



Postmortem Tissue Distribution of AB-CHMINACA Following Lethal Intoxication Compared with AB-CHMINACA Concentrations in Impaired Drivers

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Abstract

Introduction: N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide, also known as AB-CHMINACA, is a heterocyclic indazole-based synthetic cannabinoid (SC). AB-CHMINACA and other SCs have psychoactive and pharmacological effects similar to delta-9-tetrahydrocannabinol and continue to have popularity as recreational drugs. Unlike Δ⁹-THC, these drugs have severe toxicities and reported deaths. Recent studies indicate these cannabimimetic agents exert their pharmacologic effects as potent agonists at the cannabinoid 1 (CB₁) and cannabinoid 2 (CB₂) receptors. As of January 2015, AB-CHMINACA is a DEA Schedule I drug.

Objective: This report describes two post-mortem AB-CHMINACA cases, one single and one multiple drug intoxication, and three driving under the influence of drugs (DUID) cases involving AB-CHMINACA impairment.

Method: The first decedent was a 23 year old, white male recently released from a rehabilitation facility for marijuana abuse; he was last known alive about 5 hours before being found dead in the driveway at home. The second decedent was a 33 year old white female with a history of past heroin abuse and current methadone treatment. She was found at home in a state of moderate decomposition. She was last known alive two days earlier when leaving a party. The impaired drivers were males 21-34 years of age. The first two individuals were stopped by police for erratic driving and the third individual drove into a home. AB-CHMINACA and SC concentrations were measured in the various tissues: blood, urine, vitreous, gastric, liver, kidney, brain, bile and hair. Comprehensive toxicology and drug chemistry analyses were performed on multiple specimens and drug exhibits using gas chromatography/mass spectrometry. The detection of SCs and AB-CHMINACA in tissues and fluids was accomplished using ultra performance liquid chromatography/tandem mass spectrometry after liquid-liquid extraction and in hair using high performance liquid chromatography/tandem mass spectrometry after solid-phase extraction.

Results: Postmortem cases:

Case #1: AB-CHMINACA was present at 7.0, 16.9 ng/mL in the femoral and heart blood, 59.2 ng/40 mL in the gastric and 404 ng in the liver, and 46.7 ng/mL in the bile. AB-CHMINACA mono-hydroxyl metabolite was present in the urine. With the exception of caffeine and cotinine, no other drugs, including synthetic stimulants, were found to be present in the femoral blood.

Case #2: AB-CHMINACA was present at 7.1, 7.8 ng/mL in the femoral and heart blood, 115 ng/g in the liver, 26.5 ng/g in the kidney and 21.3 ng/g in the brain. AB-CHMINACA was also present in the hair, consecutive 30-day hair segments from the root end were found to contain AB-CHMINACA at 29.9, 25.9 and 37.2 pg/mg. Femoral blood from the decedent also contained 167 ng/mL methadone, 29.6 ng/mL EDDP, and < 0.05 mg/L diphenhydramine; β-phenethylamine and cotinine were reported as present. Drug Chemistry exhibits were found to contain AB-CHMINACA in both postmortem cases.

DUID cases (Cuyahoga and Lake Counties):

Case #1: Blood from the first driver contained 10.8 ng/mL AB-CHMINACA and 0.20 ng/mL AB-PINACA.

Case #2: 1.4 ng/mL of AB-CHMINACA, present in blood from the second driver.

Case #3: AB-CHMINACA was reported as present in the third driver. No additional drugs, other than those noted, were detected in the three DUID cases.

Drug Chemistry exhibits were found to contain AB-CHMINACA in the third driving case; exhibits from the first driver were found to contain AB-FUBINACA. No exhibits were submitted in the second driving case.

Conclusions: The cause of death in case #1 was ruled a single drug “acute intoxication by AB-CHMINACA” resulting in cardiac arrhythmia. AB-CHMINACA was distributed among multiple tissues with values ranging from 7.0 ng/mL femoral to 404 ng/g liver. Tissue and fluids associated with detoxification had higher concentrations of AB-CHMINACA. The cause of death in case #2 was ruled an “acute intoxication by the combined effects of AB-CHMINACA, methadone and diphenhydramine” resulting in cardiac arrhythmia. The manner of death for both cases was “accidental”. All the DUID drivers were deemed “impaired” based on a standardized field sobriety test. The lethal and the impairment/DUID range of AB-CHMINACA appears to overlap in these cases.

Key Words: AB-CHMINACA, Synthetic Cannabinoids, Postmortem, Impairment

Objective

This report describes two post-mortem AB-CHMINACA cases, one single and one multiple drug intoxication, and three driving under the influence of drugs (DUID) cases involving AB-CHMINACA impairment.

Introduction

N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide also known as AB-CHMINACA is a heterocyclic indazole-based as opposed to an indole ring based (JWH-018), synthetic cannabinoid (SC).

AB-CHMINACA and other SCs have psychoactive and pharmacological effects similar to Cannabis sativa, delta-9-tetrahydrocannabinol, (Δ⁹-THC). Recent studies indicate these cannabimimetic agents SCs exert their pharmacologic effects as potent agonists at the cannabinoid 1 (CB₁) and cannabinoid 2 (CB₂) receptors.¹⁻²

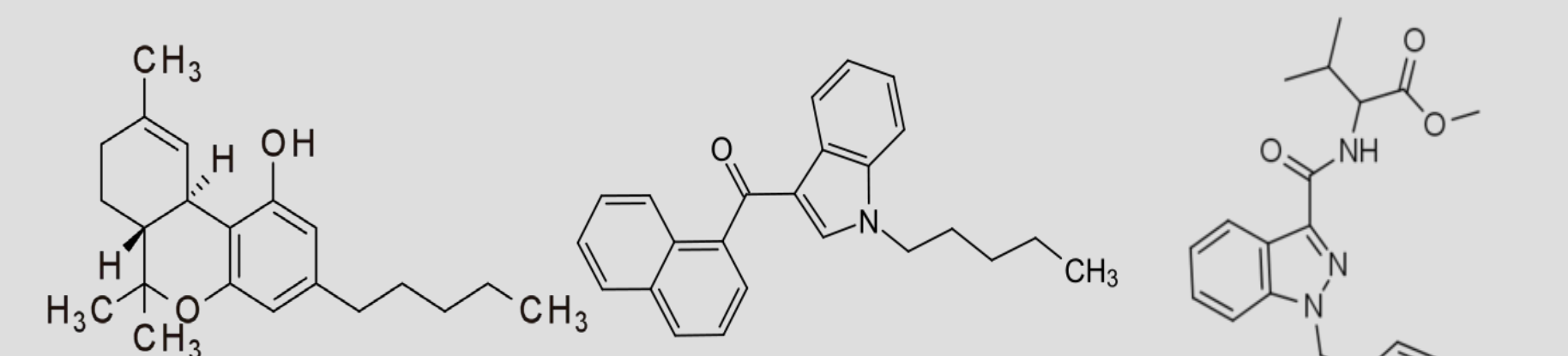
AB-CHMINACA and other SCs continue to have popularity as a recreational drugs. Unlike Δ⁹-THC, they have high abuse potential, severe toxicities, significant central nervous system, respiratory depression, and reported deaths.³⁻⁷ They have also been associated in DUID and impairment cases.⁸⁻¹⁰

As of January 30, 2015, AB-CHMINACA is a DEA Schedule I drug.⁷ The State of Ohio is also taking measures to schedule current and future synthetic cannabinoids.¹¹

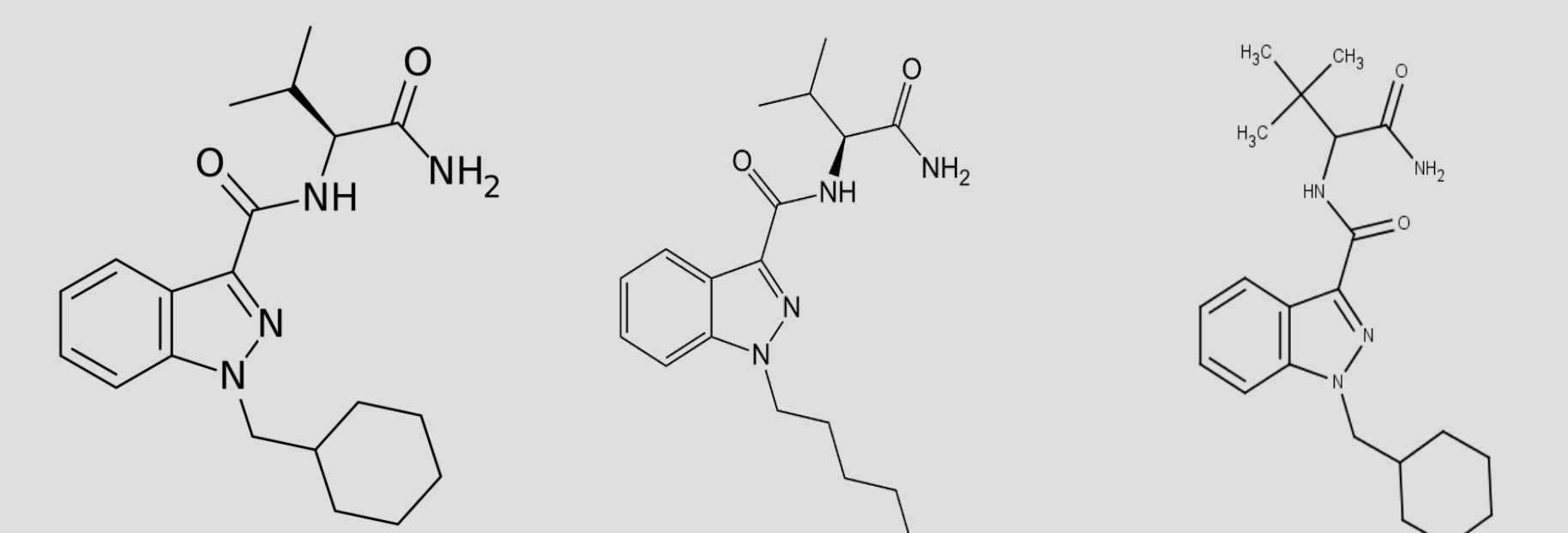
The next synthetic cannabinoid implicitly controlled as a DEA Schedule I drug is ADB-CHMINACA or MAB-CHMINACA.¹² Numerous analytical methods have been published for the analysis of synthetic cannabinoids.¹³⁻¹⁹

Structures: Δ⁹-THC and Synthetic Cannabinoids:

Δ⁹-THC JWH-18 AB-FUBINACA



AB-CHMINACA AB-PINACA ADB-CHMINACA



Case Histories:

- The first decedent was a 23 year old, single, white male recently released from a rehabilitation facility for marijuana abuse.
 - He was last known alive about 5 hours before being found dead, in the driveway at home. A packet of suspected synthetic marijuana labeled “Anonymous Potpourri” was collected at the scene.
- The second decedent was a 33 year old white female with a history of past heroin abuse and current methadone treatment. She was found at home, at the bottom of the stairs, in a state of moderate decomposition.
 - She had recently received a medically supervised methadone injection the day of her death. She was last known alive two days earlier when leaving a party. Cigarette paraphernalia was submitted to drug chemistry for analysis.
- The impaired drivers were males 21-34 years of age. The first two individuals were stopped by police for erratic driving and the third individual drove into a home.

Materials/Methods

Toxicological analysis:

- Comprehensive toxicology and drug chemistry analyses were performed on multiple specimens and drug exhibits using gas chromatography/mass spectrometry for therapeutic and drugs of abuse at the Cuyahoga County Medical Examiner's Office for the postmortem and the Driving under the influence of Drugs (DUID) cases from Cuyahoga County.

- Toxicological analysis was performed on the DUID cases from Lake County, Ohio on various specimens for drugs of abuse (9-panel ELISA screen) and for volatiles.

AB-CHMINACA and SCs Analysis:

- AB-CHMINACA and SC concentrations were measured in the various tissues: blood, urine, vitreous, gastric, liver, kidney, brain, bile and hair.

- The detection of SCs and AB-CHMINACA in tissues and fluids was accomplished using ultra performance liquid chromatography/tandem mass spectrometry after liquid-liquid extraction by AIT Laboratories, Indianapolis, IN, USA.

- Specimens were extracted at a basic pH into n-butyl chloride. Separation and detection was completed by a Waters Acquity UPLC coupled to a Waters LCT Premier XE TOF mass spectrometer as well as a Waters Acquity UPLC coupled to a Waters tandem quadrupole detector (TQD). The analytical column for both analyses was a Waters BEH C18, 2.1 x 100 mm, 1.7 μm particle size. > 0.1mg.

- The hair extraction and analysis for SCs and AB-CHMINACA were performed at Omega Laboratories, Mogadore, OH, USA, using high performance liquid chromatography/tandem mass spectrometry after solid-phase extraction using a Phenomenex Strata-X-Drug N polymeric reverse phase SPE column and an in-house method for Synthetic Cannabinoids.

- Separation and detection was accomplished by using a LC – tandem mass spectrometry (MS-MS) system consisting of an Agilent 6430 LC triple quadrupole mass spectrometer (Santa Clara, CA) operated in electrospray ionization (ESI) in positive mode, and an Agilent 1290 Infinity HPLC system.

Results

Forensic Autopsy Findings:

- Both autopsies were performed at the Cuyahoga County Medical Examiner's Office. Multiple specimens were collected and submitted for a comprehensive toxicology analysis as indicated in the tables below.

Case #1:

- Findings showed no evidence of congenital or acquired disease. There was myocardial ischemia, a 390-gram heart, pulmonary congestion and edema (right lung 660 g, left lung 640g), agonal food aspiration, leptomeningeal congestion (cerebral edema) and moderate hepatic macrovesicular steatosis (fatty liver) and obesity (292 lb).

Case #2:

- Findings showed mild to moderate decomposition changes. There was no evidence of trauma. There was congenital absence of the right kidney.

Results & Discussion

Postmortem Cases:

AB-CHMINACA: Postmortem Drug distribution among multiple matrices.

Specimen (ng/mL)	Femoral Blood	Heart Blood	Urine	Gastric	Vitreous	Bile	Liver (ng/g)	Kidney (ng/g)	Brain (ng/g)	Hair	Drug Chemistry exhibits
Case #1	7.0	16.9	*Pos	59.2 ng /40mL	Negative	46.7	404	NTDN	NTDN	NTDN	AB-CHMINACA
Case #2	7.1	7.8	NTDN	NTDN	NTDN	NTDN	115	26.5	21.3	**AB-CHMINACA	AB-CHMINACA

NTDN=No testing performed.

- Case #1:** Caffeine and cotinine were present. No other drugs, including synthetic stimulants, were present in the femoral blood. No ante-mortem admission blood samples were available for subsequent analysis. *AB-CHMINACA monohydroxyl metabolite was present in the urine. AB-CHMINACA was present in the “potpourri” paraphernalia.

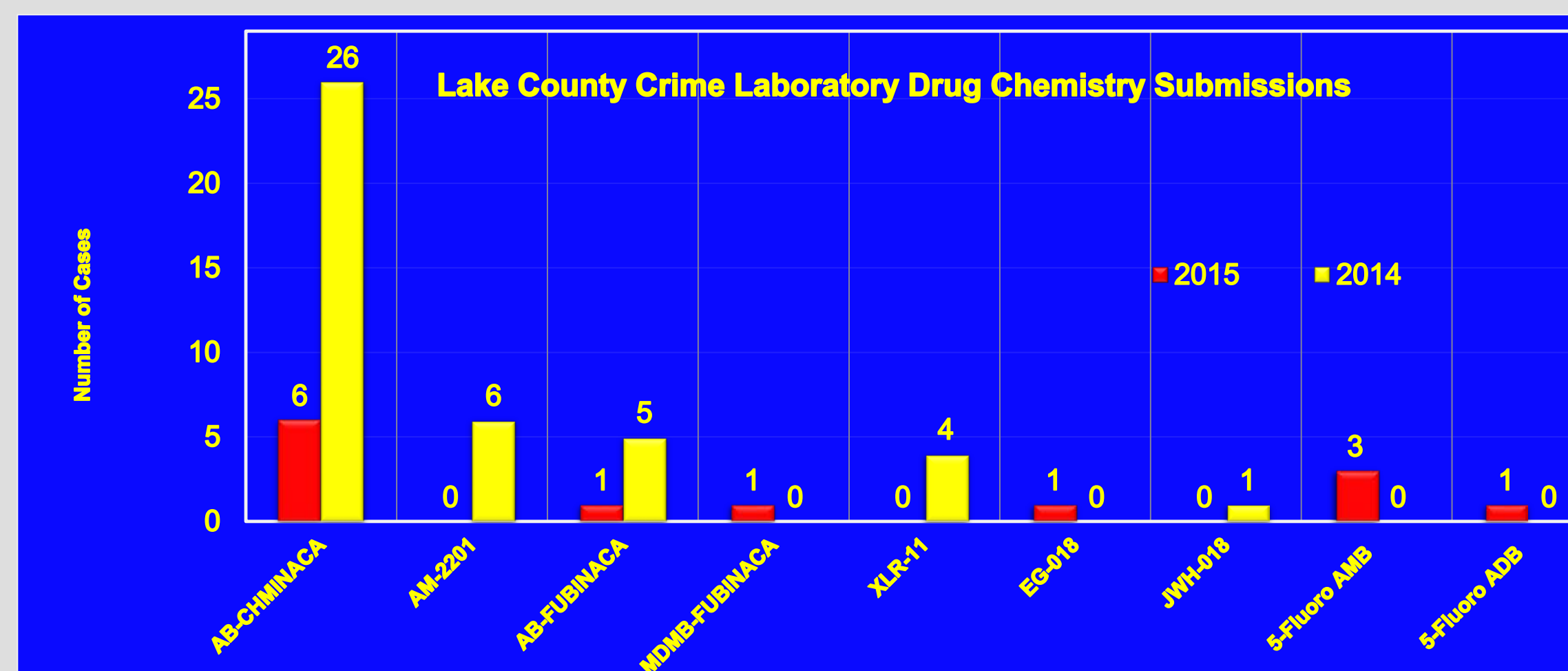
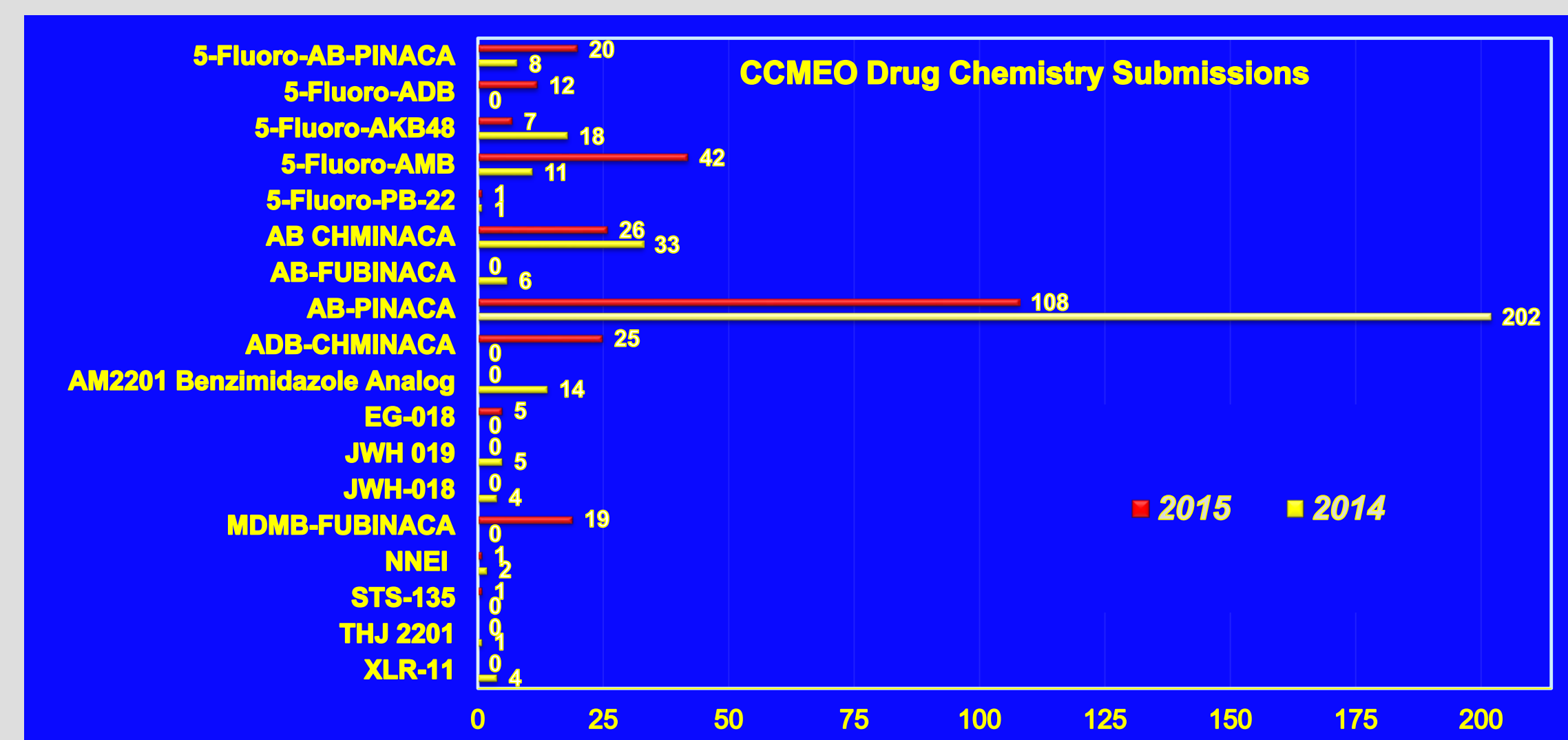
- Case #2:** Femoral blood contained 167 ng/mL methadone, 29.6 ng/mL EDDP, and < 0.05 mg/L diphenhydramine; β-phenethylamine and cotinine were present.
 - Hair: Consecutive** 30-day hair segments from the root end were found to contain AB-CHMINACA at 29.9, 25.9 and 37.2 pg/mg.
 - AB-CHMINACA was present in submitted cigarette.

DUID cases (Cuyahoga and Lake Counties):

	Driving Offense	AB-CHMINACA	AB-PINACA	Comprehensive Toxicology Testing	Drug Chemistry Results
Driver #1	Erratic Driving	10.8 ng/mL	0.20 ng/mL	None detected	AB-FUBINACA
Driver #2	Erratic Driving	1.4 ng/mL	7.8 ng/mL	None detected	None submitted
Driver #3	Drove into a House	Present	None detected	None detected	AB-CHMINACA

- Standardized sobriety tests were performed at the scene and all the drivers were considered “impaired”. No additional drugs, other than those noted, were detected in the three DUID cases.

Drug Chemistry Submissions: Synthetic Cannabinoids 2014/2015



Conclusions

- In **case #1** AB-CHMINACA was distributed among multiple tissues with values ranging from:
 - 7.0 ng/mL femoral to 404 ng/g liver.
 - The cause of death was ruled a single drug “acute intoxication by AB-CHMINACA” resulting in cardiac arrhythmia.
- In **case #2** AB-CHMINACA was distributed among multiple tissues with values ranging from:
 - 7.1 ng/mL femoral to 115 ng/g liver.
 - The cause of death was ruled, “acute intoxication by the combined effects AB-CHMINACA, methadone and diphenhydramine”, resulting in cardiac arrhythmia.
- Tissue and fluids associated with detoxification had higher concentrations of AB-CHMINACA in both cases.
- The manner of death for both post-mortem cases was “accidental”.
- All the **DUID drivers** were deemed “impaired” based on a standardized field sobriety test.
- The lethal and the impairment/DUID range of AB-CHMINACA appears to overlap in these cases.

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