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Synthetic Cannabinoids: The Newest, Almost Illicit Drug of Abuse

Synthetic cannabinoids are associated with effects similar to those of cannabis. In the United States, they are growing in popularity in tandem with legal efforts to prevent their sale. In this case, a patient presents with seizures after consuming a large quantity of a synthetic cannabinoid powder that he bought online.

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Case

A healthy 48-year-old man has a generalized convulsion after ingesting a powder he purchased through the Internet. The powder was sold as “research grade JWH-018,” with the wording “not for human consumption” listed on the packaging. The seizures continue in the prehospital setting, as well as in the ED, for approximately 15 minutes in total before ceasing after administration of lorazepam 4 mg IV. Initial vital signs after cessation of his seizures include a blood pressure of 140/88 mm Hg; pulse, 106 beats/min; respiratory rate, 22 breaths/min; temperature, 37.7°C. Physical examination is notable for mydriasis and diaphoresis with 5 beats of myoclonus in the bilateral lower extremities. Shortly after arrival in the ED, the patient is intubated for airway control. Findings on noncontrast CT of the brain are unremarkable, and EEG results are normal. Initial pertinent laboratory values include

normal electrolyte, creatinine, and glucose levels. His creatine phosphokinase level is elevated, at 2,500 U/L. Toxicology screening does not detect acetaminophen, ethanol, or salicylates.

What is JWH-018?

JWH-018 is a synthetic cannabinoid (Figure 1) that acts at both endogenous cannabinoid receptor subtypes (CB1 and CB2).¹ Synthetic cannabinoids were created shortly after the structure of Δ^9 -tetrahydrocannabinol (Δ^9 -THC; Figure 2) was elucidated in the 1960s, and their development continued for use of these substances in appetite stimulants (eg, dronabinol) and as research tools for the study of the endocannabinoid receptors. Different synthetic cannabinoids have distinct binding affinity for the cannabinoid receptors. For example, HU210 is reported to bind to the CB1 and CB2 receptors with 100 times the affinity of Δ^9 -THC.² The synthetic cannabinoids of the JWH series vary in structure from Δ^9 -THC and are classified as aminoalkylindoles. They are named for the chemist who first synthesized them, John W. Huffman, PhD (thus the “JWH” prefix). Synthetic cannabinoids recently appeared as herbal incense for sale in smoke shops and other outlets (such as gas stations). These herbal incense products contain pulverized plant material that is adulterated with one or more synthetic cannabinoids. They have been sold

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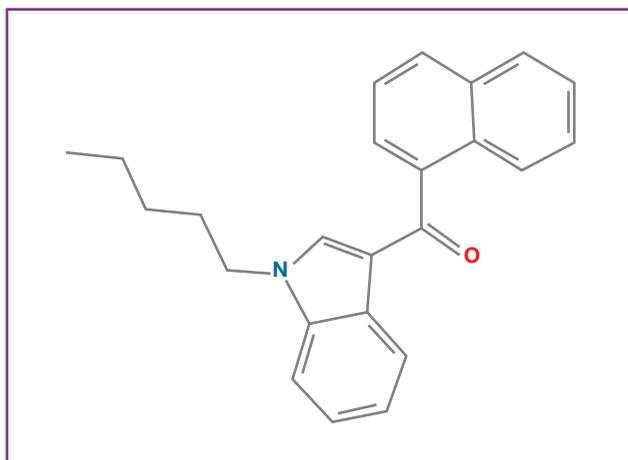


FIGURE 1. JWH-018.

under multiple names and brands, including Spice, K2 (Figure 3), K3, and Mr. Nice Guy. In a recently published case, JWH-018 and JWH-073 were found in a single product.³ They are typically labeled as “not for human consumption.” Purified JWH-018 is an off-white powder that was previously used for cannabinoid receptor research.

JWH-018–laced incense first appeared in 2007 on the European drug scene. Its use peaked after a German news report detailed “legal marijuana-like” products for sale in local smoke shops.⁴ Use in the United States has expanded over the last year, due largely to discussions in Internet forums.

What are the expected clinical effects of synthetic cannabinoids? How do synthetic cannabinoids differ from traditional cannabinoids?

The drug can be smoked, insufflated, or ingested. Some users report an experience similar to that of marijuana

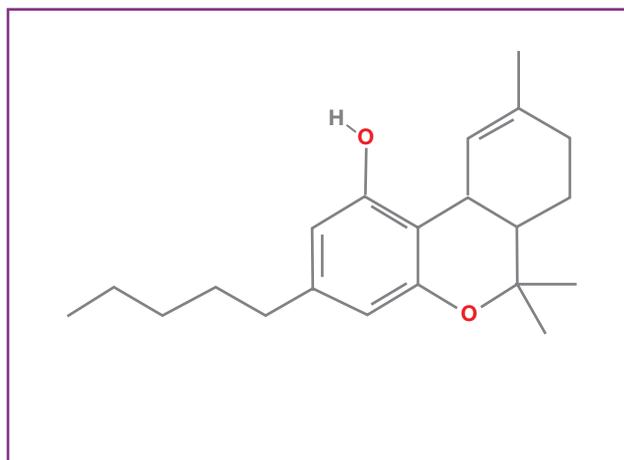


FIGURE 2. Δ⁹-Tetrahydrocannabinol.

use, while others detail a more intense high that lasts longer. Not surprisingly, online user reports indicate that finding the correct recreational dose can be difficult. Although discussion in the medical literature is limited, the majority of anecdotal accounts relay clinical effects similar to those of Δ⁹-THC. The psychoactive effects (both desired and undesired) that are described include alteration of time perception, anxiety, dysphoria, listlessness, hallucinations, and psychomotor agitation. Additional undesirable effects include nausea, vomiting, tachycardia, palpitations, and xerostomia. Seizures have not been reported in users of conventional doses of JWH-018. However, given the large volume of pure JWH-018 that this patient reportedly consumed, a dose-dependent effect is likely.

What treatment can be recommended for synthetic cannabinoid–intoxicated patients?

As with marijuana users, the majority of these patients do not require measures beyond observation along



FIGURE 3. Synthetic cannabinoid products.

with symptomatic or supportive care. Benzodiazepines are recommended for control of psychomotor agitation and abatement of seizures. Gastrointestinal decontamination has no known role in patients using synthetic cannabinoids by insufflation or inhalation. However, as with many other poisonings, it may prove beneficial in large-quantity ingestions.

What is the legal status of synthetic cannabinoids?

In November 2010, three synthetic cannabinoids (JWH-018, JWH-073, and JWH-200) were designated by the Drug Enforcement Administration (DEA) to temporary Schedule I status (ie, they have no medicinal use and high abuse potential).⁵ This temporary designation applies for 1 year and could be made permanent by legislative means. The authority for temporary schedule status was enacted by the Controlled Substances Act, specifically the Analogue Act, which essentially allows structurally similar drugs with abuse potential to be removed from sale pending investigation or legal action.⁶ Since these synthetic cannabinoids are not analogues of Δ^9 -THC, they are not under the auspices of the Analogue Act. Furthermore, the wording of the Analogue Act states that it applies to substances “intended for human consumption” and it may well be the intention of synthetic cannabinoid manufacturers to circumnavigate this law by labeling their products as “not for human consumption.” However, at this time, a temporary court injunction has halted the DEA’s emergency scheduling pending further proceedings. Many

of the synthetic cannabinoids are banned in Europe as well as parts of Asia.

Case Conclusion

The patient was extubated on hospital day 5 and had an uneventful recovery. He was subsequently discharged home in his usual state of good health.

Samples from the patient, as well as the powder he ingested, were sent for further analysis by high-performance liquid chromatography (HPLC) and gas chromatography mass spectrometry (GC/MS). The powder was found to be pure JWH-018 in crystalline form. Both JWH-018 and JWH-073 were identified in the patient’s urine with unclear implications—possibly representing either the 073 compound as a metabolite of 018 or prior use of synthetic cannabinoids. Toxicologic analysis of his urine by both enzyme-multiplied immunoassay technique and GC/MS was negative for conventional drugs of abuse, including Δ^9 -THC. **EM**

References

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