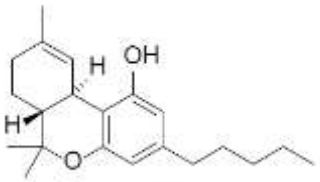
Synthetic cannabinoids

Description

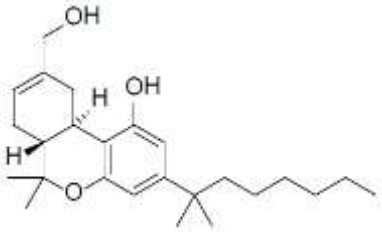
In Europe, synthetic cannabinoids were first identified in 2008 in different vegetable mixtures, called "herbal mixture" or "herbal blend", and sold as incense or air fresheners. There are products called "Spice" and sold as "not for human consumption" but despite what is stated on the labels, these "Spice" products contain synthetic cannabinoids and can produce similar effects in the consumer, when not superior, to those of cannabis. The first synthetic cannabinoids identified in this type of products are JWH-018 and JWH-073. Synthetic cannabinoids were detected in Italy from 2010 (first notification collected by the National Early Warning System).

The analyses of "herbal mixture" products, carried out by several international laboratories, showed the existence of several other synthetic cannabinoids, including, for example, JWH-122, JWH-200, JWH-250, JWH-251, JWH-081, JWH-398, JWH-019, HU-210 and CP-47,497 including its analogues with the alkylic chain C6, C8 and C9. These molecules act on CB1 receptors responsible for the psychoactive effects of cannabis, mimicking the effects.

Chemical structures of the main synthetic cannabibnoids registered by the National Early Warning System.

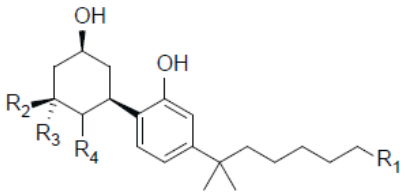


THC



HU-210

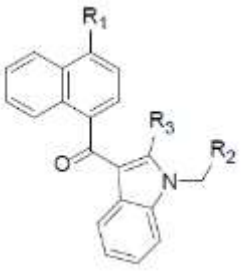
"Classic" cannabinoids



CP-47,497 (R2=R3=R4=H, R1=methyl)
CP-47,497 C6 (R1=R2=R3=R4=H)
CP-47,497 C8 (R2=R3=R4=H, R1=ethyl)
CP-47,497 C9 (R2=R3=R4=H, R1=propyl)

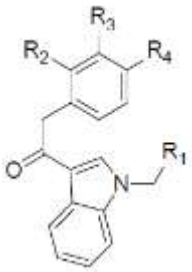
"Non classic" cannabinoids

Aminoalkylindoles:



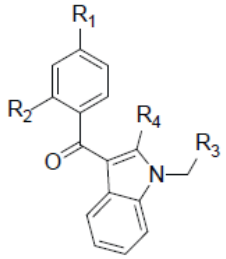
JWH-018 (R1=R3=H, R2=butyl)
JWH-073 (R1=R3=H, R2=propyl)
JWH-122 (R1=methyl, R3=H, R2=butyl)
JWH-081 (R1=OMe, R3=H, R2=butyl)

Naphtoylindoles



Phenylacetylindoles

JWH-250 (R1=butyl, R2=OMe, R3=, R4=H)



Benzoylindoles

AM-694 (R1=R4=H, R2=I, R3=5-fluorobutyl)
RCS-4 (R1=OMe, R2=R4=H, R3=butyl)
WIN 48,098 (R1=OMe, R2=H, R3=4-morpholinmethyl, R4=methyl)

Potency

The *in vitro* activity of JWH-018 and JWH-073 and its analogs JWH-019 is higher than that of Δ9-THC. The CP 47,497 exhibits agonist activity on CB1 receptors from 3 to 28 times higher than that of Δ9-THC. For this reason, consumers often use them considering as a natural alternative to cannabis, but with similar psychotropic activity. Furthermore, because of the ability of the synthetic cannabinoids identified to act as agonists on the CB1 receptors, it is possible to easily develop tolerance to these molecules.

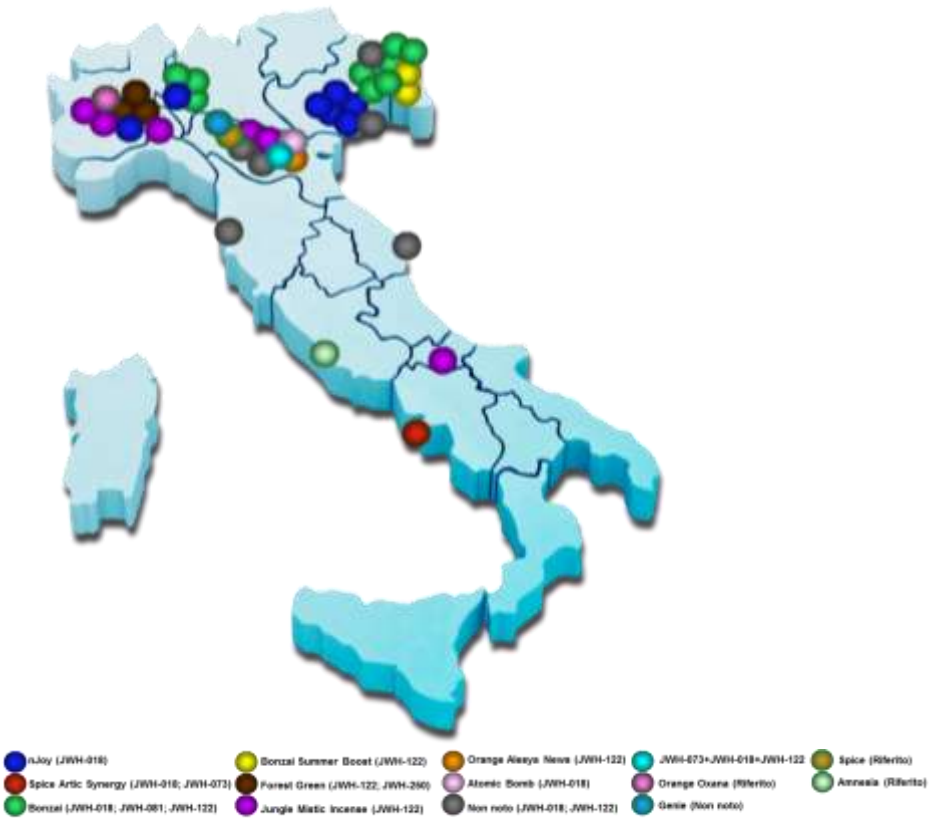
Assumption and effects

Synthetic cannabinoids are usually assumed by smoking through the consumption of cigarettes containing herbal substance containing these synthetic molecules. The effects of synthetic cannabinoids are similar, if not higher than, that caused by the consumption of cannabis. Their assumption, in fact, generates, after ten minutes, conjunctivitis, tachycardia, xerostomia and alteration of perception and mood, with effects that last for about six hours. In Germany, since 2009, there have been cases of people arriving in the emergency room after the consumption of "herbal mixture" with disorders of the cardiovascular system and the nervous system, such as tachycardia and a temporary loss of consciousness. In some cases, effects have been reported such as psychomotor agitation, panic attacks, confusional states, convulsions. Similar cases have been reported in Sweden, Austria, Romania and Italy. Cases of serious cardiovascular effects (eg, acute coronary syndrome, severe and prolonged bradycardia) and neuro-behavioral (eg, acute psychosis) are now already reported in the scientific literature and also found in the Italian series.

Acute intoxications in Italy

Since 2010, in Italy, the National Early Warning System, through notifications of its collaborating centers, has recorded 41 cases of acute intoxications related to the consumption of products found to contain synthetic cannabinoids, for which it was necessary the access to the emergency unit. The majority of cases were recorded in Northern Italy and included patients between 14 and 55 years old.

Intoxication cases by synthetic cannabinoids that needed the access to the emergency unit, registered by the National Early Warning System starting from 2010, name of products consumed by the patients and synthetic cannabinoids identified in samples analyzed.



     	**Photos of some products notified to the National Early Warning System and resulted to contain synthetic cannabinoids**
In Italy, following numerous cases of acute intoxication related to the consumption of herbal mixtures containing synthetic cannabinoids JWH-018 and JWH-073, these two molecules have been placed under regulatory control in June 2010 (Table I of the laws concerning the regulation of narcotics and psychotropic substances, prevention, treatment and rehabilitation of drug addiction of Presidential Decree 309/90 as amended). Subsequently entered into force new decrees that have placed under control other synthetic cannabinoids listed below: JWH-250; JWH-122; AM-694; CP 47,497; CP 47,497 C8 homologue and structure analogues derived from 3-phenylacetylindole; from the 3-(1-naphtoyl)indole and from the 3-benzoylindole. These molecules are not easily detectable to the normal screening tests on urine but are subsequently detected through blood tests and urine tests conducted in specialized laboratories. In case of positivity to synthetic cannabinoids driving a car, motorcycle or scooter, the law enforcement may withdraw the license, impound the vehicle, impose fines, make report to the Prefecture, pick up your passport.	**Legal status**