Straight Tox

Herbal Incensed

Synthetic Cannabinoids Detected in Herbal Incense and Smoking Blends

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I am a skeptic by nature. I am particularly circumspect about believing anecdotal accounts of just about anything. I've become even more jaded in light of the number of urban legends that otherwise intelligent people send to my inbox each week. Thus is my reason for waiting this long to cover the Spice/K2 issue. It was my contention that I should wait and see what happens. I figured that if one is willing to smoke some mix of herbs that one doesn't even know the identity of, a person is likely to get sick and have some bad experiences, as well as some real, or perhaps imagined, good experiences, i.e. placebo effect. However, there now appears to be reliable scientific evidence that at least some of these products contain potent cannabinoid-like compounds.

What are "K2" and "Spice"?

K2 and Spice are trade names for two different products, but what they have in common is that they are sold as "herbal incense" or "herbal smoking blends". These products have become very popular with teenagers across the nation who are using them in place of marijuana, fueled by their ease of purchase (internet and "head shops") and their legal status in most areas. The users of these and similar products are beginning to show up in emergency rooms with hallucinations, nausea, vomiting, hypersomnolence, agitation, and other adverse reactions.

The origins of Spice and K2 appear to be primarily in Europe, China and Korea, with many competing products, or "knock-offs", appearing for sale on the internet daily. A check of one website offered various K2 products: K2 Summit, K2 Blue, K2 Pink, K2 Mango, K2 Citron, and K2 Bubblegum, for sale at prices ranging from about $10 to $15 per gram. The

ingredient list on the package claims that it contains a number of herbal products. However, there is growing evidence that herbs are not the only active ingredients.

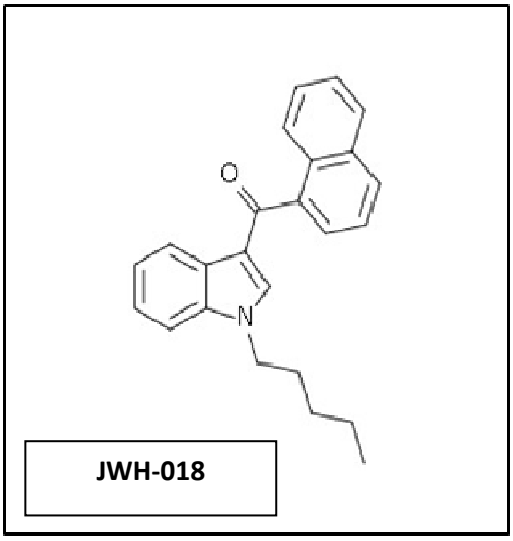
- On December 15, 2008 the German pharmaceutical company, THCPharm, announced that it had found the synthetic cannabinoid, JWH-018, in at least three versions of Spice.
- On January 19, 2009 the University of Freiburg in Germany announced that another synthetic cannabinoid known as CP 47,497 had been detected in Spice.
- In March 2009 the Drug Enforcement Administration reported in the *Microgram Bulletin* that Customs and Border Protection – Chicago Laboratory, had recently found the synthetic cannabinoid, HU-210, in "small but verifiable amounts" in "incense" labeled as "Spice Gold", "Spice Silver", "Spice Diamond", "Genie", and "Yucatan Fire".
- Not to be outdone, in October 2009 the Johnson County Criminalistics Laboratory in Mission, Kansas reported that it detected the presence of two synthetic cannabinoids, JWH-018 and JWH-073, in a K2 product submitted to the laboratory.

Synthetic Cannabinoids, a Primer:

This subject is too vast to cover in depth in an article such as this, so I will provide an overview of the various synthetic cannabinoids that have been implicated in these "herbal blends":

JWH-018

All of the "JWH" designated cannabinoids take their prefix initials from Clemson University organic chemist, John W. Huffman. Dr. Huffman's research interests include the synthesis of analogues and metabolites of THC, with the goal of developing new pharmaceutical products and elucidating the geometry of the CB_1 and CB_2 receptor.



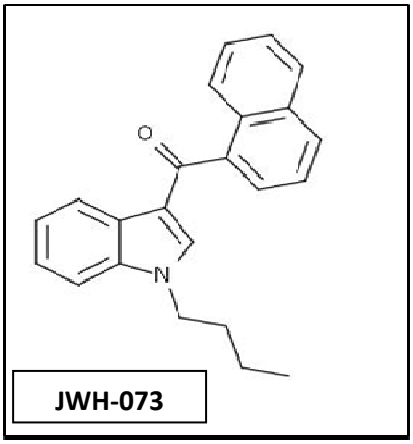
JWH-018

Dr. Huffman first synthesized JWH-018 in the mid-1990's, but notes that JWH-018 was being sold as a plant growth stimulant in China and Korea even before he published a book chapter of the synthetic scheme for this and other cannabinoid agonists.

JWH-018 has a molecular mass of 341.45 and bears the IUPAC name, Naphthalen-1-yl-(1-pentylindol-3-yl)methanone. JWH-018 acts as an agonist at both the CB_1 and CB_2 receptors with some selectivity for the CB_2, and produces marijuana-like effects of somewhat longer duration. JWH-018 is not currently scheduled in the United States.

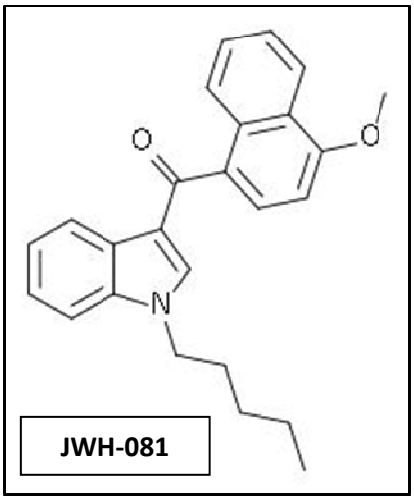
JWH-073

JWH-073 has a molecular mass of 327.42 and bears the IUPAC name, Naphthalen-1-yl-(1-butylindol-3-yl)methanone, differing by only by a methylene group in the alkyl chain on the indole portion of the molecule from JWH-018. JWH-073 is a CB_1 and CB_2 receptor agonist with approximately 5 times the affinity for the CB_2 compared to the CB_1 receptor. JWH-073 is not currently scheduled in the United States.



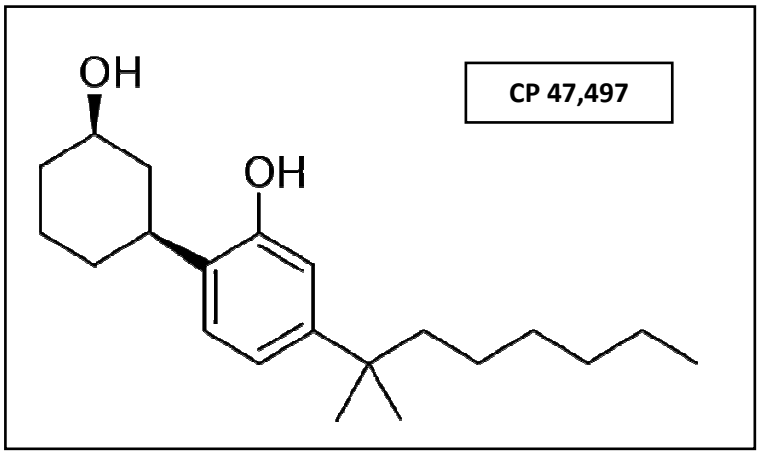
JWH-081

JWH-081 has a molecular mass of 371.47 and bears the IUPAC name, 4-methoxynaphthalen-1-yl-(1-pentylindol-3-yl)methanone, differing from JWH-018 by a methoxy group in the 4 position of the naphthalene portion of the molecule. JWH-081 is a CB_1 and CB_2 receptor agonist with selectivity for the CB_1 receptor approximately 10 times that of the CB_2 receptor. There is speculation that JWH-081 is replacing JWH-018 in herbal blends that are being marketed in states where the latter is being banned. JWH-081 is not currently scheduled in the United States.



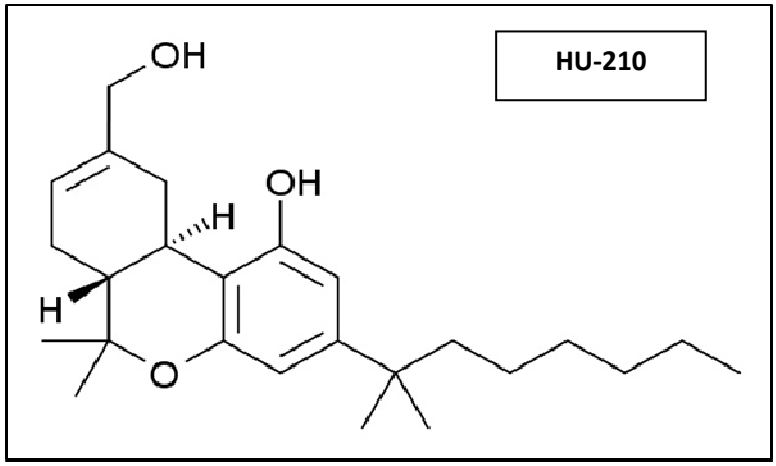
CP 47,497

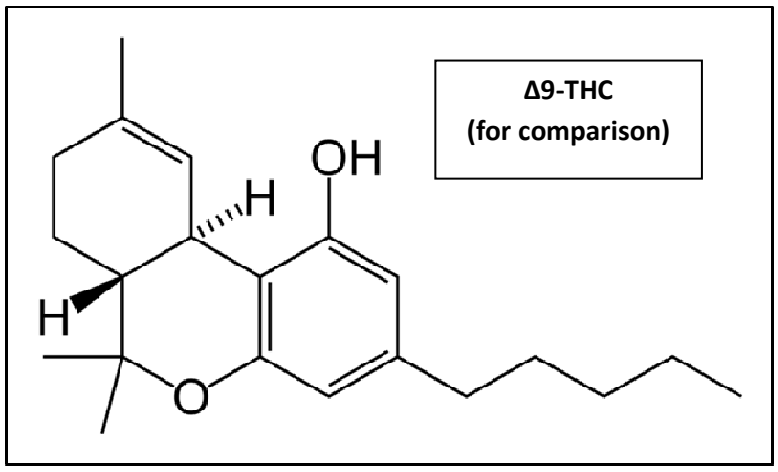
CP 47,497 has a molecular mass of 318.49 and bears the IUPAC name, 2-[(1R,3S)-3-hydroxycyclohexyl]- 5-(2-methyloctan-2-yl)phenol. CP 47,497 was developed by Pfizer in the 1980's and is reported to be a potent CB_1 agonist. CP 47,497 is not currently scheduled in the United States.



HU-210

HU-210 has a molecular mass of 386.57 and bears the IUPAC name, (6a*R*,10a*R*)- 9-(Hydroxymethyl)- 6,6-dimethyl- 3-(2-methyloctan-2-yl)- 6a,7,10,10a-tetrahydrobenzo [c]chromen-1-ol. Noteworthy is the extreme similarity to Δ9-THC, differing only in the alkyl group, an additional hydroxyl group, and the position of the double bond, which is analogous to Δ8-THC. HU-210 was first synthesized by a group at Hebrew University (thus the "HU" designation) led by Professor Raphael Mechoulam. In mice HU-210 decreased overall activity, produced analgesia, decreased body temperature, and produced catalepsy. In in-vitro studies, HU-210 bound both the CB_1 and CB_2 receptors. HU-210 is reported to be 100 – 800 times more potent than THC with an extended duration of action. HU-210 is a schedule I controlled substance in the United States.





Legality

For the most part, K2, Spice and related products are not illegal in the United States based on their stated ingredients. Their continued legal status will depend, in part, on whether they are found to universally contain synthetic cannabinoids, whether those substances are controlled, as is HU-210, and whether any of the other included cannabinoids will be deemed to fall under the Federal Analog Act, which is a rather confusing document in its own right.

Summary

The use of clandestine synthetic cannabinoids in the guise of herbal preparations appears to be an increasing problem, especially among teens. Only time will tell if the trend continues. If it does, laboratories will need to gain access to standards for these compounds and to develop assays to detect these substances, which in some incidences are many times more potent than Δ9-THC.

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