

New Synthetic Cannabinoids

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There are nearly two dozen new synthetic or semi-synthetic cannabinoids. Some are already available over the counter others are or will soon be available by prescription. Some potent synthetic cannabinoids are currently being sold over the counter in Skate Board shops, Head shops, Adult shops, gas stations and over the internet without a prescription. These super potent synthetic cannabinoids are being sold as an incense labeled “not for human consumption.” Many states are in the process of making these synthetic cannabinoids illegal. Currently, there are no specific laws barring the sale of these synthetics as long as they are sold for non-human consumption. Other synthetic and semi-synthetic cannabinoids are currently being reviewed by the FDA for potential future prescriptive use.



There are Nearly two Dozen new Synthetic and Semi-synthetic Cannabinoids and Compounds

Synthetic Cannabinoids that are currently being sold all over the U.S., over the counter, labeled “not for human consumption.” These synthetic cannabinoids are 5 to 800 times more potent than THC from marijuana:

- JWH-015, JWH-018, JWH-073, JWH-081, JWH-133, JWH-200, JWH-250, HU-210, WIN-55/212-2, CP 47/497-C6, CP-47/497-C7, CP-47/497-C8, CP-47/497-C9

Synthetic cannabinoids that are currently available by prescription or are being researched by the FDA for possible prescriptive use in the future:

- Dronabinol/Marinol®: available in U.S. by prescription, synthetic, used for; nausea, vomiting, cancer, wasting

- Nabilone/Cesamet®: same as above
- Ajulemic acid (AB-III-56, HU-239, IP-751): synthetic being studied in U.S.
- Cannador®: Semi-synth, THC/CBD compound being studied in Europe
- Rimonabant (Acomplia, Zimulti, SR141716): Synthetic antagonist, initially used in 56 countries for weight loss, pulled from the market in numerous countries because of some side-effects, currently being investigated by NIDA as an addiction treatment drug. Rimonabant blocks the effects of intoxicating cannabinoids like THC in marijuana.
- Sativex®: Semi-synth, THC/CBD compound used in Europe and Canada for pain, approved for phase III trials in the U.S.

These synthetic and semi-synthetic drugs aren't "all the same." Some of these drugs get a person high, some don't, and one even blocks the high of marijuana:

Researchers have developed over a dozen cannabinoid drugs. Some are significantly more potent than THC in marijuana. They can get a person so intoxicated that they end up in the emergency room with seizures, acute anxiety, panic, rapid heart rate and rapid respiration. Others, don't really get people very "high" at all, they are being researched for their medicinal value, and one of the synthetic cannabinoids (Rimonabant) can actually block the receptor sites where THC binds and can block the intoxicating effects of marijuana.

As you may have guessed, the synthetic cannabinoids that get people ridiculously high and intoxicated, are the ones currently being sold over the counter, as an "incense" at Skate Board shops, Head shops, Adult shops, gas stations and over the internet. The researchers who developed these chemical formulas never intended unscrupulous manufacturers to market these for human consumption under the guise of being "incense," with the moniker "for non-human-consumption" in the small print. These cannabinoids, primarily, HU-210, JWH-018, CP-47/497 and JWH-200, are being sold under a variety of trade names such as, Spice, K2, and Mojo. Some of these trade names may have tell tale signs of their actual intent. Possibly, the incense K2 is a double entendre, referring to the elevated high one may experience, like being on a mountain, and the dissociation constant (Kd) of approximately 2, that some of these cannabinoids present in neuropharmacologic research. Or in other words, K2 refers to the *super-affinity* the drug has for receptor sites in the human brain. (For example, the Kd of the synthetic cannabinoid CP-47/497 is exactly 2.1 expressed as "Kd 2.1")

Spice is a drug, labeled "incense," that has been sold in headshops in Europe (often referred to as "smartshops" in Europe), Canada and other parts of the world since around 2002. Even though the manufacturer officially warns against human ingestion of Spice, it is usually smoked for its cannabis-like effects which are believed to be caused by a mixture of synthetic cannabinoid drugs. Several different "flavors" of Spice have been marketed which have been shown to contain different proportions of the synthetic cannabinoid active ingredients, and reportedly produce subtly different effects. A large number of competing products made by other manufacturers appeared shortly after the emergence of

Spice. Of these products "Smoke" and "Skunk" were found to contain both JWH-018 and oleamide. Others, like Pandora Potpourri contain only JWH-018.

Bans and Restrictions on these Cannabinoid “Incenses”

Austria, Chile, Germany, Finland, France, Poland, Russia, South Korea, Sweden, and Switzerland have banned these incense-drugs. These synthetic cannabinoids have been classified as B-Class drugs in the U.K. Currently, there are no explicit prohibitions against these synthetic cannabinoids in the United States. Several states have developed legislation to ban these drugs. Additionally, the federal government may quickly be acting on these drugs under the Federal Analogue Act. The Federal Analogue Act was instituted largely due to amphetamine analogues, such as, MDA, MDE, DMA, MDMA, etc. However, the Federal Analogue Act basically states that the government can classify new similar drugs in the same schedule as the drug they mimic, if they are being sold for “human consumption.” In the case of Spice, it is being sold as incense for “non-human-consumption.” Therefore, the government will need to prove that the product is, in fact, actually being sold for human consumption despite the manufacturers’ claims to the contrary. Currently, the FDA’s Criminal Division has raided a few shops around the U.S. as a result of their distribution of Spice. Presumably, this has occurred as a result of reports that shop staff/owners were encouraging clients to “physically consume” the product, which violates FDA rules. HU-210 is already classified as a Schedule I drug in the United States, however many others are not classified and there are no restrictions.

Recipes not intended for “Human Consumption”

Many of these experimental cannabinoids were created by researchers in order to learn more about the endogenous cannabinoid systems within the human nervous system. Many of them were never intended for human consumption, especially those that turned out to be significantly more potent than marijuana. In fact, the cannabinoids that have been of greatest interest to researchers and physicians alike, have been those that show promising medicinal value and have “low intoxication” in clinical trials. Sativex is a compound with low-intoxication that shows great promise in the treatment of chronic pain. Currently, Sativex is in phase III clinical trials in the U.S.

Health Effects of *Super-potent* Synthetic Cannabinoids never intended for Human Consumption

"These products weren't designed for human consumption,"

--Dr. Alvin C. Bronstein, medical director of Rocky Mountain Poison Center and director of surveillance for the American Association of Poison Control Centers.

Little research has occurred on these super potent cannabinoids, such as, HU-210, JWH-018, CP-47/497 and JWH-200. These four super-potent synthetic cannabinoids appear to be the primary culprits sprayed over these so-called herbal incense blends. Since these cannabinoids were never intended for human consumption there has been literally no human research on their health effects. However,

reports are coming in from all over the U.S. regarding emergency room visits related to this incense (Spice, K2, and Mojo). The JWH series of cannabinoids were invented by John W. Huffman (JWH) at Clemson University, HU-210 was created by Raphael Mechoulam at Hebrew University (HU), and CP-47/497 was created by Pfizer in what is known as the cyclohexylphenol (CP) series.

- March 17, 2010, The Daily Record — Three Delaware residents were taken to the hospital over the weekend after smoking an herbal marijuana substitute, prompting police to issue a warning about the relatively new substance that has cropped up in the state.
- March 14, 2010, LOGAN, Utah — Cache County health officials say at least six people have been treated in the emergency room for stomach pain after smoking incense that's being used as a drug.
- February 22, 2010 — Dr. Steven Marcus of the New Jersey Poison Information and Education System issued a Feb. 22 advisory about the marijuana substitute being reported in the Midwest and the influx of teens and young adults showing up in hospital emergency rooms after smoking it. Symptoms improved after 6 to 8 hours and they were discharged.
- 2008, some emergency cases were reported in Germany ('effects on the cardiovascular and nervous system like tachycardia and, in some cases, short-term loss of consciousness'). These had been reported in the mass media and via personal communication (Poison Control Centre, Mainz).
- 2008, Italy reported a single case of a 53-year old woman with diabetes, who smoked 'Spice' and was treated in an emergency room, one hour after consumption. She was in an excited state and in psychomotor agitation that was successfully treated with benzodiazepines. For a few hours, the patient was monitored and no alteration of vital parameters was registered. After 12 hours in an emergency room, the patient was discharged in a stable condition.
- 2008, the Swedish Poison Information Centre had 51 inquiries (45 cases in total) — 40 of these cases originated from the health care system, i.e. physicians treating patients who reported use of 'Spice'.
- 2008, based on a few accounts from counseling centers in Austria, the subjective effects of 'Spice' were reported as highly variable, ranging from mild to strong, and it was reported that they could be similar to cannabis or, alternatively, completely different.
- 2008, similar reports from users in Romania suggested that 'Spice' tasted like herbal cannabis and the effects could be similar or even 'better'.

In the case of JWH-018, it can be speculated that, due to structural features, there may be some carcinogenic potential. Furthermore, accidental overdosing with a risk of severe psychiatric complications may be more likely to occur because the type and amount of cannabinoid may vary considerably from batch to batch even within the same product. In general, there may be a risk of the appearance of a full CB receptor agonist leading to life-threatening conditions if overdosed (unlike THC, which acts only as a partial agonist). HU-210 is known to induce memory deficits, and it is suspected this is likely true of all the super potent cannabinoids. Furthermore, it seems that tolerance to these synthetic cannabinoids may develop fairly fast, and arguably this might be associated with relatively high potential to cause dependence. What is clear is that further studies are needed to assess these risks reliably.

Additionally, Spice contains a variety of "herbs", on which the cannabinoids are sprayed. Little is known regarding the health effects of these plants. Some are believed to be psychoactive in addition to the synthetic cannabinoids.

Herbal components of 'Spice' (a non-exhaustive list)

Common name	Species	Family
Beach bean	<i>Canavalia maritima</i> ; syn. <i>C. rosea</i>	Fabaceae
White and blue water lily	<i>Nymphaea alba</i> and <i>N. caerulea</i>	Nymphaeaceae
Dwarf skullcap	<i>Scutellaria nana</i>	Lamiaceae
Indian warrior	<i>Pedicularis densiflora</i>	Orobanchaceae
Lion's ear/tail, Wild dagga	<i>Leonotis leonuru</i>	Lamiaceae
'Maconha brava'	<i>Zornia latifolia</i> or <i>Z. diphylla</i>	Fabaceae
Blue/Sacred lotus	<i>Nelumbo nucifera</i>	Nelumbonaceae
Honeyweed/Siberian motherwort	<i>Leonurus sibiricus</i>	Lamiaceae
Marshmallow	<i>Althaea officinalis</i>	Malvaceae
Dog rose/Rosehip	<i>Rosa canina</i>	Roseaceae

The Epidemiology of Spice

The extent of Spice consumption in the U.S. is unknown at this time. However, availability is widespread. It appears that Spice or similar herbal drugs sprayed with synthetic cannabinoids are available in most parts of the U.S. Limited emergency room data suggests that Spice is being used by adults and minors. It appears that it is also being used by military personnel. The primary synthetic cannabinoids used in Spice are undetectable on a standard Urine Drug Screen. This fact makes Spice very attractive to those who are subject to urine drug testing such as; criminal offenders, addiction treatment clients, commercial driver licensees, and others with safety sensitive jobs who are routinely subjected to urine drug test.

Resources:

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9. Uppers, Downers and Allarounds, 6th Edition, Inaba and Cohen
10. Wikipedia: JWH-018, HU-210, Spice