estimated that synthetic cannabinoids account for an 8 billion dollar industry. The primary demographic of users is **young males in their 20s-30s**. It was found ED visits involving synthetic cannabinoids increased from 11,406 to 28,531 from 2010 to 2011. A survey done in 2012 reported that among high school seniors, 11.3% admitted to have used synthetic cannabinoids. This drug use was **only second to marijuana** (36.4%).

Symptoms of intoxication with synthetic cannabinoids commonly include **conjunctival injection, diaphoresis, tachycardia, high blood pressure, agitation, vomiting, delusions, and agitation**. Case reports have noted **dystonic reactions**. Serious complications have also been reported which include **myocardial ischemia, acute kidney injury (associated with a regional batch of a product brand called "blueberry spice"), rhabdomyolysis, seizures, and death**. Many cases of death secondary to exposure are secondary to accidents and suicide due to **psychosis and paranoia**. Many reports suggest that synthetic cannabinoids can be **highly addictive and produce withdrawal symptoms with chronic users**.

Diagnosis in the ED is primarily clinical. Tests commonly performed are EKG, POC glucose, BMP, and CK to assess for rhabdomyolysis in the severely agitated patient. Synthetic cannabinoids are not detected on conventional Urine toxicology screens. Confirmatory tests via liquid chromatography and mass spectrometry are available but not clinically efficient or cost effective. The treatment is **primarily supportive** and there is no antidote. Agitation is usually treated with IM or IV **benzodiazepines**; but more evidence is emerging supporting the use of antipsychotics when the patient is exhibiting psychosis. A review article by Papanti and colleagues titled "Spiceophrenia" in 2013, studied the relationship between Spice use and psychosis. Researchers concluded that **synthetic cannabinoid use might precipitate psychosis in vulnerable individuals (adolescents with ongoing CNS maturation) or exacerbate psychosis in patients with previous psychiatric history**. Dystonic reactions can be treated with diphenhydramine and benztropine. Frequently, patients may be observed in the ED and discharged after symptomatic management. Admission may be necessary if the patient is severely/persistently agitated or other complications develop (myocardial infarction, rhabdomyolysis, etc).

Over recent years, more national attention has been brought regarding synthetic cannabinoids. In 2010 the federal government banned five synthetic compounds including JWH-018, JWH-073, JWH-200, CP 47,497 and cannabicyclohexanol for 1 year. In 2012, the Synthetic Drug Prevention Act was signed by President Obama and subsequently enacted, prohibiting the sale or possession of compounds frequently found in synthetic cannabinoid products. This made most of these synthetic cannabinoids schedule I substances. However, manufacturers are continuing to alter these analogs to try and stay ahead of the law enforcement agencies.

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