



Synthetic Cannabinoid Agonist Induced Psychosis: A Case Series

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Abstract

Synthetic cannabinoid receptor agonists, often referred to as 'synthetic cannabinoids', are a large family of chemically unrelated structures functionally similar to Δ 9-tetrahydrocannabinol (THC), the active principle of cannabis. Recreational use of synthetic cannabinoid containing compounds, commonly known as "Spice," "K2," "Blaze," and "Red X Dawn", has become increasingly popular. They are plant material coated with varying combinations of synthetic cannabinoid agonists JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol. Until recently, their sale and consumption was not regulated within the United States. Though use is prohibited in Active Duty US Military personnel, the inability, until recently, to detect use of these substances in urine drug tests has resulted in significant consumption in this population. These compounds have not been approved by the FDA for human consumption and very little is known about their toxicology and safety profile.

Objectives

To our knowledge, only one case has been reported of a psychotic episode after use of a synthetic cannabinoid compound, and this patient had a past history of cannabis induced psychotic episodes. We report a case-series of ten patients with primary psychotic presentations following the use of synthetic cannabinoids.

Methods

A retrospective case review was conducted among patients at Naval Medical Center San Diego who were admitted for "Spice" induced psychosis.

Results

The sample was comprised of 10 otherwise healthy patients admitted to the psychiatry ward at Naval Medical Center San Diego from August to December 2010. Patients ranged in age from 21 to 25 years old. Presenting diagnoses included psychosis not otherwise specified and substance-induced psychotic disorder. Specific symptoms observed included: auditory and visual hallucinations, paranoid delusions, odd/flat affect, thought blocking, disorganized speech, alolia, suicidal ideation, insomnia, psychomotor retardation and agitation, and anxiety. The role of Spice in inducing these symptoms was determined by military command, friend, family member and/or patient report, as well as urine drug test. Average length of stay was 6-10 days with 70% of patients receiving antipsychotic medication. Psychotic symptoms generally resolved between 5 and 8 days after admission. However, a few patients experienced lingering paranoid delusions and dysthymia lasting approximately 3 months at the time of writing.

Conclusions

Recreational use of synthetic cannabinoids appears to be increasing. We present a case-series of 10 otherwise healthy young patients presenting with psychosis shortly following use of these compounds. While pharmacology of many of these compounds remains little known, the protracted course of psychotic symptoms well beyond acute intoxication and sometimes extending into months beyond last consumption is concerning.



Figure 1: Common Synthetic Cannabinoid Blends, Powder form of JWH-018

Introduction

This case series describes patients who experienced prolonged psychotic episodes after smoking products known to contain combinations of synthetic cannabinoid receptor agonists, commonly referred to as synthetic cannabinoid blends or "Spice." The sample is comprised of 10 otherwise healthy patients admitted to the psychiatry ward at Naval Medical Center San Diego, from August to December 2010, for primary psychotic presentations following the use of synthetic cannabinoids and had no prior history of psychosis.

Spice Use and Psychosis

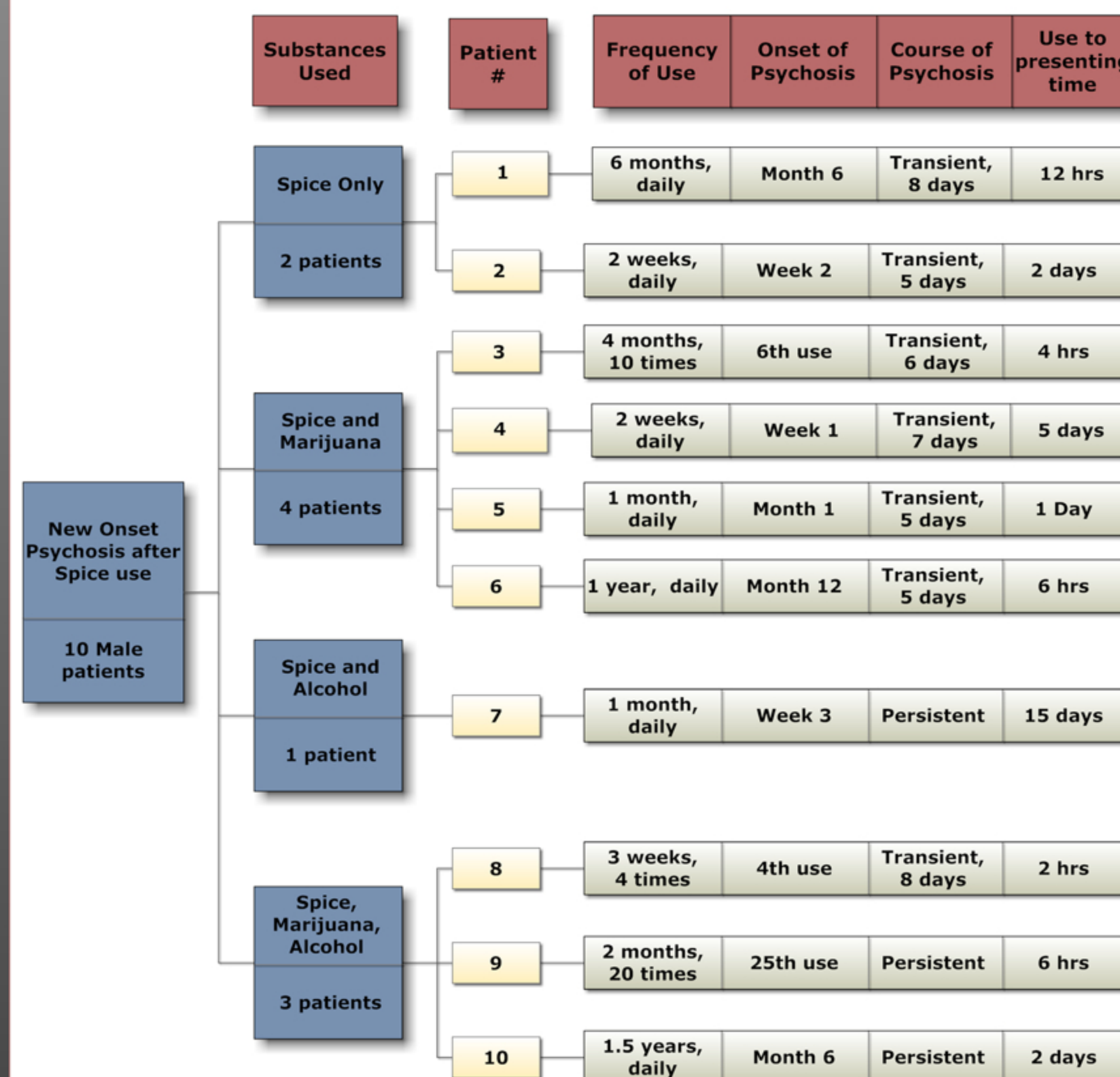


Figure 2: Substances used, duration and frequency of Spice use, onset and course of psychosis

The temporal relationship between synthetic cannabinoid consumption and psychotic symptoms was determined from information provided by friends, family members, military command, and/or patient report.

Although the majority of patients were able to report which brands of synthetic cannabinoid blends they smoked, determining the specific synthetic cannabinoids within these blends would require analyzing samples of the actual batch the patient smoked. The contents of these products are not accurately listed and are constantly changing. As such, the term Spice is used in the above figure to represent synthetic cannabinoid blends.

Patient # (all males)	Age	Psychiatric History	Family Psychiatric History
1	24	None	Father Alcohol Dependence
2	25	None	Grandfather Bipolar DO
3	22	None	None
4	24	None	None
5	22	None	Father Depression
6	25	ADHD (no Rx in 5 yrs)	None
7	22	Depression	Mother Depression, Father Alcohol Dependence
8	21	None	Father Depression
9	23	None	None
10	22	Cannabis and Alcohol Dependence	Aunt Schizophrenia

Table 1: sex, age, personal and family psychiatric history

Signs and Symptoms

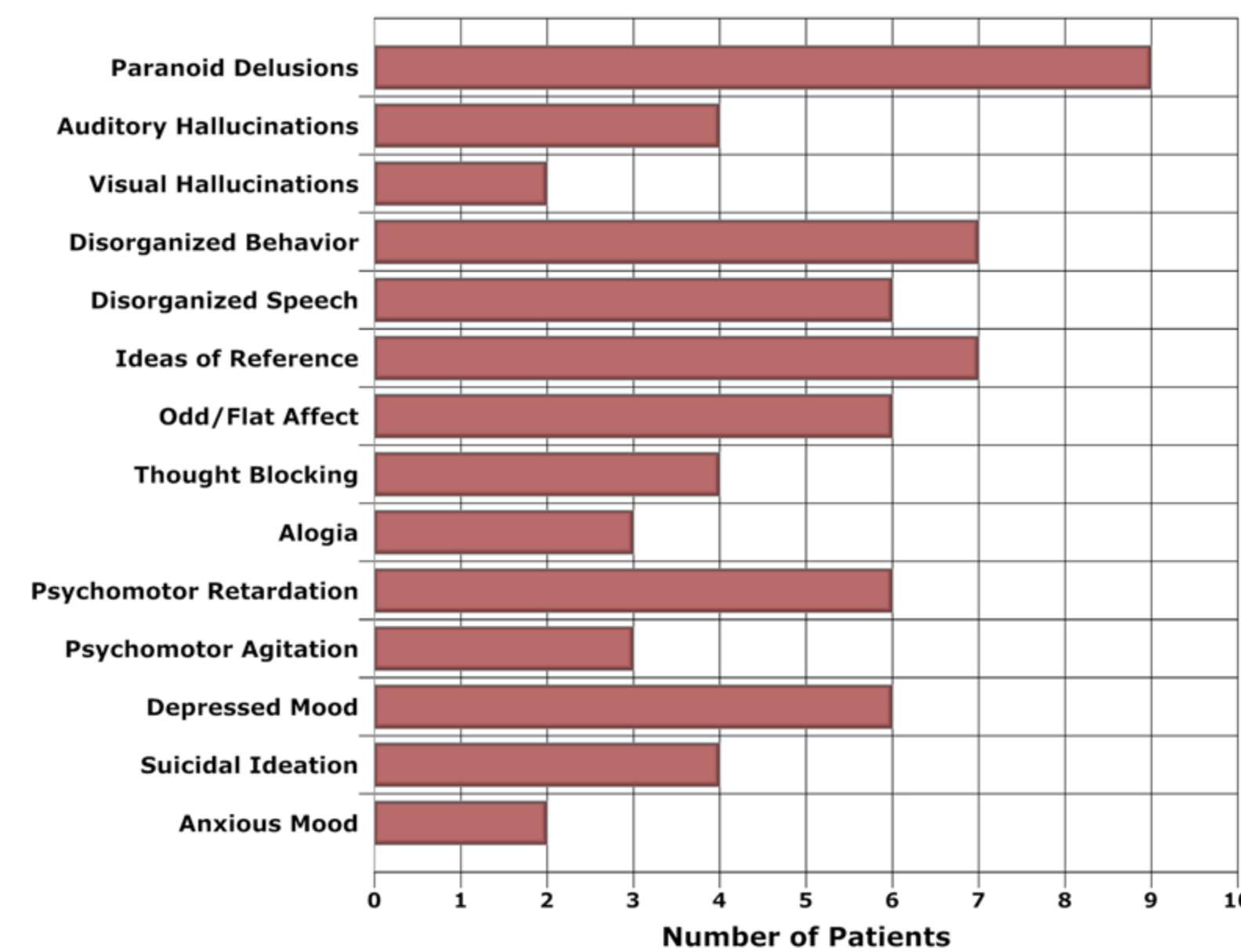


Figure 3: Signs and symptoms displayed by 10 patients hospitalized following synthetic cannabinoid agonist use

Paranoid delusions, ideas of reference, and a disorganized-confused state were the most prevalent symptoms. The paranoid delusions ranged from fixed and complex to shifting and subtle. A distinct waxing and waning stuporous appearance was common amongst these patients, often present for weeks after last use of synthetic cannabinoids. More than half of the patients had significant depressive symptoms including suicidal ideation in four. Affect was generally flat or shifting and incongruent with stated mood. Usual hospitalization was 6-10 days with 70% of patients receiving antipsychotic medication. Psychotic symptoms generally resolved between 5 and 8 days after admission.

Discussion

To our knowledge, no cases of new onset psychosis after the use of synthetic cannabinoids have been reported. Two case reports described the re-emergence of psychosis following the use of synthetic cannabinoid compounds. In one of these cases, the patient had a past history of cannabis induced psychotic episodes. A recent article out of New Zealand reported that synthetic cannabinoid agonists may precipitate psychosis in vulnerable individuals and included patients with known psychotic illness. Our case series includes patients with no known psychotic illness and describes several patients with no known psychotic predispositions who experienced prolonged psychotic episodes after smoking synthetic cannabinoid blends.

As is commonly seen with cannabis induced psychosis the majority of our patients' symptoms wore off quickly and with complete remission. It is not known whether these patients will develop long-term psychotic conditions, as is often seen in patients who have had cannabis induced psychosis. Three of our patients continue to have psychotic symptoms more than five months out from presentation. Whether synthetic cannabinoid use is actually causally linked with developing psychotic illness cannot be conclusively determined as other drug use, hereditary predisposition, and socioeconomic status may hasten the pathogenesis as is seen with cannabis induced psychosis.

The protracted presence of psychotic symptoms well beyond acute intoxication and sometimes lasting months is concerning. As such, physicians should be aware that the use of synthetic cannabinoids can be associated with psychosis and investigate possible use of synthetic cannabinoids in patients with inexplicable psychotic symptoms.

Did synthetic cannabinoid agonists induce psychotic episodes?

- Temporal relationship between use and psychosis
- No past psychotic history
- Nine out of ten of the patients had no family history of psychosis
- Two of the patients used only synthetic cannabinoid blends

Pharmacology

Synthetic cannabinoid receptor agonists are a large family of chemically unrelated structures functionally similar to Δ 9-tetrahydrocannabinol (THC), the principal psychoactive component of cannabis. They bind to the same cannabinoid receptors (CB1/CB2) in the brain as THC—mainly in areas such as the hippocampus, basal ganglia, cortex, amygdala, and cerebellum, areas linked to behaviors seen with cannabis intoxication. They were developed by pharmaceutical and academic laboratories, over the past 40 years, primarily as potential pain relievers, but chemists have not been able to separate the psychoactive effects from the desired effects. There are more than a hundred developed synthetic cannabinoids which fall into one of four structurally different groups. Representatives from all four groups have been found in synthetic cannabinoid blends.

Chemical structures

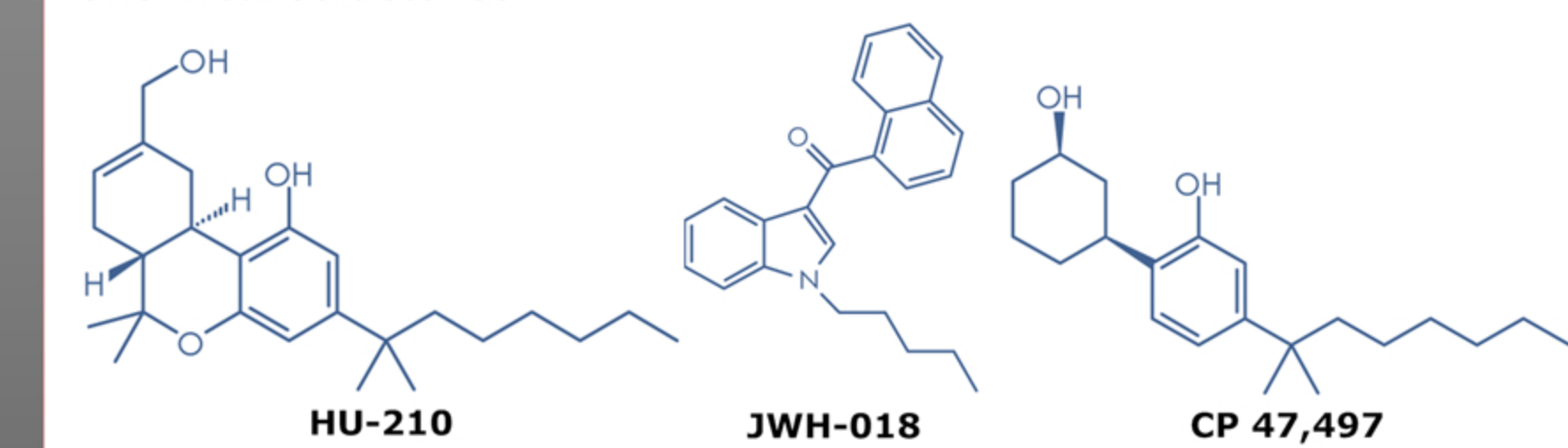


Figure 4: Chemical structures of three popular synthetic cannabinoid receptor agonists

Common components of synthetic cannabinoid blends include HU-210, JWH-018, and CP-47,497 – these structures are shown above. Many of the synthetic cannabinoid receptor agonists in these products are full agonists, as compared to THC which is a partial agonist, and many are much more potent than THC. For example, HU-210 is reported to have 100 times the potency of THC, as measured by Ki.

Potency for inducing psychosis compared to cannabis

- Synthetic cannabis blends lack cannabidiol, which has antipsychotic effects
- Many synthetic cannabinoids are full agonists, as compared to THC which is a partial agonist
- Many synthetic cannabinoids have 100 or more times the potency of THC
- Users overdose often as contents and concentrations are not stable between and within products

Legal Actions

The United States Drug Enforcement Administration (DEA) used its emergency scheduling authority to temporarily ban five synthetic cannabinoids: JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol. This action will make possessing and selling these chemicals or the products that contain them illegal in the U.S. for at least one year while the DEA and the United States Department of Health and Human Services (DHHS) further study whether these chemicals and products should be permanently controlled. Moreover, all five branches of the military prohibit their personnel from possessing or using synthetic cannabinoids associated with products such as Spice and K2.

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*The views of this presentation are those of the individual authors and do not necessarily represent those of the Department of the Navy, Department of Defense, or the U.S. Government.