Approved: 02/01/10

Date

MINUTES OF THE SENATE PUBLIC HEALTH AND WELFARE COMMITTEE

The meeting was called to order by Chairman Jim Barnett at 1:30 p.m. on January 13, 2010, in Room 546-S of the Capitol.

All members were present.

Committee staff present:

Nobuko Folmsbee, Office of the Revisor of Statutes Renae Jefferies, Office of the Revisor of Statutes Terri Weber, Kansas Legislative Research Department Jan Lunn, Committee Assistant

Conferees appearing before the Committee:

Senator Vicki Schmidt

Kyle Smith, Topeka Police Department, Kansas Peace Officers' Association Master Deputy Chris Farkes, Johnson County Sheriff's Department

- Senior Forensic Scientist Jeremy Morris, Johnson County Sheriff Department
- Ed Klumpp, Kansas Association of Chiefs of Police

Richard Samaniego (speaking on behalf of Thomas R. Stanton), Kansas County and District Attorneys

Sheriff Kenneth McGovern, Douglas County Sheriff Department

Others attending:

See attached list.

Senator Barnett welcomed all committee members, introduced the staff, and introduced new member, Senator Terrie Huntington, who has replaced Senator Wysong. Senator Barnett introduced Brian Hagen, Rose Hill High School; Nicholas Ediger and Aaron Slater, Hillsboro High School; Dan Rahe, Emporia High School; Mark McCoy; Chelsea Turkin, Lyndon High School; and Carolyn Cole, State Advisor, all representing the Technology Student Association.

Chairman Barnett opened the hearing on <u>SB 348 - Criminalizing certain synthetic cannabinoids</u>, adding to schedule I controlled substances list.

Nobuko Folmsbee, revisor of statutes office, briefed committee members on <u>SB 348</u> which amends the list of Schedule I controlled substances by adding the chemical compounds HU-210, JWH-018, and JWH-073 to the hallucinogenic substances category.

Senator Vicki Schmidt spoke in favor of <u>SB 348</u> explaining that all three compounds for addition to the Schedule I controlled substances list are synthetic cannabinoids (<u>Attachment 1</u>). JWH-018 and JWH-073 are the ingredients in K2 herbs, and HU-210 is a similar chemical appearing on the federal schedule but not on the State schedule. Senator Schmidt provided a history of the compounds, the DEA classification of Schedule I, and information from the DEA regarding the three compounds. She indicated that the risks of smoking the compound have not been studied but may be likely to break down into carcinogens in the body. Further, these compounds are sold as herbal materials which are coated with synthetic cannabinoids. They pose a real danger and should not be seen as safer alternatives to illegal substances.

Kyle Smith, Topeka Police Department and a member of the Kansas Peace Officers' Association, spoke in support of <u>SB 348</u>. Mr. Smith indicated approximately a dozen countries, including Canada, France, and Germany have banned one or more of these substances (<u>Attachment 2</u>). He expanded on the effect of these substances and encouraged favorable passage of this legislation. Senator Haley inquired whether these substances really should be added to the controlled substance list at this particular time. Mr. Smith indicated there is strong evidence these drugs are being abused, and any intoxicant should be controlled especially when no long-term studies have been conducted related to potential harm.

Master Deputy Christopher Farkes from the Johnson County Sheriff's Office was recognized. Master Deputy Farkes supports <u>SB 348</u> and reports he became aware of unregulated synthetic cannabinoids in September 2009 (<u>Attachment 3</u>). Through investigation with high school juveniles and probation officers, he learned admitted marijuana smokers had switched to smoking these substances while under court supervision. These substances do not show a positive reading in a urinalysis test, but they provide the same effect as smoking marijuana. Master Deputy Farkes encouraged passing this legislation to benefit Kansas public health and safety.

Senior Forensic Scientist, Jeremiah Morris, with the Johnson County Sheriff's Office Criminalistics

Unless specifically noted, the individual remarks recorded herein have not been transcribed verbatim. Individual remarks as reported herein have not been submitted to the individuals appearing before the committee for editing or corrections. Page 1

Minutes of the Senate Public Health and Welfare Committee at 1:30 p.m. on January 13, 2010, in Room 546-S of the Capitol.

Laboratory offered testimony in support of **SB 348.** He reported that HU-210, JWH-018, and JWH-073 are laboratory produced compounds that are structurally different from tetrahydrocannabinol (THC) (<u>Attachment 4</u>); however, laboratory research has determined these compounds have more potent psychoactive effects (from 3 to over 100 times) than THC. Currently, there is nothing known about long-term health or psychological effects for these synthetic cannabinoids; published literature has expressed concern about the lack of information regarding metabolism or toxicity of these substances; concerns exist related to dosing and overdosing; and the issue of addiction and withdrawal symptoms linked to chronic abuse exists. Senator Haley inquired how the substances are administered; Mr. Morris indicated that the substances are either sprayed or sprinkled and some individuals choose to smoke them. Senator Barnett requested that a study or reference citation relative to the carcinogen effect of these products be submitted to the committee members (<u>Attachment 5</u>). Senator Brungardt asked how HU-210, JWH-018 and JWH-073 are detected if positive results are not indicated in a urine specimen, and he inquired about the toxicology of the drugs. Mr. Morris indicated that specimens undergo numerous other tests to determine drug presence. In regard to drug toxicology, Mr. Morris discussed military concerns related to toxicology screens.

Chairman Barnett recognized Ed Klumpp, Kansas Association of Chiefs of Police, who supports <u>SB 348</u>. Mr. Klumpp testified that these new drugs are gaining popularity among high school students, parolees, and persons on probation. He reported that scheduling these drugs is an important step toward protecting youth and others from negative effects and potential addiction (<u>Attachment 6</u>). Senator Kelly inquired as to the penalties for possessing these drugs, should legislation be passed. Mr. Klumpp indicated the penalty would be the same as for possessing marijuana which is a Class A misdemeanor (first offense). The second offense results in a Level 8 felony. Senator Haley questioned whether Kansas would be the first State to pass legislation such as that being proposed. Mr. Smith indicated there were 13 countries which had passed similar legislation; he was unaware of any other states that have passed legislation currently.

Richard Samaniego (representing Thomas R. Stanton) from the Kansas County and District Attorneys Association was introduced. Mr. Samaniego supported <u>SB 348</u> (<u>Attachment 7</u>). He reported that HU-210 is already listed as a Schedule I drug under federal law. Mr. Samaniego testified that benzylpiperazine (BZP) is a synthetic drug similar to Ecstacy and has become an increasingly abused drug in Kansas; the drug is ten to twenty times more potent than amphetamine and is included on the federal Schedule I list of controlled substances. Mr. Samaniego requested amendment of <u>SB 348</u> to include BZP.

Senator Kelly questioned the fiscal note for <u>SB 348</u> as to whether accurate and reasonable cost information was included. Senator Barnett requested the committee secretary contact the Division of Budget for a revised fiscal note reflecting reasonably accurate information.

Kenneth McGovern, Sheriff of Douglas County, testified in support of **SB 348**. He provided examples of several incidents involving these drug and furnished information retrieved from the Internet related to synthetic cannabinoids; he expressed concern regarding use by school age youth and extenuating negative concerns such as use while driving. Sheriff McGovern urged committee members to take decisive action against this threat to the health and safety of Kansas communities (Attachment 8).

Written testimony was submitted by:

Eric A. Voth, MD, FACP, Chairman, The Institute on Global Drug Policy (<u>Attachment 9</u>) Senator Mike Petersen, District 28 (<u>Attachment 10</u>)

Senator Barnett closed the hearing on SB 348.

Senator Vicki Schmidt moved to amend the effective date of **SB 348** as publication in the Kansas Register; Senator Colver seconded the motion. The motion passed.

Senator Haley indicated that he could support the addition of BZP to the Schedule I list, however, he could not support the addition and criminalizing of HU-210, JWH-018, and JWH-073 in the same bill. Given the lack of studies supporting harmful health or psychological outcomes by using these substances, Senator Haley indicated addition of these drugs to the controlled substances list could be premature and are not required at this point in time, particularly in light of fiscal challenges currently faced by the State. Senator Haley suggested that BZP be added to the Schedule I Controlled Substances List separately from the drugs listed in <u>SB 348</u>

Upon a motion by Senator Vicki Schmidt to amend **SB 348** to include the addition of benzylpiperazine (BZP) to the list of Schedule I drugs and a second by Senator Huntington, the motion passed with

CONTINUATION SHEET

Minutes of the Senate Public Health and Welfare Committee at 1:30 p.m. on January 13, 2010, in Room 546-S of the Capitol.

Senator Haley voting in opposition to the amendment..

Senator Vicki Schmidt moved to pass out favorably **SB 348** as amended; the motion was seconded by Senator Mary Pilcher-Cook. The motion passed with Senator Haley voting in opposition to favorable passage of **SB 348**.

The next meeting is scheduled for January 14, 2010.

The meeting was adjourned at 2:32 p.m.

PUBLIC HEALTH AND WELFARE GUEST LIST January 13, 2009

NAME	AFFILIATION
DAVID HUTCHPHUS	KANSAS BURLAY OF (AVESTICATION)
EDKUMP	KACP/KPOA/KSA
STAN HEFPLEY	ICBT ZAB
Barbara Hollingsworth	The Topeka Capital-Journa
DAVID BURGER	JOHNSON COUNTY SHERIFF'S OFFICE
BOB KELLER	11 II I
Baby Jallisins	Ko Assoc Osteapethic Med
famel tomes	United Health Guoup
Michelle Leterson	Capitol Atrategies
Alade Spiess	America Concertorization
Critico buitar	Kansas State Norsas Assoc
Steve Lawis	Douglas County Sherriff Spitting
Les McGoron.	Donglas Com of Sheriff Stran
Jeremiah Morris	Johnson County Sheriff's Office
CHRISTOPHER FRAKES	JOHNSON COUNTY SHERSFR'S Office
Richard Semaricy a	Kenner & Associates
H. SCOTT ASKEW	SHAWNEE County Sheriff's office
Christing Morrig	KS Bd. of Pharmacy
Deb Billingsley	11 /1
Sherrene Sones-Sorataly Aulu Shelys	AAMS
	KHI New,
leigh Keck	Hein Law Firm

STATE OF KANSAS

SENATOR, 20TH DISTRICT 2619 S.W. RANDOLPH CT. TOPEKA, KANSAS 66611 (785) 267-4686

STATE CAPITOL—ROOM 542-N TOPEKA, KANSAS 66612 OFFICE: 785-296-7374 vicki.schmidt@senate.ks.gov



SENATOR VICKI SCHMIDT ASSISTANT MAJORITY LEADER

COMMITTEE ASSIGNMENTS

CHAIR: ETHICS AND ELECTIONS VICE-CHAIR: PUBLIC HEALTH AND WELFARE MEMBER: INTERSTATE COOPERATION TRANSPORTATION WAYS AND MEANS

JOINT COMMITTEES

CHAIR: ADMINISTRATIVE RULES AND REGULATIONS MEMBER: HEALTH ROLICY OVERSIGHT INFORMATION TECHNOLOGY

Testimony Presented to PUBLIC HEALTH AND WELFARE COMMITTEE Senator Vicki Schmidt January 13, 2010 SB 348

Chairperson Barnett distinguished members of the Senate Public Health and Welfare Committee:

Thank you for the opportunity to provide testimony on SB 348. This bill adds 3 chemical compounds (all synthetic cannabinoids) to Schedule I, which subjects them to our drug laws. K2 herbs have JWH-018 and JWH-073 on them, while HU-210 is a similar chemical that already appears in the federal schedule, but not ours. I have included the information from the DEA website on these compounds.

K2 contains the two synthetic cannabinoids and was created at Clemson University. John W. Huffman is the chemistry professor that had an undergraduate student working in his lab create JWH-018, which is named after Huffman's initials. The original research was designed to help find new pharmaceuticals and understand the chemistry of the brain. The risks of smoking this compound have not been studied, and may be likely to break down into carcinogens in the body.

I have attached some news articles on K2, the DEA classification of Schedule I and the information from the DEA on the three compounds. I tank you for your consideration and ask that you pass SB 348 out of the committee favorably. As always, I am happy to stand for questions.

Public Health and Welfare Date: Attachment:

01/13/10

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STATE OF KANSAS

SENATOR, 20TH DISTRICT 2619 S.W. RANDOLPH CT. TOPEKA, KANSAS 66611 (785) 267-4686

STATE CAPITOL—ROOM 542-N TOPEKA, KANSAS 66612 OFFICE: 785-296-7374 vicki.schmidt@senate.ks.gov



SENATOR VICKI SCHMIDT ASSISTANT MAJORITY LEADER

> SCHEDULE I DRUGS Excerpt from DEA

COMMITTEE ASSIGNMENTS

CHAIR: ETHICS AND ELECTIONS VICE-CHAIR: PUBLIC HEALTH AND WELFARE MEMBER: INTERSTATE COOPERATION TRANSPORTATION WAYS AND MEANS

JOINT COMMITTEES

CHAIR: ADMINISTRATIVE RULES AND REGULATIONS MEMBER: HEALTH POLICY OVERSIGHT INFORMATION TECHNOLOGY

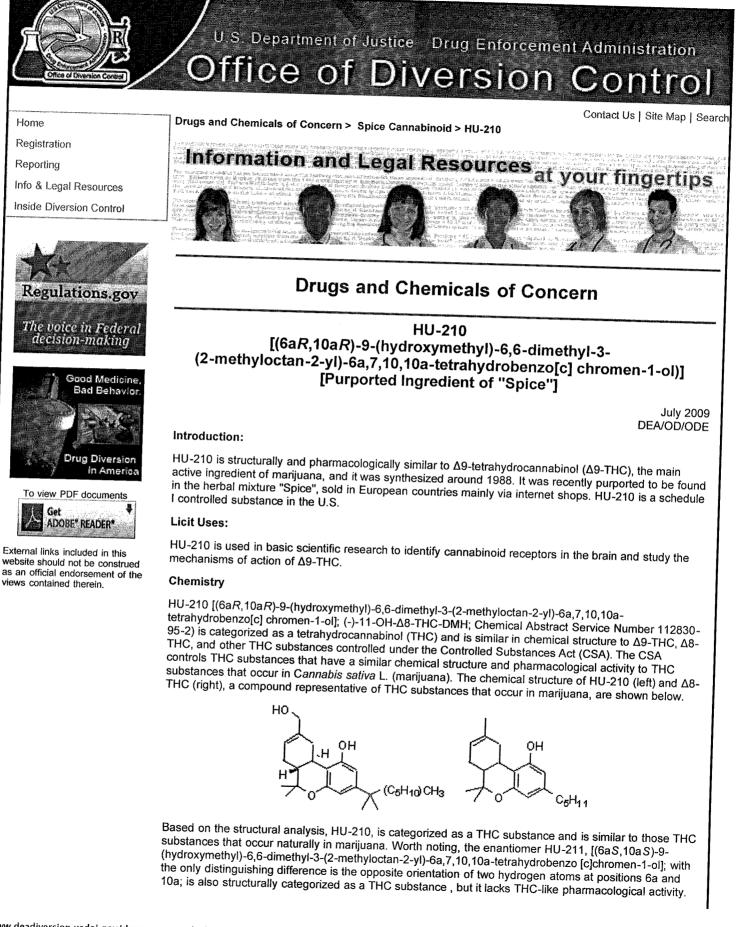
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(1) Schedule I. -

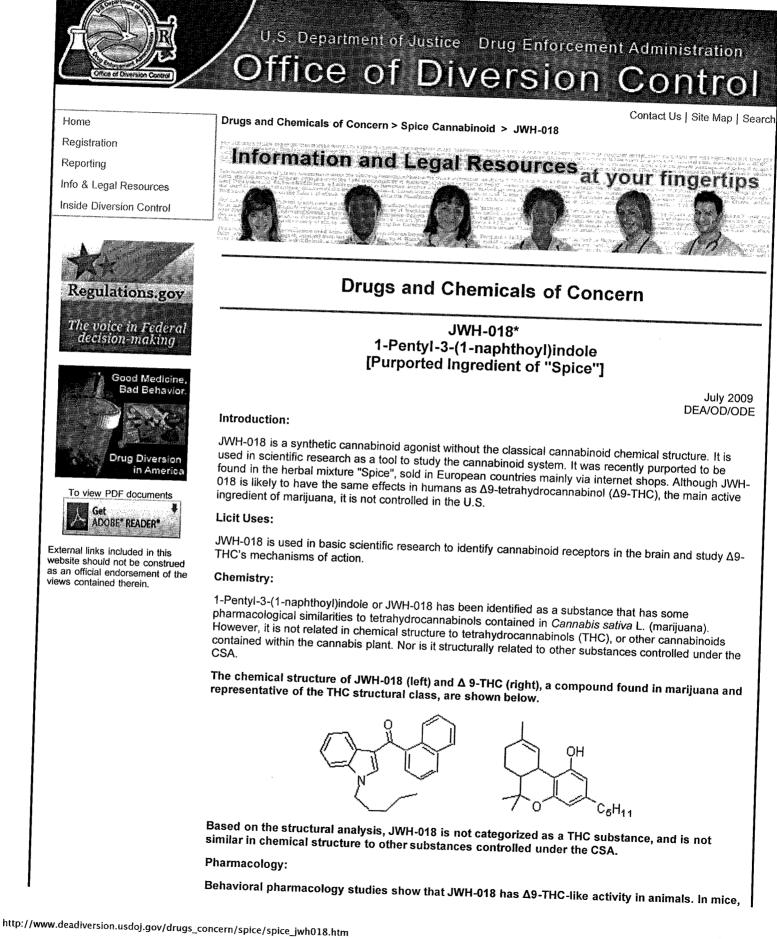
(A) The drug or other substance has a high potential for abuse.

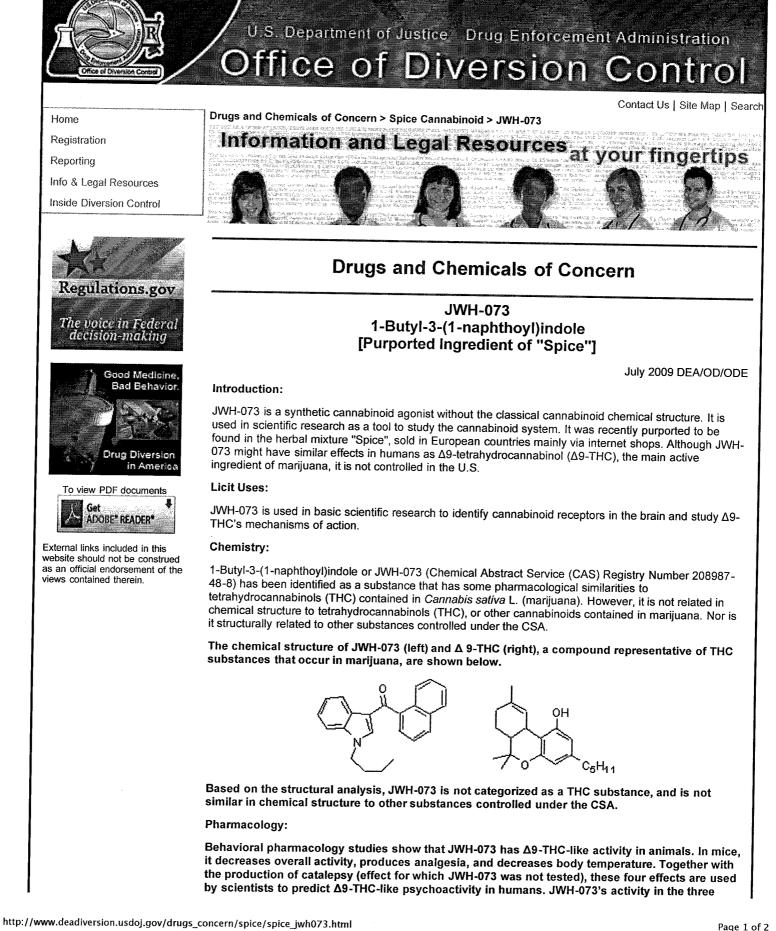
(B) The drug or other substance has no currently accepted medical use in treatment in the United States.

(C) There is a lack of accepted safety for use of the drug or other substance under medical supervision.



Page 1 of 2





A legal pot gets the attention of police

By DAVID KLEPPER

The Star's Topeka correspondent

It burns like marijuana, works like marijuana and it sort of looks like it, too.

And it's perfectly legal.

It's called K2, and area police confirm that the little bags of dried herbs are starting to pop up among teens and young adults.

Although it may be new on the local drug scene, K2 and similar brands have the attention of a Kansas lawmaker who said she would consider outlawing the substance. That's because the health risks of smoking one of these dubious doobies is unknown. Some European countries already have moved to ban it.

"It is new on the scene here," said Johnson County Sheriff's Deputy Tom Erickson. "It's just been a few weeks since we found out it was being sold locally."

Available for sale online and at a store in Lawrence, K2 comes in a small pouch. Inside is a mix of dried herbs that look like oregano but are laced with chemicals designed to mimic the effects of marijuana. Other brands go by the names Spice, Genie and Zohai.

Because the active ingredients are just a few atoms away from the real thing, the synthetic stuff isn't covered by laws banning marijuana. This means K2 and similar products are legal — even though the effects are identical to pot.

Johnson County police first discovered the drug was being used by ex-convicts on probation. They turned to K2 hoping it wouldn't show up on drug tests as marijuana. Now police are finding it in high schools.

The Sacred Journey, a botanical store in Lawrence, sells bags of K2 for \$15 to \$30. A store manager declined to comment, but an employee said K2 should be burnt as incense and isn't meant to be smoked. A competing brand is marketed online as "plant food."

The Johnson County Crime Lab ran an analysis on K2. Although it tested negative for THC, the active ingredient in marijuana, it was positive for synthetic cannabinoids. These are chemical compounds created in a lab that act on the brain like THC.

K2 contains two synthetic cannabinoids created at Clemson University. Chemistry professor John W. Huffman said an undergraduate student working in his lab actually created one of the compounds, called JWH-018 after Huffman's initials.

Huffman said his research was designed to help find new pharmaceutical drugs and a deeper understanding of brain chemistry. He had no intention of inventing a new way to get high.

"But I'm not the least bit surprised," Huffman said. "If you make something illegal, like marijuana, people will look for an alternative."

Yet the fake marijuana may be more dangerous than the real McCoy, according to Huffman. He noted that unlike with marijuana, the risks of smoking synthetic cannabis haven't been studied. His research suggests the compounds likely break down in the body into carcinogens.

The manufacturer behind K2 and similar brands remains a mystery. No information is available about the company or individuals making the products. Huffman said he thought much of the new synthetic cannabis comes from labs in Asia.

He suspects the manufacturer turns the synthetic cannabinoid into powdered or liquid form and mixes it with otherwise harmless herbs.

Britain, Germany, Poland, France, South Korea and Russia have moved to ban the sale of synthetic cannabis within the past year. Kansas may not be far behind.

State Rep. Peggy Mast, an Emporia Republican, hadn't heard about K2 until informed by The Kansas City Star. But she's worried enough to suggest the state should take action.

"I would be very happy to sponsor a bill to make this illegal," Mast said.

Mast sponsored legislation a few years ago that outlawed the hallucinogenic plants jimson weed and salvia divinorum.

Johnson County Sheriff's Deputy Chris Farkes worries that teens may assume synthetic cannabis is safe because it's legal.

"I've even talked with parents who say, 'Oh, it's completely legal so I don't " Farkes said. have a problem with my kid smoking it,'

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But Huffman isn't so sure outlawing his creation will help much.

"You ban one and they'll come up with another one," he said.

Senate Public Health and Welfare January 13, 2010 Testimony in Support of SB 348 Kyle G. Smith Topeka Police Department Kansas Peace Officers' Association

Chairman Barnett and Members of the Committee,

I appear today on behalf of the City of Topeka Police Department and Kansas Peace Officers' Association in support of SB 348.

This legislation would add three synthetic cannabinoids to schedule I of the controlled substances act. These three drugs, commonly referred to on the street as K2 or Spice but by the trade names HU-210, JWH-018 and JWH-073 have been developed and are being abused as synthetic versions of marijuana.

Approximately a dozen countries, including Canada, France and Germany, have placed one or more of these analogs on their controlled substance schedules and abuse of the drugs is increasing here in Kansas. There have been numerous reports of abuse by juveniles and others, of these products, sold as 'incense', being ingested by smoking the product. While we have limited scientific research, from media and internet accounts it would appear that the pharmacological effect is similar to pretty strong marijuana. Coupled with the danger of other health concerns from ingesting untested materials, it would seem prudent to place these drugs on the Schedules here in Kansas as well.

I would note that there has been some misunderstanding of the current legality of these drugs under current Kansas law. Kansas statutes do provide for prosecution of possession of analogs of controlled substances. An analog is defined as a having a similar chemical structure and pharmacological effect as a controlled substance. I believe that possession of these drugs could be prosecuted under K.S.A. 65-4162/21-36a06, but it would require substantial expert testimony by forensic scientists. I believe it would be better, easier and provide retailers and users more notice, if we explicitly included these drugs in the schedules.

Thank you for your time and consideration. I would be happy to answer any questions.

Public Health and Welfare Date: Attachment:

01/13/10 2 FRANK P. DENNING SHERIFF

> TELEPHONE 913-791-5800

FAX 913-791-5806



DAVID A. BURGER UNDERSHERIFF

DUTY HONOR SERVICE

KEVIN D. CAVANAUGH UNDERSHERIFF

125 N. CHERRY OLATHE, KANSAS 66061 WWW.JOCOSHERIFF.ORG

To: Chairperson Barnett, Vice-Chairperson Schmidt, and distinguished members of the Senate Public Health and Welfare Committee.

From: Master Deputy Chris Farkes

Date: January 13th, 2010

Chairperson Barnett and Committee Members,

My name is Deputy Chris Farkes and I'm a fourteen year veteran of the Johnson County Sheriff's Office. I appear before the committee today in support of Senate Bill 348.

I first became aware of the growing usage of unregulated synthetic cannabinoids in September, 2009. Through my interviews with high school age juveniles and probation officers, I learned that admitted marijuana smokers had switched to smoking K2 while they were under court supervision. I further learned the reason for this switch was the fact that the use of K2 would not show as a positive reading in a urinalysis test and yet would provide the same "high" as smoking marijuana.

I purchased packages of the four known versions of the product and submitted samples to the Johnson County Criminalistics Laboratory for analysis. The results of the analysis showed K2 was a composition of various organic plant materials which contained no identified controlled substances but it did contain two manmade compounds, JWH-018 and JWH-073. Both of these compounds were identified as unregulated synthetic cannabinoids.

I was surprised to learn that these newly created synthetic cannabinoids did not appear in the Kansas Controlled Substances Schedule, nor was the compound HU-210, also a synthetic cannabinoid. HU-210 was recently listed by the Federal Government as a Schedule I Controlled Substance but had yet to be added to the Kansas Controlled Substances.

Adding the synthetic cannabinoids to the Kansas Controlled Substances will allow for their proper regulation and oversight while benefiting the public safety and welfare of all Kansans. I ask the Committee to vote favorably on Senate Bill 348 which seeks to add JWH-018, JWH-073 and HU-210 to the list of Kansas Controlled Substances.

Master Deputy Christopher Farkes Johnson County Sheriff's Office

> Public Health and Welfare Date: Attachment:

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DAVID A. BURGER UNDERSHERIFF

KEVIN D. CAVANAUGH UNDERSHERIFF

FRANK P. DENNING SHERIFF

GARY R. HOWELL LABORATORY DIRECTOR

> TELEPHONE 913-826-3209

FAX 913-826-3286 CRIMINALISTICS LABORATORY 6000 LAMAR MISSION, KANSAS 66202 WWW.JOCOSHERIFF.ORG

DUTY HONOR SERVICE

Date: January 12, 2010

To: Chairperson Barnett, Vice-Chairperson Schmidt, and distinguished members of the Public Health and Welfare Committee.

My name is Jeremiah Morris and I am a Senior Forensic Scientist with the Johnson County Sheriff's Office Criminalistics Laboratory. I offer testimony today in support of Senate Bill 348, which seeks to amend K.S.A 65-4105 to add HU-210, JWH-018, and JWH-073 to the list of Schedule I controlled substances.

Marijuana and its active component tetrahydrocannabinol (THC) are both listed as schedule I controlled substances federally and in the State of Kansas. Recently, a number of herbal incense mixtures marketed in Kansas, the United States, and worldwide, have been found to contain a number of synthetic cannabinoids, particularly HU-210, JWH-018, and JWH-073. In October 2009, our laboratory detected the presence of JWH-018 and JWH-073 in a product called K2, an herbal smoking blend with rising popularity among Johnson County teenagers. Although our laboratory has not detected the presence of HU-210 in any submitted samples, we received reports that area teenagers were talking about an herbal smoking blend known to contain this compound.

HU-210, JWH-018, and JWH-073, are laboratory produced compounds and are structurally different from THC and other components in marijuana; however, laboratory research by Clemson University and the Hebrew University has determined that these compounds have more potent psychoactive effects than THC. They have a greater affinity to receptor sites in the brain which are thought to be responsible for most of the overt pharmacological effects of THC and other natural cannabinoids. Preliminary studies indicate that the three synthetic cannabinoids under consideration are anywhere from three to over 100 times more potent than THC.

The presence of HU-210, JWH-018, and JWH-073 in herbal smoking blends is extremely troubling for a number of reasons. First, detailed and exhaustive health and safety studies have yet to be performed on these compounds. Nothing is known about long term health or psychological effects for these synthetic cannabinoids. Published literature has expressed concern about the lack of information regarding metabolism of these compounds and whether or not metabolites are toxic or pharmacologically active. No studies have been done reporting the safety of combustion products from smoking these cannabinoids. Second, because these synthetic cannabinoids are being added to the herbal products, there is concern about dosing consistency and the risk of accidental overdoses. Overdoses and hospitalizations related to products containing synthetic cannabinoids have been reported in Missouri and Germany. Finally, preliminary research has found examples of addiction and withdrawal symptoms linked to chronic abuse of products containing JWH-018 and other synthetic cannabinoids. Adolescents and other members of the public may assume that these herbal smoking blends are both safe and non-addictive because they are "legal." In reality, the presence of HU-210, JWH-018, and JWH-073 in these blends present serious risks to users because the chemicals are very potent psychoactively and may present serious health risks to users.

In summary, the Johnson County Sheriff's Office Criminalistics Laboratory supports Senate Bill 348 and the amendment to K.S.A 65-4105 to include HU-210, JWH-018, and JWH-073, as Schedule I controlled substances. This bill will prohibit illicit possession and abuse of these synthetic cannabinoids but not restrict legitimate research, either.

Respectfully, Jeremiah Morris Senior Forensic Scientist, Johnson County, KS Sheriff's Office

> Public Health and Welfare Date: Attachment:

ORIGINAL PAPER

Identification of in vitro metabolites of JWH-015, an aminoalkylindole agonist for the peripheral cannabinoid receptor (CB₂) by HPLC-MS/MS

Qiang Zhang · Peng Ma · Richard B. Cole · Guangdi Wang

Received: 22 May 2006 / Revised: 18 July 2006 / Accepted: 28 July 2006 / Published online: 6 September 2006 © Springer-Verlag 2006

Abstract The in vitro microsomal metabolism of JWH-015, a ligand that exhibits a high binding affinity at the peripheral cannabinoid receptor CB₂, has been studied. A total of 22 metabolites were identified and structurally characterized. The metabolites are products of: 1) monohydroxylation on the naphthalene ring (m/z 344, M20) and M21), indole ring (m/z 344, M17 and M18), or the N-alkyl group (m/z 344, M14); 2) arene oxidation leading to dihydrodiols (m/z 362, M12 and M15); 3) dihydroxylation on the naphthalene ring (m/z 360, M7) or indole ring (m/z360, M13), resulting from a combination of monohydroxylations on both the naphthalene and indole rings (m/z 360,M16), or a combination of monohydroxylations on the naphthalene ring and on the N-propyl group (m/z 360, M9); 4) trihydroxylation (*m*/z 378, M1, M3, M4, M6, and M10); 5) N-dealkylation (m/z 286, M19); 6) N-dealkylation and monohydroxylation on the naphthalene ring (m/z 302,M11); 7) N-dealkylation and dihydrodiol formation from arene oxidation (m/z 320, M2 and M5); 8) dehydrogenation after monohydroxylation on the N-alkyl group (m/z 326,M22); 9) dehydrogenation and monohydroxylation on the indole ring (*m*/z 342, **M8**).

Keywords JWH-015 \cdot Metabolites \cdot CB₂ agonist \cdot HPLC-tandem mass spectrometry

Q. Zhang · P. Ma · G. Wang (⊠) Department of Chemistry, Xavier University of Louisiana, New Orleans, LA 70125, USA e-mail: gwang@xula.edu

R. B. Cole Department of Chemistry, University of New Orleans, New Orleans, LA 70148, USA

Introduction

Shortly after the discovery of the central cannabinoid receptor, CB1, located primarily in the brain [1], a peripheral cannabinoid receptor, CB₂, that is mainly expressed in immune cells was identified and cloned [2]. CB_1 is believed to be responsible for the psychotropic and antinociceptive effects of cannabinoids, whereas the physiological role of CB₂ is not well understood [3]. However, recent studies show that CB₂ is also involved in pain perception [4, 5], providing evidence that CB₂ may be expressed in neural cells [6, 7]. There has been growing interest in separating potential therapeutic functions of cannabimimetic compounds from psychotropic side effects, and many ligands that exhibit stronger binding affinity to CB₂ than to CB₁ have been discovered [3]. These include agonists WIN55212-2 [8], JWH-015, JWH-051, JWH-057 [9], and L768242 [10], and antagonists SR144258 [11] and AM 630 [12, 13]. WIN55212-2 and JWH-015 are aminoalkylindoles that behave as CB₂ receptor agonists. Howeyer, while WIN55212-2 also shows a strong affinity for CB₁, JWH-015 has very little binding affinity for CB₁. The in vitro metabolism of two aminoalkylindoles has been studied in our laboratory [14, 15]: WIN55212-2 which is an agonist for both CB1 and CB2, and AM 630 which behaves primarily as a CB2-selective antagonist/inverse agonist [13, 16].

There has been no report on the metabolism of JWH-015, a CB_2 -selective agonist, and it is unknown whether there is any difference between its metabolic pathways and those of other aminoalkylindoles that function differently. In the current study, we investigate the in vitro metabolism of JWH-015. Metabolites were generated by incubating JWH-015 with rat liver microsomes. The incubation products were subjected to separa-

Public Health and Welfare Date: Attachment: tion by high-performance liquid chromatography (HPLC) and the metabolic products were identified and structurally characterized by tandem mass spectrometry (MS/MS).

Experimental

Materials

JWH-015 was purchased from Tocris Cookson (Ellisville, MO). HPLC-grade solvents (acetonitrile, methanol, and water) were purchased from Fisher Scientific (Fair Lawn, NJ). All other chemicals were purchased from Sigma-Aldrich Co. (St. Louis, MO). Rat liver microsomes were purchased from Gentest Corporation (Woburn, MA) and stored at -80 °C prior to use.

Microsomal Incubations

Stock solutions of 20 mM JWH-015 were prepared in DMSO and added in 1-µL aliquots as substrate to individual incubation aliquots. Rat liver microsomes containing 1.5 mg/mL of protein were pre-incubated at 37 °C for 30 min. The 0.2-mL incubation aliquots contained 75 mM potassium phosphate (pH 7.4), 17 mM magnesium chloride, 7 mM NADPH, 17 mM glucose-6-phosphate, and 1.2 units of glucose-6-phosphate dehydrogenase. Incubation times ranged from 0.5 to 4 h. Incubations were halted by placing the incubation vials in an ice bath followed by addition of an equal volume of methanol (0.2 mL). The quenched incubation mixtures were stored at -20 °C until analysis. Prior to HPLC separation, microsomal proteins were precipitated by centrifugation at room temperature, and the solvent was evaporated with a stream of nitrogen at 37 °C. The residual solution was applied to 6-mL SUPELCO C₁₈ solid-phase extraction (SPE) columns pretreated with water and methanol. The columns were washed with HPLC-grade water and eluted with methanol, and the effluents were again concentrated by a nitrogen stream at 37 °C.

Blank samples

Control incubations were performed under identical conditions with heat-inactivated microsomes (heated to 100 °C for 10 min). In addition, incubations were carried out in the absence of NADPH or in the absence of microsomes. To locate matrix interferences arising from microsomes and buffer components, blank incubations were done where all elements were present except the drug compounds.

HPLC-UV analyses

Initial analyses of the incubation products were performed by using a Shimadzu HPLC system equipped with a UV-Vis SPD-10ADVP detector (Shimadzu Instruments Co. Colombia, MD). A 2.1×150 mm, 4-µm-pore-size ODS HPLC column (Phenomenex, Torrence, CA) was used for separation. The mobile phase flow rate was set at 0.3 mL/min, with gradient elution starting at 10% acetonitrile and 90% water for 5 min, followed by a linear increase to 70% acetonitrile in 17 min, and a linear change to 100% acetonitrile in 5 min. Eluted components were detected by UV absorbance (λ_{max} at 270 nm). At least three injections were performed for each incubation aliquot; no significant qualitative or quantitative run-to-run variations were found.

LC/MS and LC/MS/MS analyses

A Phenomenex ODS HPLC column (2.1×150 mm, 4-µm pore size) coupled to a C_{18} guard column (2×18 mm, 5 μ m, Supelco, Bellefonte, PA) was used for separation. A Shimadzu LC-MS 2010 was used for initial screening of metabolic products generated from the microsomal incubations. HPLC mobile phase flow rate was set at 0.20 mL/min, with gradient elution starting at 10% acetonitrile and 90% water for 5 min, followed by a linear increase of acetonitrile composition to 100% in 18 min. MS/MS experiments were performed on a Ouattro II triplequadrupole tandem mass spectrometer equipped with an electrospray ionization (ESI) source (Quatro II, Micromass Inc., Beverly, MA). The ESI "needle" potential was set at 3.46 kV and the cone voltage was set at 70 V for MS scans and 62-67 V for MS/MS measurements. In MS/MS experiments examination of collision-induced dissociation of selected precursors takes place in the central hexapole collision cell; argon was used as the collision gas at collision energies between 17 and 20 eV and a CID pressure of 1.9×10^{-4} mbar. The ion source temperature was held at 250 °C.

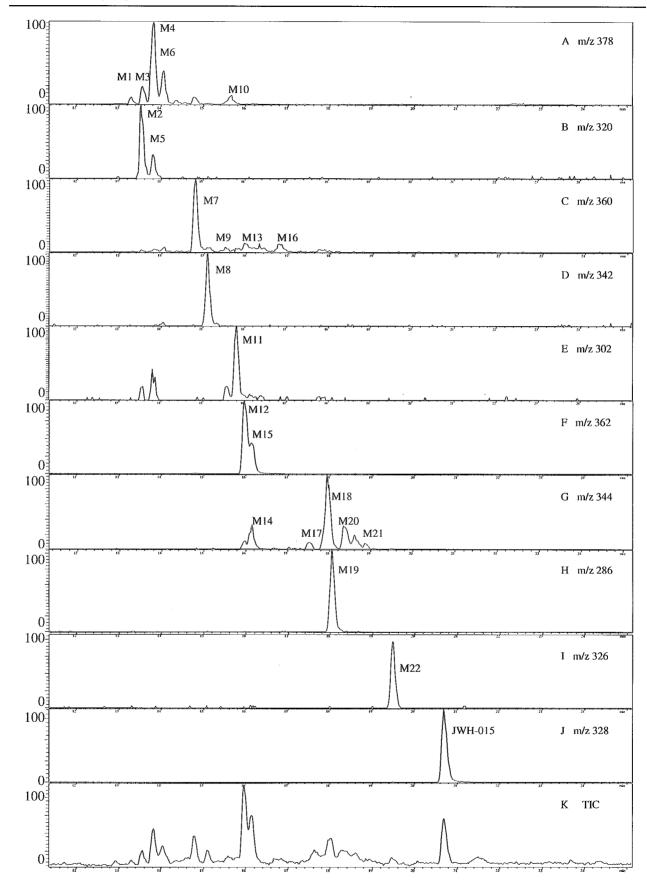
Results and discussion

Detection and structural assignments of the metabolites were based on the appearance of the diagnostic ions in HPLC/MS/MS analysis. As shown in Fig. 1, a total of 22 metabolites of JWH-015 (i.e., M1–M22) were identified from the total ion and reconstructed ion chromatograms (RICs) by screening for molecular and fragment ions that

Fig. 1 Total ion chromatogram (TIC, K) and reconstructed ion chromatograms (RIC, A-J) of a rat microsomal incubation product of JWH-015. The identified metabolites are labeled *M1* through *M22*, and the parent compound is labeled *JWH-015*

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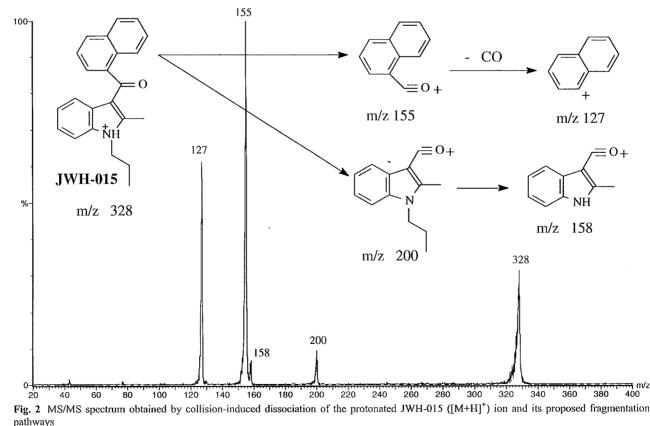
are related to those of the parent compound JWH-015. Figure 2 is a product ion spectrum obtained by collisioninduced dissociation (CID) of the protonated JWH-015 molecule. Four fragment ions were observed as diagnostic ions for structural characterization of potential metabolites that upon CID may yield identical or related product ions. In Fig. 2, the two product ions at m/z 155 and m/z 127 represent two naphthyl fragments, whereas the two product ions at m/z 200 and m/z 158 correspond to two fragments with charge retention on the indole moiety. The metabolites, while structurally modified by p450 enzymes, are expected to yield one or more analogous fragments that are related to these fragment ions of JWH-015.

For each of the 22 distinct peaks shown in the RICs (Fig. 1), tandem mass spectra were acquired to confirm that they represent JWH-015 metabolites whose product ions are either identical or related to the four diagnostic fragment ions of JWH-015. In panel A of Fig. 1, a total of 5 metabolic products, assigned as M1, M3, M4, M6, and M10, were detected, each yielding a single predominant ion at m/z 378. Examination of the tandem mass spectrum of each peak indicates that these metabolites represent structural isomers differing in the site of oxidation. All five metabolites bear a dihydrodiol function on the naphthyl ring and a third hydroxyl group either on the indole ring or on the N-propyl chain. Variation of the dihydrodiol site on

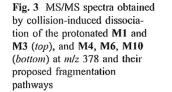
the naphthyl moiety can also result in two structural configurations. Thus, M1 and M3 are attributed to two metabolites with a hydroxylated indole ring and a dihydrodiol group on the naphthyl ring, whereas M4, M6, and M10 are metabolites that have the hydroxylated propyl side chain. This conclusion is arrived at after examining the product ion spectrum of each of the five metabolite peaks. The protonated M1 and M3 yielded fragment ions containing the indole moiety that are 16 amu higher than those of JWH-015; the protonated M4, M6, and M10 produced fragment ions containing the indole ring that are identical to those of JWH-015. Additional fragment ions from M4, M6, and M10 provided evidence that the propyl chain has been hydroxylated. For illustration, two product ion spectra are shown in Fig. 3, one for M1 and M3, and one for M4. M6. and M10.

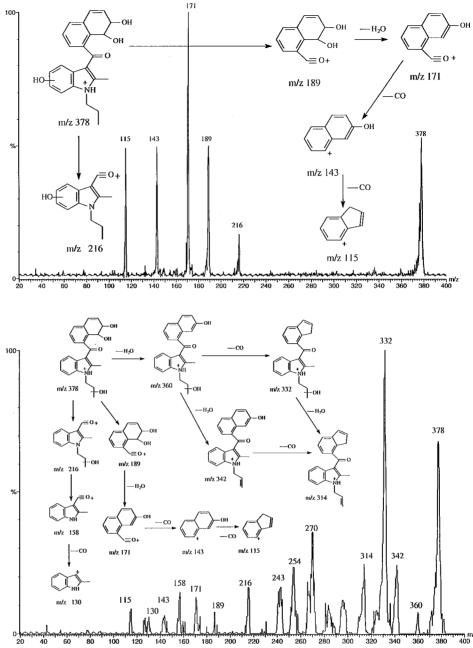
Appearing next in the RICs are M2 and M5, two isomeric metabolites whose protonated molecules at m/z320 yielded nearly identical product ion spectra. As shown in Fig. 4, these two metabolites are products of *N*-dealkylation and dihydrodiol formation on two different sites of the naphthyl ring. Comparing to the product ion spectrum of JWH-015, it is clear that the fragment ion of M2 and M5 at m/z 189 corresponds to that of JWH-015 at m/z 155, the former with 34 amu higher due to the introduction of two additional hydroxyl groups. Because

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of *N*-dealkylation, another fragment ion of the metabolites at m/z 158 is 42 amu lower than its corresponding fragment ion of JWH-015 at m/z 200.

The RIC obtained for m/z 360 shows four metabolites identified as M7, M9, M13, and M16. The first two metabolites, M7 and M9 are identified as products of dihydroxylation on the naphthyl ring (Fig. 5). Thus, a metabolite product ion at m/z 187 is analogous to the product ion at m/z 155 in Fig. 2; both M7 and M9 yield fragment ions at m/z 200 and m/z 158 that are identical to those of JWH-015, confirming that the indole moiety is intact in M7 and M9. Metabolite M13 was identified as a product of dihydroxylation on indole ring, as evidenced by the presence of a fragment ion at m/z 232 (MS/MS spectrum not shown) that is 32 amu higher than the fragment ion of JWH-015 at m/z 200. On the other hand, fragment ions of M16 (precursor m/z 360, not shown) suggest that hydroxylation occurred on the naphthyl ring as well as on the indole moiety. For example, the fragment ion of M16 at m/z 216 that contains the indole moiety, corresponds to the fragment ion of JWH-015 at m/z 200; the fragment ion from M16 containing the naphthyl ring at

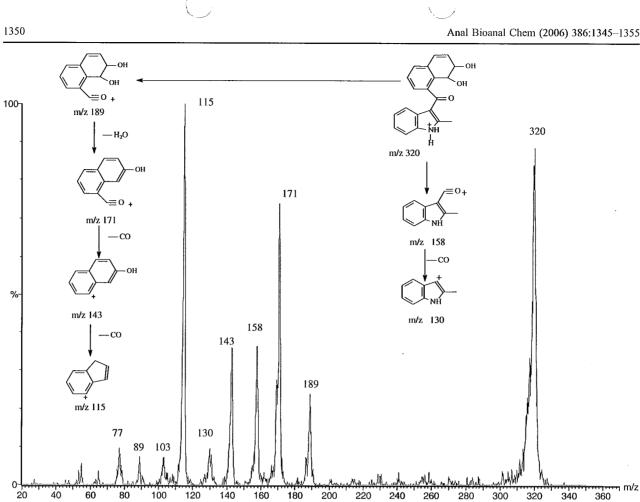


Fig. 4 MS/MS spectrum obtained by collision-induced dissociation of the protonated ion at *mlz* 320 (M2 and M5) and its proposed fragmentation pathways. Only one position of the dihydrodiol group on the naphthyl ring is shown

m/z 143 is also 16 amu higher than the fragment ion from JWH-015 at m/z 127.

M11 is the sole metabolite that yields a high-abundance protonated molecule at m/z 302 as shown in panel D of Fig. 1 (other peaks did not give fragment ions related to the parent compound JWH-015). Its product ion spectrum indicates that M11 is hydroxylated on the naphthyl ring and has lost the propyl group via N-dealkylation (Table 1). Eluting next is metabolite M8 that shows a protonated molecule at m/z 341. Compared to the parent compound, two structural modifications may have occurred on M8: the hydroxylation of the indole ring and the formation of a double bond (dehydrogenation) on the propyl chain. As illustrated in Fig. 6, the structural assignment is supported by the presence of a fragment ion at m/z 214 which is 14 amu higher than the corresponding fragment ion from JWH-015, and the presence of ions at m/z 155 and m/z 127, indicating that the naphthyl moiety of the metabolite is intact.

Two metabolites were identified in the RIC of m/z 362, which are two dihydrodiols, presumably differing in the site of dihydrodiol formation on the naphthyl ring. As shown in Fig. 7 that is the product ion spectrum of the protonated **M12** or **M15**, the only structural modifications on **M12** and **M15** have occurred on the naphthyl ring, as evidenced by the intact indole and the *N*-propyl moieties (m/z 200, 158). On the other hand, the fragment ion at m/z 189 is exactly 34 amu higher than the corresponding one from the parent compound (m/z 155, Fig. 2), suggesting the dihydrodiol structure on the naphthyl moiety. Again, only one possible dihydrodiol configuration is shown in Fig. 7 for illustration.

At least 5 metabolites were detected that yield protonated molecules at an identical m/z value of 344. Indeed these metabolites were all metabolic products of monohydroxylation on the *N*-propyl chain (M14), the indole ring (M17, M18), or the naphthyl ring (M20, M21). As listed in Table 1, the structure of M14 is deduced by the presence of the intact naphthyl ring (m/z 155, 127) and the observation of an ion at m/z 326, most likely a product of dehydration of the hydroxylated propyl group that occurred in the gas phase. The presence of fragment ions at m/z 155, m/z 127, and m/z 216 leads to the conclusion that monohydroxylation has occurred within the indole ring moiety for M17 and M18.

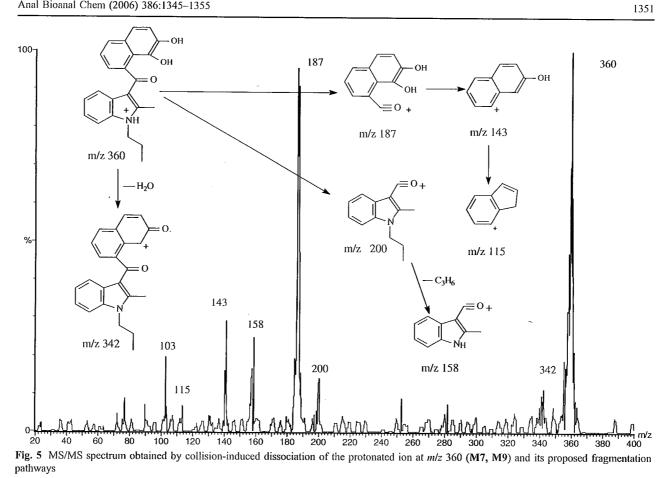
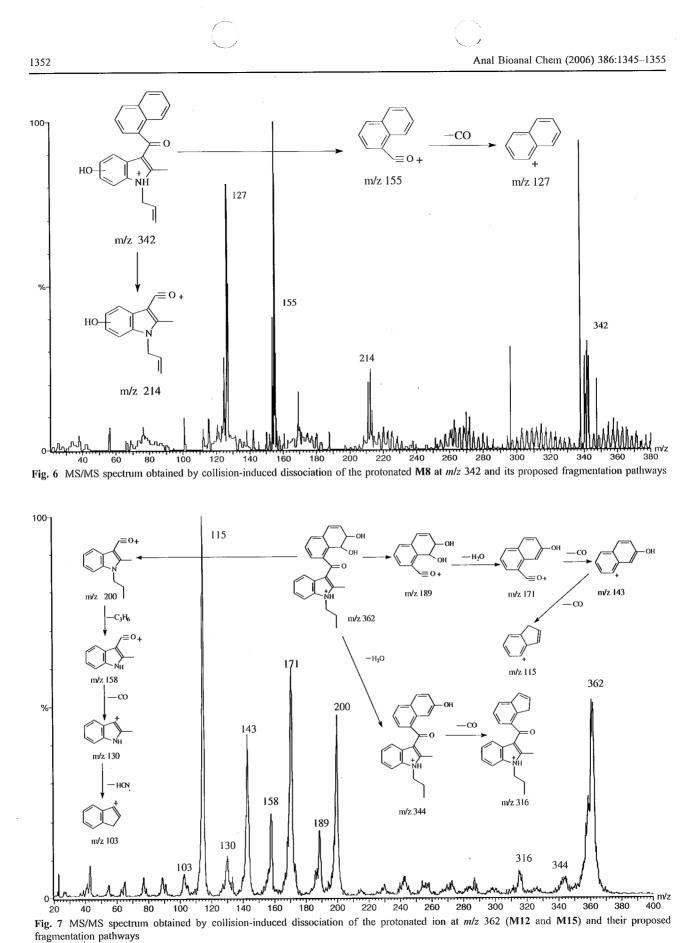


Table 1 [M+H]⁺ and the characteristic fragment ions (*m/z*) of JWH-015 and its 22 identified metabolites (M1-M22)

Compound	$[M+H]^+$	Diagnostic product ions	Other
Parent (JWH-015)	328	200, 158; 155, 127	
M1	378	216; 189, 171, 143, 115	
M2	320	158, 130, 103; 189, 171, 143, 115	89
M3	378	216; 189, 171, 143, 115	174, 146
M4	378	216, 158, 130; 189, 171, 143, 115	198; 360, 342, 314
M5	320	158, 130, 103; 171, 143, 115	302; 77
M6	378	216, 158, 130; 189, 171, 143, 115	360, 342, 332, 314
M7	360	200, 158, 130; 187, 171, 143,	342, 314, 299, 271
M8	342	214; 155, 127	
M9	360	200, 158, 103; 187, 143, 115	342
M10	378	216, 158, 130; 189, 171, 143, 115	360, 342, 332, 314
M11	302	158, 130; 171, 143, 115	
M12	362	200, 158, 130, 103; 189, 171, 143, 115	
M13	360	232; 155, 127	
M14	344	155, 127	326, 296, 283, 254
M15	362	200, 158, 130, 103; 189, 171, 143, 115	344, 316
M16	360	216, 188, 160; 171, 143, 115	,
M17	344	216; 155, 127	
M18	344	216; 155, 127	
M19	286	158, 130, 103; 155, 127	77
M20	344	200, 158; 171, 143, 115	
M21	344	200, 158, 171, 143, 115	
M22	326	155, 127	283

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The sole chromatographic peak observed at m/z 286 represents M19, a metabolite that has lost the propyl group. Thus, the fragment ion of JWH-015 at m/z 200 corresponds to that of M19 at m/z 158 as a result of the loss of C_3H_6 (42 amu); the naphthyl ring fragment ions remain the same in the metabolite (Fig. 8). Finally, the metabolite M22 observed at m/z 326 with the only modification being dehydrogenation on the propyl group, consistent with the mass difference of 2 amu between JWH-015 and M22.

To account for all 22 detected metabolites, several metabolic pathways were proposed as illustrated in Fig. 9. In one pathway the parent compound undergoes oxidation on the naphthyl ring via an epoxide intermediate, which undergoes either enzymatic hydrolysis to yield two isomeric dihydrodiol metabolites **M12** and **M15**, or spontaneous rearrangement to give two monohydroxylated metabolites **M20** and **M21**. Further oxidation of these metabolites at different sites accounts for six more metabolites observed at m/z 378 (**M1**, **M3**, **M4**, **M6**, **M10**) and m/z 360 (**M7**). It is noted that only two possible dihydrodiol sites are assigned for all 9 metabolites that contain the dihydrodiol function based on a previous study of the in vitro metabolism of

WIN55212-2 [14], also an aminoalkylindole with a naphthyl ring. In that study, it was found that the two major metabolites containing the dihydrodiol structure had only assumed two dihydrodiol configurations on the naphthyl ring instead of four theoretically possible ones.

In the second metabolic pathway JWH-015 is oxidized at the aminoalkyl chain to give a monohydroxylated metabolite M14 at m/z 344, which upon hydroxylation on the indole ring gives rise to M9 at m/z 360. Dehydration of M14 leads to M22 at m/z 326 which can be oxidized on the indole ring to generate M8 at m/z 342. The third metabolic pathway is responsible for four metabolites where M17 and M18 (m/z 344) are first formed by hydroxylation on the indole ring and two isobaric metabolites M13 and M16 at m/z 360 are then formed by further hydroxylation on the indole ring and naphthyl ring, respectively. Finally, the fourth metabolic pathway accounts for four metabolites that are characterized by the loss of the aminoalkyl group. The metabolite M19 at m/z 286 is a result of dealkylation on the nitrogen atom, which upon oxidation is converted to two isomeric dihydrodiol metabolites M2 and M5 at m/z 320. However, monohydroxylation of the naphthyl ring yields only M11 at m/z 302.

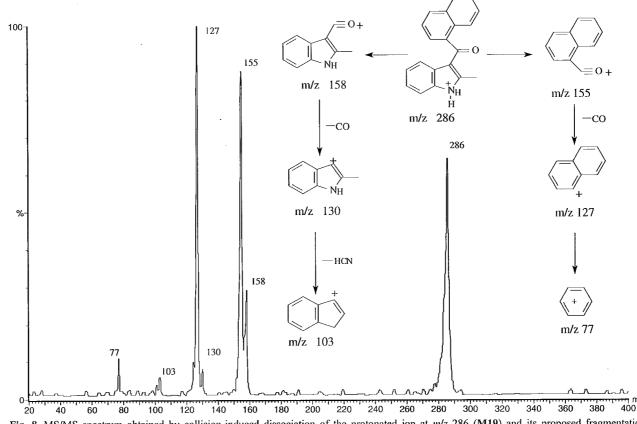


Fig. 8 MS/MS spectrum obtained by collision-induced dissociation of the protonated ion at m/z 286 (M19) and its proposed fragmentation pathways



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m/z



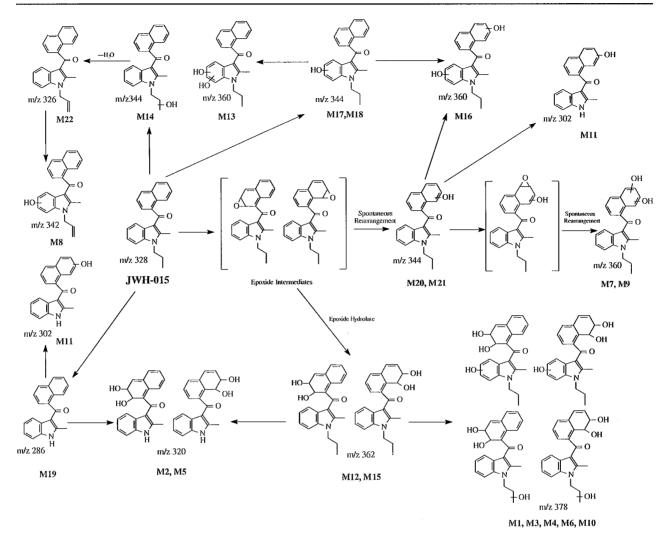


Fig. 9 Proposed metabolic pathway of JWH-015

Conclusion

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An analytical method based on HPLC coupled with tandem mass spectrometry has been developed and JWH-015, an aminoalkylindole cannabinoid, shows unique metabolic pathways that differ from other types of cannabinoid ligands such as Δ 1-THC and SR141716A. For example, the major microsomal metabolite of Δ 1-THC in rat is 7-hydroxy- Δ 1-THC, a product of alkyl hydroxylation, and for SR141716A, which is a diarylpyrazole, all structural modifications as a result of metabolism occur on the terminal group of the 3-substituent [17]. The major metabolic pathway of JWH-015, like WIN55212-2 [14] and AM-630 [15], is characterized by the formation of dihydrodiols via the arene oxide pathway. There are also extensive metabolic structural modifications on other parts of the JWH-015 molecule that were not observed in the metabolism of other aminoalkylindoles. For instance, the N-dealkylation appears to be a unique pathway to JWH-015

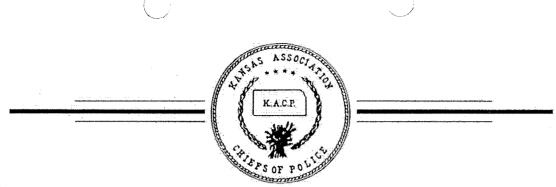
neither shared by WIN55212-2 nor by AM-630. Such metabolic transformations may have implications on the extent to which cannabimimetic properties are retained or removed in the metabolites of JWH-015.

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Testimony to the Senate Public Health and Welfare Committee In Support of SB 348

January 13, 2010

Mr. Chairman and Committee Members,

The Kansas Association of Chiefs of Police supports SB438 which proposes adding three synthetic drugs to the Schedule 1 drugs. Some of our agencies are starting to see regular abuse of these new synthetic drugs. Reports I have received indicate they are gaining popularity among high school students, parolees, and persons on probation in some areas of our state.

These drugs reportedly produce the same physiological effects as high quality marijuana. Although our experience with these new drugs is limited and long term effects are not yet clear, reports indicate these drugs may be more addictive than marijuana and probably have some carcinogenic effects as well.

We believe adding these synthetic drugs of abuse to the schedule 1 drugs is an important step toward protecting our youth and others from the negative effects and potential addiction caused by these synthetic drugs. More importantly it will take these drugs of abuse off the open access of retail outlets in the state.

We urge you to recommend this bill favorably for passage.

& Kipp

Ed Klumpp Legislative Committee Chair eklumpp@cox.net Phone: (785) 235-5619 Cell: (785) 640-1102

Public Health and Welfare Date: Attachment:

01/13/10

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Kansas County & District Attorneys Association 1200 SW 10th Avenue Topeka, KS 66604 (785) 232-5822 Fax: (785) 234-2433 www.kcdaa.org

TO: Senator Barnett, Chair Senate Public Health and Welfare
FROM: Thomas R. Stanton Deputy Reno County District Attorney Past President, Kansas County and District Attorneys Association
DATE: January 13, 2010

RE: Written testimony in support of Senate Bill 348

Chairman Barnett and Members of the Committee:

Senate Bill 348 seeks to add synthetic cannabinoids to Schedule I of the Uniform Controlled Substances Act. The legislation should be favorably considered by this committee. According to material posted on the Drug Enforcement Agency website, HU 210 is a synthetic cannabinoid which is "hundreds of times more potent than THC," the active ingredient in marijuana. Because of this, an extremely small amount the drug is psychologically active. It is, therefore, referred to as a "stealth" drug. The drug is already listed as a Schedule I drug under federal law. It is, thus, a drug which must be controlled in Kansas.

One concern with this legislation is in the form of the legislation. K.S.A. 2008 Supp. 65-4105 lists the drugs assigned to Schedule I. Subsection (d)(24) reads as follows:

(24) Tetrahydrocannabinols 7370

Synthetic equivalents of the substances contained in the plant, or in the resinous extractives of Cannabis, sp.and/or synthetic substances, derivatives, and their isomers with similar chemical structure and pharmacological activity such as the following: Delta 1cis or trans tetrahydrocannabinol, and their optical isomers Delta 6 cis or trans tetrahydrocannabinol, and their optical isomers Delta 3,4 cis or transtetrahydrocannabinol, and its optical isomers (Since nomenclature of these substances is not internationally standardized, compounds of these structures, regardless of numerical designation of atomic positions covered.)

As you can see, the statute already addresses synthetic equivalents of THC. In fact, the listed DEA control number for HU210 is 7370, the same as for THC. It would, therefore, be more prudent to add HU 210 to the non-exclusive list of known synthetic cannabinaoids as follows:

Public Health and Welfare Date: Attachment:

01/13/10

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Synthetic equivalents of the substances contained in the plant, or in the resinous extractives of Cannabis, sp.and/or synthetic substances, derivatives, and their isomers with similar chemical structure and pharmacological activity such as the following: Delta 1cis or trans tetrahydrocannabinol, and their optical isomers Delta 6 cis or trans tetrahydrocannabinol, and their optical isomers Delta 3,4 cis or transtetrahydrocannabinol, and its optical isomers (6aR, 10aR)-9-(hydroxymethyl)-6, 6-dimethyl-3-(2-methyloctan-2-yl)-6a,7,10,10-tetrahydrobenzo[c]chromen-1-ol, known also by trade or other name: HU-210, and its optical isomers (Since nomenclature of these substances is not internationally standardized, compounds of these structures, regardless of numerical designation of atomic positions covered.)

It should be noted that the DEA information suggests that there are at least six other compounds that are similar to HU 210, and my research has not yet identified those drugs. If those drugs are similarly federally controlled, they should be included in this legislation.

The DEA website suggests that the other two drugs listed in SB 348, JWH 018 and JWH 073, may not be specifically designated as Schedule I controlled substances. One article on the website stated that JWH 073 is on the DEA's list of Drugs and Chemicals of Concern. However, Kansas can certainly place these drugs in K.S.A. 65-4105(d)(24) as identified controlled synthetic cannabinoids.

There is at least one other bill before the legislature this term which was introduced in the House Corrections committee by the KCDAA to add BZP (benzylpiperazine) to the list of schedule I drugs. BZP is a synthetic drug similar to MDMA (Ecstacy) which has become an increasingly abused drug in Kansas, especially in urban areas. The DEA website states the drug is ten to twenty times more potent than amphetamine. This drug has also been listed as a schedule I drug on the federal level. The KCDAA respectfully requests an amendment to SB 348 to include BZP.

Thank you for the opportunity to present written testimony on this matter. We urge your full support and favorable recommendation of SB 348 with the friendly amendments suggested in this testimony. I would be happy to answer any questions upon request.

Kansas County & District Attacheys Association Proposed Amendment - Senate Public Health January 2010

SB 348

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1	(24)	Tetrahydrocannabinols	7370
2		Synthetic equivalents of the substances contained in the plant, or in the	
3		resinous extractives of Cannabis, sp. and/or synthetic substances, deriv-	
4		atives, and their isomers with similar chemical structure and pharma-	
5		cological activity such as the following: Delta 1 cis or trans tetrahydro-	
6		cannabinol, and their optical isomers Delta 6 cis or trans	
7		tetrahydrocannabinol, and their optical isomers Delta 3,4 cis or trans	
8		tetrahydrocannabinol, and its optical isomers (Since nomenclature of	
9		these substances is not internationally standardized, compounds of these	
10		structures, regardless of numerical designation of atomic positions cov-	
11		ered.)	
12	(25)	Ethylamine analog of phencyclidine	7455
13		Some trade or other names: N-ethyl-1-phenyl-cyclo-hexylamine;	
14		(1-phenylcycłohexyl)ethylamine; N-(1-phenylcycłohexyl)ethylamine;	
15		cyclohexamine; PCE.	
16	(26)	Pyrrolidine analog of phencyclidine	7458
17		Some trade or other names: 1-(1-phenylcyclo-hexyl)-pyrrolidine; PCPy;	
18		PHP.	
19	(27)	Thiophene analog of phencyclidine	7470
20		Some trade or other names: 1-{1-(2-thienyl)-cyclohexyl}-piperidine; 2-	
21		thienylanalog of phencyclidine; TPCP; TCP.	
22	(28)	1-[1-(2-thienyl)-cyclohexyl] pyrrolidine	7473
23		Some other names: TCPy.	
24	(29)	2,5-dimethoxy-4-ethylamphetamine	7399
25		Some trade or other names: DOET.	
26	(30)	Salvia divinorum or salvinorum A; all parts of the plant presently clas-	
27		sified botanically as salvia divinorum, whether growing or not, the seeds	
28		thereof, any extract from any part of such plant, and every compound,	
29		manufacture, salts, derivative, mixture or preparation of such plant, its	
30		seeds or extracts.	
31	(31)	Datura stramonium, commonly known as gypsum weed or jimson weed;	
32		all parts of the plant presently classified botanically as datura stramo-	
33		nium, whether growing or not, the seeds thereof, any extract from any	
34		part of such plant, and every compound, manufacture, salts, derivative,	
35		mixture or preparation of such plant, its seeds or extracts.	
36	(32)	(6aR,10aR)-9-(hydroxymethyl)-6, 6-dimethyl-3-(2-methyloctan-2-yl)-	
37		6a,7,10,10a-tetrahydrobenzo[c]chromen-1-ol	7370
38		Some trade or other names: HU-210.	
39	(33)	1-Pentyl-3-(1-naphthoyl)indole	
40	. ,	Some trade or other names: JWH-018.	
41	(34)	1-Butyl-3-(1-naphthoyl)indole	
42	/	Some trade or other names: JWH-073.	
43 /	(e)	Any material, compound, mixture or preparation which c	ontains
	(-)	······································	
/			

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(35) benzylpiperazine; Some trade or other names: BZP

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- INTELLIGENCE ALERT -

"SPICE" - PLANT MATERIAL(S) LACED WITH SYNTHETIC CANNABINOIDS OR CANNABINOID MIMICKING COMPOUNDS

The Customs and Border Protection (CBP) - Chicago Laboratory (Illinois) recently received five small, resealable, bright foil packets containing dull olive-colored plant material(s), labelled as "Spice Gold," "Spice Silver," "Spice Diamond," "Genie," and "Yucatan Fire" incense (see Photo 1, right, and Photos 2 - 3, next page), all reputedly laced with various synthetic cannabinoids or synthetic cannabinoid mimicking compounds, notably "HU-210" [(6aR,10aR)-9-(hydroxymethyl)-6,6-dimethyl-3-(2-methyloctan-2-yl)-6a,7,10,10a-tetrahydrobenzo[c] chromen-1-ol); see Figure 1, next page]. The exhibits were selected from a shipment containing approximately 1,500 such packets that were detained by a CBP agricultural specialist at an express parcel service hub in Wilmington, Ohio. The items were not smuggled but were rather part of a formal entry. Standard marijuana analyses (microscopy) of the materials were negative. Analysis of extracts by



Photo 1 - Packages are about 2 x 3 inches.

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GC/MS in the scan mode with split injection indicated only the presence of a large amount of vitamin E and other, smaller amounts of various natural products. However, when the extracts were derivatized with N,O-bis(trimethylsilyl)acetamide and injected splitless with selected ion monitoring, HU-210 was found in very small but verifiable amounts in every packet (not quantitated). The results were confirmed against a standard. These were the first such submissions to the laboratory.

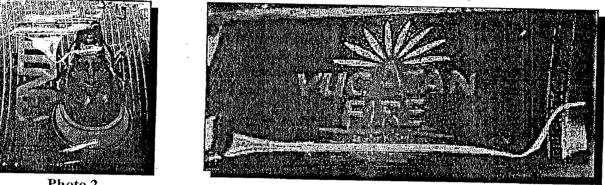
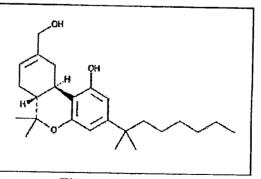


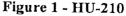
Photo 2

Photo 3

[Additional Laboratory and Editor's Notes: In addition to the above-named products, there are at least two other such herbal products: "Skunk," and "Sence." These products are currently being encountered nationwide. They, and the synthetic cannabinoids and cannabinoid mimic compounds they contain, are also the subjects of widespread discussion and speculation on the Internet. Based on anecdotal reports, HU-210 is hundreds of times more potent than THC; thus, the trace amounts detected in the above case are physiologically active, and these materials may be viewed as "stealth marijuana." The reference standard of HU-210 used in this case was purchased from Cayman Chemical of Ann Arbor, Michigan. The ions selected for the analysis were m/z 446 (100%), 530 (molecular ion), 447, 474, and 356. Note that HU-210 is named in several different ways; for example: (6aR,10aR)-3-(1,1'-dimethylheptyl)-6a,7,10,10a-tetrahydro-1-hydroxy-6,6-dimethyl-6H-dibenzo[b,d]pyran-9-methanol. HU-210 is controlled (Schedule I) in the U.S. (See: http://www.deadiversion.usdoj.gov/drugs_concern/spice/spice_hu210.htm), and products containing it and similar cannabinoids are controlled within the U.S. and in a number of other countries, including Austria, Canada, Germany, the Netherlands, and Switzerland. In addition to HU-210, there are at least half a dozen other compounds with similar

structures, plus several unrelated compounds that have cannabinoid mimicking effects (notably JWH-018 (1-pentyl-3-(1-naphthoyl)indole)), that are being used to adulterate the plant materials in "Spice" and similar products. An article presenting mass spectral data and background information on these compounds was recently published on line (not yet published in hard copy); see: Auwarter V, Dresen S, Weinmann W, Muller M, Putz M, Ferreiros N. "Spice" and other herbal blends: Harmless incense or cannabinoid designer drugs? Journal of Mass Spectrometry 2009.]





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JWH-073 (PURPORTED "SPICE" INGREDIENT) IN VIRGINIA

The Virginia Department of Forensic Science's Central Laboratory received a small glass vial containing a light yellow powder. Analysis of the powder (total net mass 0.27 gram) by color tests (Marquis - yellow to brown, Mecke - yellow), TLC, AccuTOF-DART, GC/FID and GC/MS indicated 1-Butyl-3-(1-naphthoyl)indole, also known as JWH-073. JWH-073 is a cannabimimetic indole and is included in the DEA's list of Drugs and Chemicals of Concern. It has been purported to be an ingredient in "Spice" herbal mixtures. This is the laboratory's first encounter with a "Spice" chemical.

[Editor's Notes: For more information about Spice, see: Microgram Bulletin 2009:42(3):23-24.]

* * * * *

OXYCONTIN® MIMIC TABLETS SEIZED IN VIRGINIA

The DEA Mid-Atlantic Laboratory recently received 59 round, green tablets imprinted with "80" on one face and "CDN" on the opposite face, suspected OxyContin®. The tablets (film-coated over a cream-colored interior) averaged 1.0 centimeter in diameter by 0.5 centimeters thick, and weighed approximately 303 milligrams. The tablets were presumptively identified by markings to contain 80 milligrams of oxycodone. Analysis of the tablets (total net mass 17.9 grams) by GC/MS, GC/FID, FTIR-ATR, CE and LC identified not oxycodone, but rather heroin, *l*-ephedrine, *d*-pseudoephedrine and phenylpropanolamine (not quantitated). Tramadol was also presumptively identified as the primary ingredient in the tablets. This is the first known submission of OxyContin® mimic tablets containing heroin, *l*-ephedrine, *d*-pseudoephedrine and phenylpropanolamine to the Mid-Atlantic Laboratory.

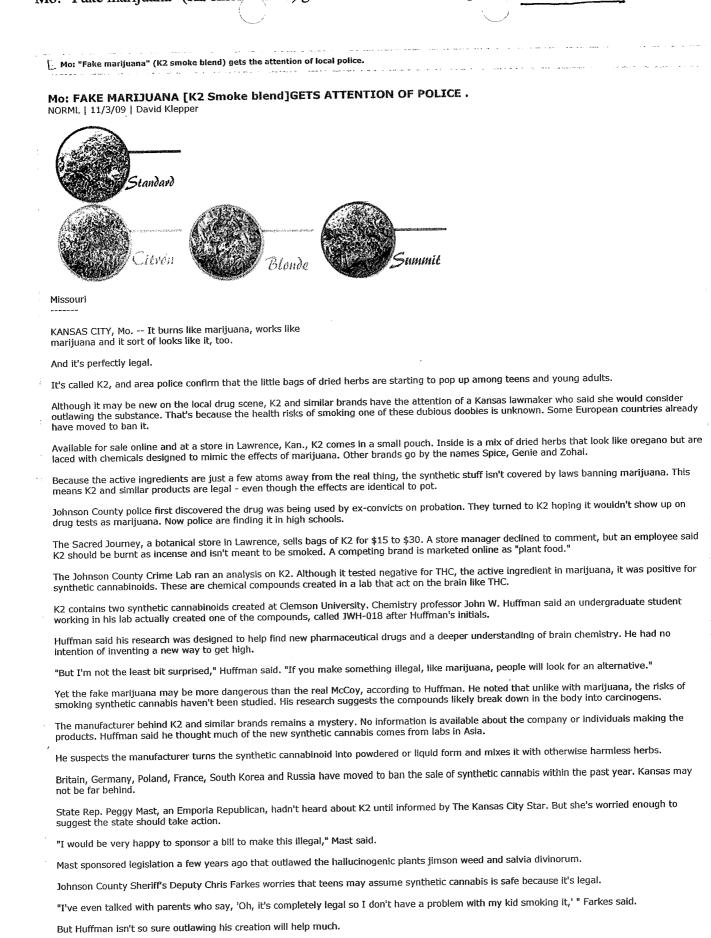
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SELECTED REFERENCES

[The Selected References section is a compilation of recent publications of presumed interest to forensic chemists. Unless otherwise stated, all listed citations are published in English. Abbreviated mailing address information duplicates that provided by the abstracting service. Patents and Proceedings are reported only by their *Chemical Abstracts* citation number.]

- Howard C, Gilmore S, Robertson J, Peakall R. A cannabis sativa STR genotype database for Australian seizures: forensic applications and limitations. Journal of Forensic Sciences 2009;54(3):556-563. [Editor's Notes: A genetic database was established with the aim of documenting the genetic diversity of Cannabis sativa in Australia for future utilization in forensic investigations. Contact: School of Botany and Zoology, The Australian National University, Canberra, ACT 0200, Australia.]
- Jermain JD, Evans HK. Analyzing Salvia divinorum and its active ingredient salvinorin A utilizing thin layer chromatography and gas chromatography/mass spectrometry. Journal of Forensic Sciences 2009;54(3):612-616. [Editor's Notes: Presents results of the subject analyses. Contact: Scientific Investigations Division, San Bernardino County Sheriff's Department, San Bernardino, CA 92415.]





http://www.marijuana.com/drug-war-headline-news/133868-mo-fake-marijuana-k2-smoke... 1/13/2010

Drug info - K2 Smoke Blend - Drugs Forum

Page 1 of 2

	an a
Ratha O Silver Member	Join Date: 14-06-2009 Location: US Posts: 58
Re: K2 Smoke Blend	•
SWIM is a pretty large male (in a big way, not a round way) weigh pounds. SWIM received 3 grams each of K2 Citron and and K2 Bloc compare to Enigma and Ex-Ses Platinum at this point.	ing in at over 230 nde. SWIM can only
Both Citron and Blonde are light in color and texture, springy, sligh appreciates given that he is still using a drugstore tobacco pipe with make small amounts of product difficult to use. The texture makes to work with than Enigma and the few Spice-alikes SWIM has expe- almost makes the whole scary "SWIM has no idea what this stuff he less pressing given the harmless, even friendly appearance of the	th a deep bowl that can them more enjoyable erienced. The texture has in it" issue seem
Both blends seem to share a smell, but SWIM can't put his finger of mentioned pineapple, which SWIM does not really smell, but SWIM getting past the sort of grain-y and pepper-y smell he detects in b from Blonde is much stronger than from Citron. Whatever it is, it h SWIM somewhat enjoys. (SWIM preferred the taste of the Citron.)	1 has a hard time oth products. The smell nas an earthiness that
SWIM found the effects of both Citron and Blonde to be significant or borderline) and reproducible. However, after using Blonde, usin largely ineffectual until all effects had cleared from SWIM's system from around 100mg to up to 250mg of each. Onset was within one following a couple of deep, held draws. SWIM felt the effects most an intermittent cognitive dampening of both input and output. No or euphoria, although SWIM was alone with no one to interact with changed the experience.	g Citron to re-up was a. SWIM has used doses a to a few minutes dy in the head, sort of spontaneous creativity
The effects were moderately floaty head and somewhat tired eyes good mental relaxation. There were few body effects according to floaty feeling of mild incoordination common to almost any buzz. I feeling, SWIM otherwise experienced no tiredness or lethargy wha eyes was a feeling rather than a need, there was no urge to close	SWIM aside from the Despite the tired eyes tsoever. Even the tired
The effects of Citron were very much like those of Blonde, with Blo more pronounced and lasting longer. Both blends had extremely s SWIM. Citron had a duration of perhaps 15 minutes with a brief per or two at very most. Blonde had a duration of 20 to 30 minutes, w little stronger and a little longer, and which then tailed off more sle abruptly disappeared. The duration for both was under half an hou higher level of effect over more of that timeframe and also retained the second half hour. There was a mild sensation of heart palpitatio occur more with Citron than Blonde, but it was primarily perception increase in heart rate, and none of this lasted for long.	hort durations for eak that lasted a minute with a peak that was a owly than Citron until it ur, but Blonde gave a ed some tired-eye into ion that seemed to
It has also been very easy for SWIM to re-up on just a hit from Blo effects, thanks to the relatively quick onset.	onde to prolong the

Most interesting is that aside from a very mild tension above the eyes, just barely enough to notice, SWIM discerns no physical or mental after-effects, does not feel mentally slow

http://www.drugs-forum.com/forum/showthread.php?t=92322

1/13/2010

and is not remotely physically tired. Within an hour, SWIM is completely back to normal. This is in contrast to SWIM's experience with Enigma, which has both head and body effects that are routinely persisting for several hours, with vestiges of a swimmy/floaty head feeling lasting for many hours beyond. SWIM is a big fan of Enigma, which is the only blend he's experienced any euphoria with so far, but if the K2 blends continue working this way SWIM will keep them around and enjoy them for their short duration.

Overall for SWIM:

- both Citron and Blonde imparted a calm, introspective mental state, a sort of disconnect without feeling dumb
- neither imparted euphoria or creativity, but SWIM was alone and cannot say for sure
- neither had more than a faint hangover, within an hour all systems seemed "go," no lethargy, no apathy, no confusion
- Citron's effects extremely short-lived. In practice, SWIM would probably only purchase Blonde, but if time was even tighter and SWIM wanted something that was even shorter acting to fit into SWIM's schedule, Citron would be right there
- SWIM would rate this a good notch below Enigma in terms of the breadth, duration and quality of effects, but if SWIM had to meet busy schedules and/or interact with others frequently either Citron or Blonde would be high on his list
- SWIM cannot compare these products to Ex-Ses Platinum, as SWIM has been unable to discern any significant effects after a bad first attempt with a small amount of the product
- SWIM is even more curious about these products given their very short duration

29-06-2009, 21:16	
	Join Date: 10-05-2008 Location: .
Lou1024 O	Posts: 110
Silver Member	
Re: K2 Smoke Blend	and the second
After further examination, swim finds K2 smoke blend to be very pr	omising.
Swim now believes that this may in fact not contain a synthetic can have a "chemical" feel that was felt almost immediately with blends duration is also typical of herbs like baybean and wild dagga.	nabinoid. It does not s like Spice Gold. It's
Upon contacting the vendor which provided the K2 smoke blend, th a well done baybean extraction he tested at one point felt somewhat	e owner claimed that at similar.
Only a few hits are needed to attain full effects, anymore than that waste. There appears to be a cap on how high you can get. Redosir minutes also appears to be meaningless. The user must wait about before a redose will effectively work. All three types (Standard, Blog effective, but there are a few differences:	ng after about 20 45 minutes to an hour
<u>Blonde-</u> The "heaviest" of the three. Very mild body buzz, but certa change of awareness and perception as with cannabis. Lasts the lor 30 minute duration for main affects and mild aftereffects for about minutes. No excessive tiredness is felt, only a small headache.	ngest with about a 20-
<u>Citron-</u> Citron has a similar duration to Standard, but is a bit more similar relaxation and change of awareness to Blonde, but its durat short, with half the aftereffects.	powerful. Provides ion is about half as
Standard- Duration is about the same as Citron with similar effects	
Note that all three types promoted relaxtion rather than a tired haze. Swim could go on with his day after 45 minutes. Total baseline is hit very quickly. "Haziness" is one reason why swim really dislikes cannabis. K2, on the other hand, is free from haziness. The minutes kept lucid and aware. Paranoia and anxiety are very very slim.	
K2 has become swims favorite smoke blend due to its short duration hangover. Swim is also comforted by the fact that it may be a natur have to worry about the possible negative side effects of a chemica	Iral blend, and not
K2 is a wonderful blend. For swim, it is a notch above cannabis.	
 Reputation Comments on this post: Good information with comparisons. 	



STEVE M. HORNBERGER UNDERSHERIFF

111 E. 11TH STREET LAWRENCE, KS 66044-2990 PHONE: (785) 841-0007 FAX: (785) 841-5168 January 13, 2010 KENNETH M. MCGOVERN SHERIFF KENNETH L. MASSEY UNDERSHERIFF

3601 E. 25TH STREET LAWRENCE, KS 66046 - 5616 PHONE: (785) 830 - 1000 FAX: (785) 830 - 1085

To: Chairperson Barnett, Vice-Chairperson Schmidt, and distinguished members of the Senate Public Health and Welfare Committee.

Chairperson Barnett and Committee Members,

I am Ken McGovern, Sheriff of Douglas County, and I stand before you today in support of Senate Bill 348.

Our department's mission is to provide effective and efficient public safety services to the citizens of Douglas County. As Sheriff I am obliged to take a stand when I see a problem on the horizon that likely threatens that public safety. I believe the product K-2, and any like it, is just such a problem.

Our concerns began in early November 2009 with media inquiries about any problems we were seeing with the herbal mixture K-2, which was being sold in Lawrence. Since its sale was legal, our joint drug enforcement unit had not had any dealings with it, other than hearing it produced a high similar to marijuana. We have since taken a closer look at K-2, and the concerns law enforcement has with its spreading use. Other experts will testify about its chemical composition, but it is generally known to contain synthetic cannabinoids, compounds designed to create a marijuana-like high. A quick search of the internet produced quite a volume of information.

Besides being available in at least one store in Lawrence, K-2 is also marketed on-line through "Twisted Herbs", a company with a Topeka address. Costs range from 3 grams for \$15 to 9 grams for \$75. They do have a disclaimer that K-2 is "not for human consumption", unlikely to be heeded by those purchasing it to smoke. On the web site <u>www.drugs-forum.com</u>, there are numerous reviews of K-2 by users, describing and rating the high they experience. Some of the reviews are dated as early as June 2009.

Use by any of our school age youth is a real concern. It is difficult enough battling the negative effects of alcohol and other illegal drugs, without having to worry about a "legal" drug. Add to the mix driving, and the negative possibilities are enormous.

Our Sheriff's Office has had several encounters involving K-2 within our facilities. We confiscated two 3 gram packages of K-2 and a pipe from an inmate who had his work release revoked. He was likely smoking it to get high and trying to technically not violate his work release orders. The compounds in K-2 will likely not be detected by any of our field drug tests. We also had a belligerent subject show up for his court first appearance. He was loudly saying he was legal because it was K-2, and offered to sell it to others around him.

In conclusion, I see this new "legal" drug as an epidemic that threatens the youth of the State of Kansas. When we were threatened with the outbreak of the H1N1 flue, the government took decisive action at every level. It is time for this committee, and the Kansas Legislature, to take decisive action against this new threat to the health and safety of our communities. I urge the passing of Senate Bill 348.

Sheriff Kenneth M. McGovern

Public Health and Welfare Date: Attachment:

01/13/10 8 Members of the committee:

I am writing to support SB 348 which is intended to gain control of the explosively popular new drug of abuse, K-2.

K2 abuse has already been seen around Kansas and sporadically throughout the United States. It is considered a fairly potent intoxicant, and is showing up particularly among young people. One of the major difficulties is that there is a significant lack of systematic research as to the long-term effects of the drug. Reports of its use, however, point to significant intoxication and difficulty with coordination.

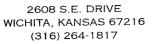
Among street drug abusers, K2 is referred to as the new marijuana. It is most disturbing that there is such a surge in use among young people. That alone should compel us to move swiftly and aggressively. The major ingredients of K2 potentially lend themselves to becoming elements of synthetic drugs of abuse resembling marijuana.

I encourage the committee to move aggressively to help prevent future problems with a serious new drug of abuse. It is relatively rare that we have the opportunity to stop or significantly slow the onset of a new drug of abuse. By passing this legislation, Kansas will be at the forefront of the country in moving to shut down a harmful new problem drug.

Sincerely,

Eric A. Voth, M.D., FACP Chairman The Institute on Global Drug Policy

Public Health and Welfare Date: Attachment: STATE OF KANSAS



STATE CAPITOL, ROOM 242-E TOPEKA, KANSAS 66612 (785) 296-7355 mike.petersen@senate.ks.gov



COMMITTEES VICE CHAIR: UTILITIES MEMBER: LOCAL GOVERNMENT TRANSPORTATION JOINT COMMITTEE ON INFORMATION TECHNOLOGY

SENATOR MIKE PETERSEN

SB 348

I would like to thank the Chair and committee members for the expedient scheduling of this hearing.

The substances being banned in this bill are being used in mixtures which have chemical properties simmular to THC (tetrahydrocannadbianol) found in marijuana and are being sold as incense. Smoking these may cause impaired judgment and reduced fine motor skills. Mixtures being sold have not been thoroughly tested for long tern negative health impacts. Reports have been published that the mixtures do not show up in basic drug screenings. We need to be concerned that the increased attention to these products may cause more people to think that because they are legal they are safe.

For the safety of our consumers and all citizens of our State we need to take a proactive stance on this issue quickly

Senator Mike Petersen District 28

Public Health and Welfare Date: Attachment:

01/13/10 10