

## **“Spice” it Up – A New Way to Get High What Pharmacists Need to Know**

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On November 24, 2010, the DEA issued a notice of intent to place five synthetic cannabinoids into Schedule 1 of the Controlled Substances Act.<sup>1</sup> These cannabinoids (JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol) are used in research laboratories to identify cannabinoid receptors in the brain and study the mechanism of action of delta-9-tetrahydrocannabinol ( $\Delta^9$ -THC), the main cannabinoid in marijuana.<sup>1,2</sup> In recent years, however, they have been gaining popularity as “legal” alternatives to cannabis and sold under the names “K2” and “Spice,” among others.<sup>2</sup> Additionally, the marijuana-like substances found in K2 and Spice will not trigger a positive result on a drug test.<sup>1</sup>

The mechanism of action of cannabinoids involves interaction with the CB1 and CB2 receptors.<sup>3,4,10</sup> CB1 receptors are found mostly in the central nervous system and are responsible for anti-emetic and psychotropic effects, while CB2 receptors are mainly in the periphery and are responsible for pain mediation and immune modulation.<sup>4</sup> John W. Huffman, organic chemist at Clemson University, is credited with first synthesizing the novel “jwh” cannabinoids in 1995 and researching their affinity for the CB1/CB2 receptors.<sup>5,10</sup> The most well-known synthetic compound, JWH-018, has a threefold higher affinity for CB1 than CB2 and a fourfold higher affinity for CB1 than THC, which may explain in part the mind-altering effects that occur when synthetics are abused and why JWH-018 is one of the main components in Spice.<sup>6,10</sup>

By 2004, Spice was already being sold in Europe, and in 2009 usage rose in the US and Canada.<sup>1</sup> From January to June 2010, the Texas poison centers alone received 99 phone calls with 87 exposures to the new synthetics.<sup>7</sup> Understandably, K2 and Spice are attractive marijuana substitutes to law-conscious individuals, and the products can be easily found in head shops, convenience stores, and on the internet for prices less than marijuana.<sup>1,8</sup> Marketed as herbal incense and “not for human consumption,” these blends have slipped past authorities for years, but subjects utilizing internet forums testify to the psychogenic effects of the incense when smoked.<sup>1,9,10</sup> Users sharing tales of their “trips” on the forums also remark that the synthetic versions bring less euphoria, and for some, frightening experiences, such as the fear of having a “heart attack” and feeling as if the heart was “bouncing around in [the] chest”.<sup>10,11</sup>

The unpleasant side effects described, along with hallucinations, seizures, and dependency, have gained media attention in light of the DEA’s decision to ban synthetic marijuana.<sup>8</sup> A case report describes the dependence syndrome and withdrawal phenomena of a 20-year-old male patient who initially smoked 1g (increased to 3g after decreasing effects) of “Spice Gold” for 8 months.<sup>11-13</sup> He continued to use Spice despite negative cognitive effects and potential loss of employment.<sup>13</sup> Due to experience with previous unpleasant withdrawal symptoms, the patient requested voluntary hospital admission and medical assistance to help him in drug withdrawal. On admission, he appeared anxious and insecure, and on day two he complained about increasing internal unrest and trouble sleeping.<sup>12,13</sup> By day four he had developed a strong craving for Spice, profuse sweating, nightmares, nausea, tremor, and headaches.<sup>13</sup> He also experienced a heart rate of 125 beats/min and a blood pressure of 180/90 mmHg that remained elevated for two days.<sup>12,13</sup> The patient was eventually released and returned to the hospital four months later with a good report. It should be noted that the phenomena reported are confounded by the patient’s underlying diagnosis of ADHD and longstanding “inner unrest” for which he self-medicated with Spice and cannabis.<sup>13</sup> Although dependence is rare among cannabis users, it may be more common among users of synthetics.<sup>5</sup>

There is sizeable disparity in the amount of cannabinoid found among different synthetic products. Lindigkeit et al<sup>9</sup> demonstrated that CP 47,497 concentrations varied between 3.0-11.0 mg/g, JWH content could be as little as 2.3 mg/g, and JWH-073 content could be as much as 22.9 mg/g in various products.<sup>9</sup> As with other products that are not FDA regulated, the amount of cannabinoid is inconsistent among products and even within one brand, which significantly endangers patient safety. Since JWH-018 has a fourfold greater affinity for CB1 than THC, consumers may be using much more than they had originally intended.

Although the DEA’s ban may effectively remove five synthetic cannabinoids from the market, it is unlikely that the “legal high” trend will disappear in the near future. Makers of the incense blends have anticipated DEA legislation and are prepared to market other synthetic analogs to anxious customers.<sup>12</sup> As pharmacists, we must be prepared to counsel patients on the potential dangers associated with using synthetic cannabinoids and recognize the symptoms of synthetic marijuana intoxication in spite of a negative drug screen.

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