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BEFORE THE

UNITED STATES SENTENCING COMMISSION

FOR A PUBLIC HEARING ON FENTANYL AND SYNTHETIC CANNABINOIDS

PRESENTED

DECEMBER 5, 2017

Thank you for the opportunity to address the Commission regarding the chemical structure underlying synthetic cannabinoids. One of the most well known cannabinoids, Δ9-tetrahydrocannabinol (THC), is the primary psychoactive constituent of marijuana (Figure 1: The chemical structure of Δ9-tetrahydrocannabinol (THC)Figure 1). As the Commission will hear, it produces psychoactive effects by acting on a specific part of the central nervous system known as the cannabinoid receptors. Other substances that act on these cannabinoid receptors are, like THC, also known as cannabinoids. Synthetic cannabinoids are a large family of synthetic (manmade) substances, irrespective of their chemical structure, that act on these same receptors.

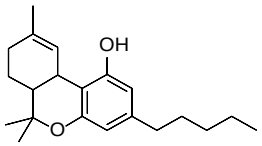


Figure 1: The chemical structure of Δ9-tetrahydrocannabinol (THC)

Beginning in 2010, the Drug Enforcement Administration (DEA) witnessed a rapid proliferation of synthetic cannabinoids introduced in the illicit drug market. Before their emergence on the illicit market, these substances were synthesized and used as research tools to investigate biological systems in legitimate scientific laboratories. The researchers published the chemical structures they invented and the pharmacological results in patents and peer reviewed papers. By doing so, they inadvertently provided a roadmap for illicit manufactures years later.

As a result of the widespread abuse of these synthetic cannabinoids, and increasing reports of adverse health effects, in March of 2011 DEA utilized its emergency authority to temporarily control five of these synthetic cannabinoids. The chemical structures of the five synthetic cannabinoids can be seen below in Figure 2. Prior to their introduction on the illicit market, all five of these substances were initially synthesized for legitimate research purposes.

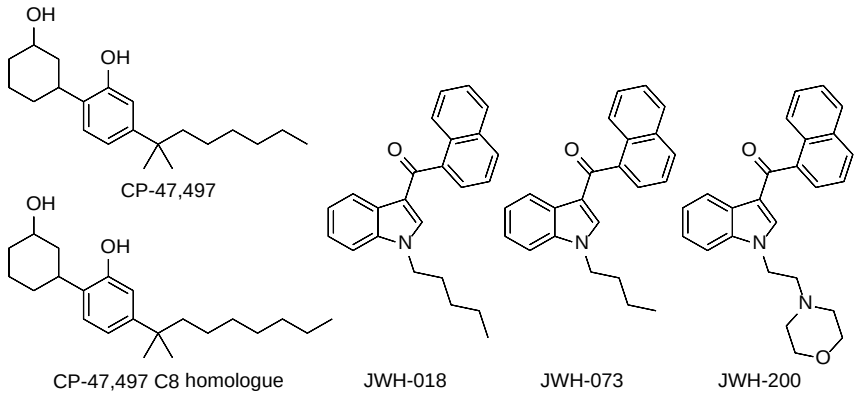
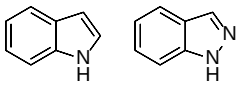


Figure 2: The chemical structures of five synthetic cannabinoids emergency controlled on March 1, 2011

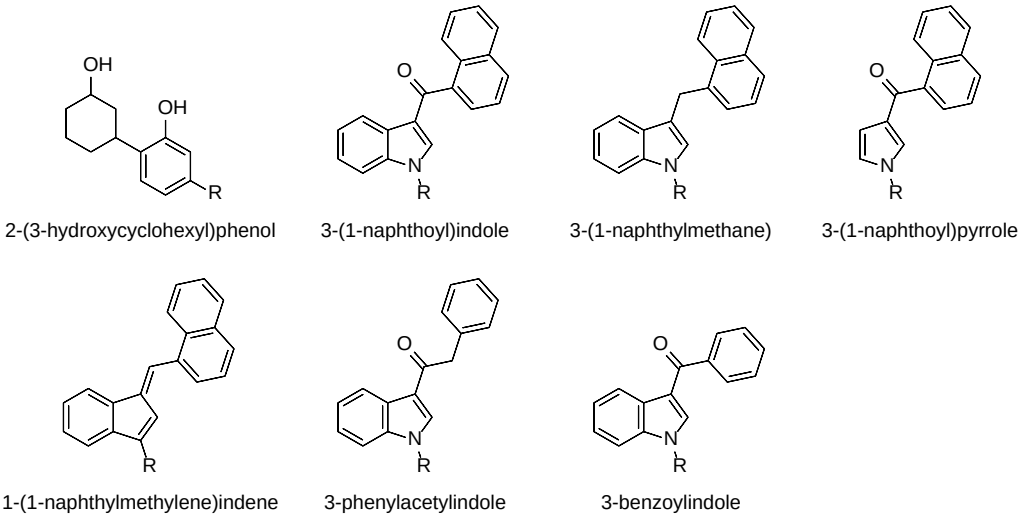
Two of these substances, CP-47,497 and CP-47,497 C8 homologue, have some structural features in common with THC, whereas the remaining three, JWH-018, JWH-073, and JWH-200, are not structurally similar to THC. These three substances represent a subset of synthetic cannabinoids that are derived from indole. To date, there are 31 synthetic cannabinoids listed in Schedule I that are derived from indole or indazole (Figure 3).



indole indazole

Figure 3: The chemical structures of indole and indazole

In an attempt to combat this rapid proliferation of new synthetic cannabinoids, Congress provided a new mechanism to control these dangerous drugs based on a two-part test defining "cannabimimetic agents" that includes chemical structure (Figure 4), and pharmacological tests to evaluate the effect on a specific cannabinoid receptor. This legislation, known as the Synthetic Drug Abuse Prevention Act (SDAPA), was signed into law on July 9, 2012.



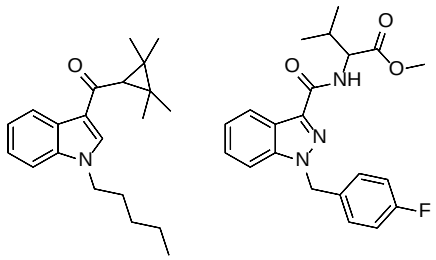
2-(3-hydroxycyclohexyl)phenol 3-(1-naphthoyl)indole 3-(1-naphthylmethane) 3-(1-naphthoyl)pyrrole

1-(1-naphthylmethylene)indene 3-phenylacetylindole 3-benzoylindole

Figure 4: Structural groups included in the Synthetic Drug Abuse Prevention Act

After the proposed legislation was made public, but before it became law, drug traffickers started adapting to the proposed controls. DEA witnessed a decrease in synthetic cannabinoids that fit the SDAPA structural definitions, whether or not they were specifically listed, and an emergence of other synthetic cannabinoids, such as UR-144. These replacement synthetic cannabinoids, still derived from indole or indazole, were similar in chemical structure to JWH-018 and others, but chemically modified in such a way that they did not meet the structural definition of a "cannabimimetic agent" under SDAPA.

Many of the new synthetic cannabinoids on the illicit market, like UR-144 or FUB-AMB (Figure 5), were first reported in legitimate scientific and patent literature. Other substances had not been reported prior to their introduction on the illicit market. These novel substances have included additional modifications to, or are hybrids of previously encountered synthetic cannabinoids.



UR-144

Emergency Controlled
May 16, 2013

FUB-AMB

Emergency Controlled
November 3, 2017

Figure 5: Examples of synthetic cannabinoids derived from indole (left) and indazole (right)

With the endless pool of synthetic cannabinoids published in legitimate scientific studies, and the propensity for illicit manufacturers to mix and match substitutions from this vast pool, there are thousands of possible synthetic cannabinoids to be derived from indole or indazole. Moving beyond this subset of synthetic cannabinoids, there are even more substances in the scientific literature that are not derived from indole or indazole that could produce the same THC-like psychoactive effects. Thus, unlike synthetic cathinones, synthetic cannabinoids cannot be defined as a single class based on chemical structure. As others will explain, however, synthetic cannabinoids do share similar pharmacological effects.

Thank you for the opportunity to discuss the chemical structure of synthetic cannabinoids. I welcome the chance to answer any questions the Commission may have during the upcoming hearing.