

## SPICE

### OVERVIEW:

There are numerous smokable herbal mixtures which have been marketed under the brand name of Spice since 2004 including Spice Gold, Spice Diamond, Spice Silver, Spice Artic Energy, Black Mamba, etc. These products and many other herbal preparations have been sold over the Internet and in specialized shops throughout the world. Although these herbal mixtures have been advertised as incense or bath salts and labeled “not for human consumption”, when smoked Spice products reportedly have similar effects to cannabis. Most of the labels on the Spice packages list a variety of potentially psychoactive plants such as Indian Warrior, Lion’s Tail, White and Blue Water Lily, and Dwarf Skullcap. These plants have traditionally been known as marijuana substitutes; therefore, users could expect similar effects to that of smoked cannabis.

In 2008, forensic investigations were undertaken by the German and Austrian governments to identify the psychoactive ingredients in Spice. It was determined that the psychoactive effects of Spice were due to added synthetic cannabinoids rather than the herbal plants. The investigations identified JWH-018 a synthetic cannabinoid receptor (CB) agonist as the active ingredient in Spice. Although the chemical structure of JWH-018 differs significantly from THC (the psychoactive ingredient in marijuana), it produces similar effects and has been reported to be more potent than THC. Subsequent investigations in 2009, identified another synthetic cannabinoid, CP- 47,497. Later in 2009, the United States Drug Enforcement Administration (DEA) reported that another potent synthetic cannabinoid, HU-210 had been identified.

Since 2008, several other synthetic cannabinoids including JWH-073, JWH-398, and HU-210 have been identified. All of these compounds act as either CB1 or CB2 agonists or partial agonists and produce cannabis like effects. At present, it appears that producers buy Spice like compounds from labs in Asia which offer cheap raw materials, dissolve the compounds in a solvent, spray the solution onto herbal mixtures, and then evaporate the solvent before packaging the products.

### HISTORY:

Cannabis sativa, commonly known as marijuana has been used for centuries as a therapeutic agent and recreational drug. The active components of marijuana are classified as cannabinoids with the main psychoactive ingredient being THC (delta 9 tetrahydrocannabinol). In addition to the psychoactive qualities, THC also demonstrates many therapeutic properties such as anti-emetic, analgesic, anti-nausea related to chemotherapy for cancer, and anti-convulsive effects. Because of these medicinal properties, synthetic cannabinoids have been researched and developed over the past 40 years as potential pharmaceutical agents, intended

primarily for pain management and appetite stimulant. However, some of these synthetics are now being used as THC substitutes for abuse purposes.

There are several categories of synthetic cannabinoids including:

- **Classical cannabinoids** which were developed in the 1960's and include HU-210 (HU stands for Hebrew University), Nabilone, and Dronabinol. HU-210 is reported to have 100 times the potency of THC.
- **Non classical cannabinoids** such as the cyclohexylphenol (CP) series was developed by Pfizer in the 1970's and include CP-47,497, CP-59,540, and other analogues. The CP analogues are reported to have 5-10 times the potency of THC.
- **The aminoalkylindoles** were developed in the 1990's by J.W. Huffman et.al., at Clemson University. These compounds bear the initials of the inventor and include JWH-018, JWH-015, JWH-073, JWH-398, and JWH-250. JWH-018 is reported have five times the potency of THC.
- **Miscellaneous non-synthetic compounds** which possibly include fatty acid amides (oleamide) with cannabinoid like activity. Although this compound has been found in Spice, it appears to have the least efficacy as a cannabinoid receptor agonist.

All of these agents have been identified in Spice and other herbal products. However because these are produced by illegal labs, there is no evidence that they are consistently present in all Spice products, nor is there any quality control to assure purity and safety. Another concern for law enforcement is the rapid development of second and third generation replacement products which seem to appear as soon as the first generation compounds are prohibited. Due to the sheer number of potentially psychoactive agents possible, it may be relatively easy to avoid control measures which target individual chemical components.

### **PHARMACOLOGY:**

Cannabinoids are a structurally diverse family of compounds that can be classified into three groups:

1. ***Phytocannabinoids*** – which are found in the cannabis plant. THC is the most prevalent natural compound to be isolated.
2. ***Endocannabinoids*** -- which are produced within the body and include natural substances such as anandamide.
3. ***Synthetic cannabinoid receptor agonists*** – which are a large family of chemically unrelated structures which act like THC, but are more potent. Although these

compounds were developed as medicinal agents, it has been difficult to separate the desired properties from the undesired psychoactive effects and abuse potential.

All of these compounds act on specific cannabinoid receptors (CB) located in the central nervous system (CNS) and throughout the body.

CB1 is a receptor expressed in the CNS in several areas of the brain including the hippocampus, cortex, and amygdala. The binding of cannabinoids to the CB1 receptor in these and other areas of the brain contributes to its psychoactive effects such as euphoria, drowsiness, memory lapses, lack of concentration and disorientation. CB2 is a family of cannabinoid receptors found in peripheral immune cells and seems to be involved in pain perception, management, and inflammatory responses. As stated earlier, to date it has been difficult to develop a medicinal compound that activates the CB2 agonist, but bypasses the psychoactive actions of CB1.

At present, much more research is needed regarding the metabolism and toxicology of synthetic cannabinoids. Accidental overdosing may be likely with synthetics because the type and amount of cannabinoid may vary considerably from batch to batch. In addition, detection of these synthetics can be difficult (see below).

#### **METHODS OF USE:**

Spice can be smoked alone or in combination with marijuana and other drugs and it can also be consumed orally. Because Spice is an unregulated mixture of dried herbs sprayed with synthetic cannabinoid substances like JWH-018 or Hu-210, it is difficult to determine actual dosage contained within a product. The usual dose for smoking is between 3-20 milligrams. The initial onset of the effects of smoking JWH-018 begins within 10 minutes and peaks by 30 minutes. The onset of effects of smoking CP-47,497 begins within 10 minutes and may last for 5-6 hours. As a general rule, drugs that are smoked act more quickly and have a more profound effect than drugs that are administered orally.

#### **EFFECTS:**

Because different ratios of JWH-018 and CP-47,497, and other analogues are used in the various herbal blends, it is difficult to know exactly what is being consumed and equally difficult to predict the short- and long- term effects. The subjective effects of Spice are reported as being highly variable, ranging from mild to strong with feelings of relaxation and mild euphoria.

Common effects include:

- red eyes,
- impaired reaction time and motor coordination,
- intense anxiety and agitation,
- possible tremors, seizures, or convulsions,
- elevated heart rate and blood pressure,

- vomiting,
- hallucinations,
- breathing problems,
- numbness and tingling in extremities,
- profuse sweating,
- depression,
- headaches

### **LONG TERM EFFECTS:**

To date, there are very limited, animal model data on the pharmacological effects of Spice and other synthetic cannabinoid compounds. A lack of data and controlled testing make it difficult to determine the long-term effects of these compounds. Smoking any kind of herbal product may cause a variety of health related concerns similar to smoking tobacco products. Some users have commented that smoking Spice is very harsh on the throat.

Some clinical reports suggest that chronic Spice users demonstrate signs of addiction syndrome and withdrawal symptoms that closely resemble those seen in cannabis dependence.

### **DETECTION TESTS AND PERIODS:**

Commonly used drug screens typically are not able to detect synthetic cannabinoid compounds. The US military does have drug screening tests which detect these compounds; however, they are expensive and not commonly available. Some very sophisticated research labs also have mass spectrometry techniques that can detect these agents; however, again these are very expensive and not commonly available.

Recently, Redwood Toxicology Laboratories (RTL) in California announced that it has developed a urine test for JWH-018 and JWH-073. The company reports that the testing window is up to 72 hours for both of these compounds. Presumably, if there is the demand, other labs will develop testing technology in the near future.

### **INCIDENCE OF USE:**

Due to its marijuana like effects, Spice and other synthetic cannabinoids appear to be used primarily by teens, young adults, and individuals on probation or parole. At present, there are only anecdotal accounts regarding Spice use rates although based on reports it is likely significant and increasing in areas where these products are still legal. Consumers can easily access these products through the Internet or “headshops”.

**LEGAL STATUS:**

**Currently synthetic cannabinoids are not federally controlled in the United States; however, they are banned in many European countries. In 2009, the DEA labeled it as a “drug of concern”. Due to concern by communities and legislatures, many states have either passed bills or are in the process of passing legislation that controls or prohibits Spice and/or cannabinoid like. The use of Spice and related products is prohibited throughout the U.S. military services.**

## Spice References

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