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Fact Sheet

SPICE, K2 AND THE PROBLEM OF SYNTHETIC CANNABINOIDS

By Paul Cary

Many drug courts are experiencing a significant and disturbing surge in client's use of synthetic cannabinoids. In many areas of the country "herbal incense" can be legally purchased and smoked with impunity as specific drug detection methods slowly become available. Products such as Spice and K2 have been widely reported as producing many of the same physiological effects as marijuana. Without laws to control its distribution, courts face a significant challenge in addressing the problem of synthetic cannabinoids.

What Are Synthetic Cannabinoids?

Synthetic cannabinoids represent the most recent advent of "designer drugs." Designer drugs are pharmaceuticals, created or reformulated (if the drug already exists) to avoid current laws (such as the Control Substance Act) by modifying the molecular structures of drugs to varying degrees. The clandestine manufacturers' ability to successfully modify a drug chemically (so as to retain its pharmacological activity while changing the structure enough to skirt existing legal controls) drives the designer drug market. The goal is to satisfy users' demands for popular drugs that can be obtained without prescriptions or other legal constraints.

The developmental history of designer drugs includes alternative esters of opium in the 1920's, synthetic hallucinogens (modifications of LSD and PCP) in the 1960's, MDMA (ecstasy) and methcathinone in the 1980's and the derivatives of anabolic steroids used in major league baseball in the last decade. Synthetic cannabinoids are but the latest example of "look-a-like" drugs created to indulge users attempting to evade established restrictions.

Synthetic cannabinoids are marketed under dozens of product names including Zombie World, Bad to the Bone, Black Mamba, Blaze, Fire and Ice, Dark Night, Earthquake, Berry Blend, The Moon and G-Force. Dispensed in small packets (1-5 grams each), nearly all contain the moniker "herbal incense," along with the disclaimer "not for human consumption." Synthetic cannabinoids are retailed widely on the internet,

through "head" shops, alternative medicine stores, and can even be purchased on eBay. While the content of each product is unique, all of these products contain differing varieties of herbs and other botanicals. The list below is typical:

- **Canavalia rosea:** *commonly known as beach bean or bay bean – vine found in tropical and subtropical beach dunes*
- **Nymphaea caerulea:** *also known as Blue Egyptian water lily*
- **Scutellaria nana:** *perennial herb also known as Dwarf skullcap*
- **Pedicularis densiflora:** *known commonly as Indian warrior – a perennial herb*
- **Leonotis leonurus:** *also known as Lion's Tail and Wild Dagga – a perennial shrub native to southern Africa*
- **Zornia latifolia:** *a perennial herb*
- **Nelumbo nucifera:** *known by a number of names including Indian Lotus, or simply Lotus – aquatic perennial commonly found in China*
- **Leonurus sibiricus:** *commonly called Honeyweed or Siberian motherwort, herbaceous plant native to Asia*

While some of these plant species can produce mild psychoactive or hallucinating effects if consumed, the significant marijuana-like effects are not associated with the plant materials themselves. The dried/crushed/chopped botanicals are sprayed with a liquid form of synthetic cannabinoids, thus greatly enhancing their potency and creating the classic marijuana "high" when the herbal incense is smoked.

These synthetic cannabinoids go by such innocuous identifiers as:

- *HU-210*
- *HU-211*
- *CP 47,497*
- *JWH-018*
- *JWH-073*

This is but a partial listing. The origins of these compounds are actually quite legitimate. HU-210 and HU-211 were synthesized in 1988 at Hebrew University in Israel. HU-210 has anti-inflammatory properties and HU-211 is an anesthetic agent. CP 47,497 was developed by the pharmaceutical manufacturer Pfizer in 1980, and is also an analgesic drug. JWH-018 and JWH-073 were developed by a researcher at Clemson University in 1995 for use in THC receptor research. The researcher was John W. Huffman, hence the prefix JWH. Synthetic cannabinoids are particularly useful in experiments designed to determine the precise relationship between the structure of drugs, like delta 9-THC, and brain receptor activity. By making incremental modifications to the cannabinoid molecule, researchers are able to identify THC's active sites, which promote our understanding of how marijuana effects the human body.

Growing Popularity

The first appearance of synthetic cannabinoids sold as herbal incense occurred on the Internet in 2004. While Europe was the first target market and misuse of herbal incense was widespread there by 2008, its manifestation in this country did not lag far behind. Reports of synthetic cannabinoids use in the US began in earnest in 2008 and by 2009 products like Spice and K2 were nearly epidemic in parts of the country. In late 2008, the first article appeared in the scientific literature (University Hospital in Freiburg, Germany) describing the chemical analyses linking the incense to synthetic cannabinoids. The Drug Enforcement Administration's Office of Diversion Control published a one-page update on Spice in its Year 2008 Annual Report.

Effects On Synthetic Cannabinoids Users

The reported pharmacological effects of smoked synthetic cannabinoids are very similar to that of marijuana. This comes as no surprise given that Spice and K2 are THC agonists – meaning they chemically bind to the same brain receptor (CB1) and trigger many of the same responses as marijuana. The physiological effects of synthetic cannabinoids include:

- *Increase heart rate & blood pressure*
- *Altered state of consciousness*
- *Mild euphoria and relaxation*
- *Perceptual alterations (time distortion)*

- *Intensification of sensory experiences*
- *Pronounced cognitive effects*
- *Impaired short-term memory*
- *Increase in reaction times*

Some reports indicate that JWH-018 binds to the CB1 receptor with even greater affinity than marijuana. Researchers in Japan have surveyed over 40 herbal preparations on the market and determined that the concentration of synthetic cannabinoids varied by a factor of fifteen, which likely explains the variability of the intensity of effects reported by users. Prolonged use of the synthetic cannabinoids has also led to publications indicating that, like marijuana, Spice and K2 can produce withdrawal symptoms and dependency syndromes similar to those identified in chronic marijuana smokers. Recently, the American Association of Poison Control Centers reported 567 cases in 41 states in which people had suffered adverse reactions to Spice during the first half of 2010. As opposed to only 13 cases reported in all of 2009. The long-term health ramifications of smoking synthetic cannabinoids remain unstudied.

Laws Regarding Synthetic Cannabinoids

At the present time, there is no federal ban on most of the synthetic cannabinoids. As a result, the current legal status of synthetic cannabinoids is an evolving patchwork of local and state laws. Products such as Spice and K2 have been banned in approximately a dozen states and in some local jurisdictions. More such prohibitions are making their way through many state legislatures.

As is often the case with designer drugs, the ability to detect these compounds through drug testing lags behind the popularity of their emergence. At the writing of this article, there are no screening tests capable of detecting synthetic cannabinoids in urine. Due to the fact that pure synthetic cannabinoids and their metabolites are difficult to obtain and combined with the reluctance of manufacturers/laboratories to invest significant resources in what may be a transient abuse trend, the prospects for either on-site, rapid tests or laboratory-based screening appears unlikely. However, there are several national laboratories that have begun to offer urine synthetic cannabinoid testing commercially, utilizing sophisticated LC/MS/MS technology. While these tests afford drug courts with some detection options, many questions remain unresolved: Which of the many synthetic cannabinoids/metabolites will be detected by these tests (likely to vary between laboratories)? What are the appropriate detection cutoff levels? What is the detection window for synthetic cannabinoids? To what extent will LC/MS/MS testing be useful without a preliminary screening test? Will the costs associated with testing for synthetic cannabinoids influence the court's ability to provide effective abstinence monitoring?

As an alternative to or as an addition to testing, courts are urged to use existing community supervision personnel to extend the court's surveillance reach. Increased search and seizure practices employing probation, law enforcement and court marshals can be effective in monitoring client behaviors in situations where drug testing approaches are insufficient. For clients suspected of synthetic cannabinoids abuse, searches should be frequent, random, unannounced and occur during non-governmental hours. An intrusive inspection of a client's home, car, school, work, "hangouts" and other restricted areas provides a visible message to all participants as to the court's monitoring vigilance. Some courts have established sanctions of greater severity if evidence of synthetic cannabinoids is identified – believing that the use of these drugs by clients is a purposeful attempt to perpetrate a fraud on the court (since current testing for synthetic cannabinoids is limited).

It is unclear as to whether the phenomenon of synthetic cannabinoids is a passing fancy or a substance abuse trend that will remain taxing to client monitoring efforts. With an uncertain legal future and limited drug detection strategies, in the short term, evaluating synthetic cannabinoids usage will continue to be a challenging endeavor for drug court programs.

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References

Due to the nature of this subject matter and the limited amount of scientific information on synthetic cannabinoids, much of the source material used in this publication was obtained from news organizations, relevant web sites and personal communications with government officials, researchers, laboratory directors and actual synthetic cannabinoids users. Other source materials included the following:

1. *Analytical Profile of Two Synthetic Cannabinoids – JWH-018 ND JWH-073,* Malinda Combs and Jeremiah A. Morris, in Journal Clandestine Laboratory Investigating Chemists Association, Volume 20, Number 2, April 2010.
2. *The Synthetic Cannabinoid HU210 Induces Spatial Memory Deficits and Suppresses Hippocampal Firing Rate in Rats,* RG Pertwee, RE Hampson, G Riedel in British Journal Pharmacology, Volume 151(5): 688–700, July 2009.
3. *Spice* – Request for Information, DEA – Office of Diversion Control, National Forensic Laboratory Information System, Year 2008 Annual Report.
4. DEA, Drugs and Chemicals of Concern, July 2009.
5. *Spice Drugs as a New Trend: Mode of Action, Identification and Legislation, I.* Vardakou, C. Pistos, and Ch. Spiliopoulou, in Toxicology Letter, in Press.
6. *Understanding the Spice Phenomenon,* A Wohlfarth, W Weinmann in Bioanalysis, May 2010, Vol. 2, No. 5, Pages 965-979.
7. *Withdrawal Phenomena and Dependence Syndrome After the Consumption of "Spice Gold",* Ulrich S. Zimmermann, Patricia R. Winkelmann, Max Pilhatsch, Josef A Nees, Rainer Spanagel, Katja Schulz in Deutsches Ärzteblatt International Dtsch Arztebl Int 2009; 106(27):464–67.
8. *Identification of a Cannabinoid Analog as a New Type of Designer Drug in a Herbal Product,* Nahoko Uchiyama, Ruri Kikura-Hanajiri, Nobuo Kawahara, Yuji Haishima and Yukihiro Goda in Chemical & Pharmaceutical Bulletin Vol. 57 (2009), No. 4 p. 439.
9. *Spice and Other Herbal Blends: Harmless Incense or Cannabinoid Designer Drugs?,* Auwärter, V., Dresen, S., Weinmann, W., Muller, M., Putz, M., Ferreiros, N., in Journal of Mass Spectrometry, Volume 44, 832–837, 2009.
10. *Design, Synthesis, and Pharmacology of Cannabimimetic Indoles,* Huffman, J.W., Dai, D., Martin, B.R., Compton, D.R., in Biomedical Chemistry, Volume 4, 563–566, 1994.
11. *Consideration of the Major Cannabinoid Agonists.* in Advisory Council on the Misuse of Drugs (ACMD), July 2009.
12. *The Growing Buzz on 'Spice' -- the Marijuana Alternative,* by Michael W. Savage, Washington Post Staff Writer, Saturday, July 10, 2010.
13. *Spice: A Never Ending Story?,* Rainer Lindigkeit, Anja Boehme, Ina Eiserloh, Maike Luebbecke, Marion Wiggermann, Ludger Ernst, Till Beuerle, in Forensic Science International Volume 191, (2009) 58–63.
14. *Fact Sheet – A Selection of Internet-Based Information* – JWH-018, Nathalie Deprez and Marc Roelands, Scientific Institute of Public Health, Brussels, November 2008.

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