CASE REPORT

TOXICOLOGY

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Driving Under the Influence of Synthetic Cannabinoid Receptor Agonist XLR-11*

ABSTRACT: The case of a 22-year-old male Caucasian driver is presented. He was involved in a traffic collision. At the roadside, he displayed blank stare and mellow speech with a barely audible voice. A DRE found low body temperature, rigid muscle tone, normal pulse, lack of horizontal and vertical gaze nystagmus, nonconvergence of the eyes, dilated pupil size, and normal papillary reaction to light. A standard toxicology DUID protocol was performed on the driver’s whole blood including ELISA and GC-MS drug screens with negative results. Additional drug screening was undertaken for bath salts and synthetic cannabinoid receptor agonists by LC-MS/MS by a commercial laboratory and identified the synthetic cannabinoid receptor agonist XLR-11 in the driver’s blood. XLR-11 was subsequently quantified at 1.34 ng/mL. This is the first documented case involving a driver operating a motor vehicle under the influence of the synthetic cannabinoid receptor agonist XLR-11.

KEYWORDS: forensic science, forensic toxicology, human performance forensic toxicology, driving under the influence of drugs, drug recognition expert, synthetic cannabinoid receptor agonist, spice, blueberry spice, XLR-11, San Francisco

Recreational use of synthetic cannabinoid receptor agonists, also known as “spice,” has increased in popularity in recent years (1). The term “spice” refers to a wide variety of herbal mixtures that produce experiences similar to those of cannabis and which are marketed as safe highs or legal alternatives to marijuana (2). Many of these compounds were first synthesized by the South Carolina-based academic organic chemistry research group of John W. Huffman who attempted to synthesize marijuana metabolites and analogues for their promise in treating nausea and glaucoma and as appetite stimulants (3). Many of these compounds also appear to incorporate Huffman’s initials (JWH) in their names: JWH-019, JWH-073, etc. There has been a recent explosion of “spice” compounds worldwide, and legislative representatives, law enforcement agencies as well as forensic and analytical laboratories have a difficult time keeping up with the myriad of new compounds continuously appearing on the streets marketed to the general public as “incense” or “fake weed” (4). In San Francisco, there has been an increase of synthetic cannabinoid receptor agonists in cases coming under the jurisdiction of the Forensic Laboratory Division of the Office of the Chief Medical Examiner of the City and County of San Francisco including postmortem forensic toxicology cases as well as human performance forensic toxicology cases (e.g., drug-facilitated sexual assaults). In the present case report, the case of a 22-year-old Caucasian male driver is presented in which the only psychoactive compound detected in his blood was the synthetic cannabinoid receptor agonist XLR-11. His driving pattern, behavior and demeanor, performance on field sobriety tests as well as results of the toxicologic analyses performed on his whole blood are also included making this the first documented case in San Francisco or elsewhere presenting the entire spectrum of observations and findings in a driver driving under the influence of XLR-11.

Case Report

Two uniformed police officers riding in a marked police car were flagged down by a member of the public alerting them to an accident at 1245 h in the afternoon. The officers quickly located a cargo truck stopped in the number 1 lane of a busy street and a female (W2), later identified as the driver of the car the truck had collided with, standing at the open passenger door of the stopped cargo truck. There was also a male (S1), later identified as the cargo truck’s driver, standing at the open passenger door of the truck. The truck’s engine was running and the keys were in the ignition. W2 stated to the officers that “this guy hit my car and I think he is really high on weed.” The officers noticed the characteristic odor of marijuana on the breath and clothing of S1 who was also reported to have “watery, bloodshot eyes.” When S1 was asked by the officers if he was injured in any way, he answered after a long pause and said he was not hurt. The officers noted that when S1 spoke, he had slurred speech. For the safety of all parties involved, the officers directed them to move onto the sidewalk but S1 appeared not to comprehend the officers’ instructions. One of the officers then attempted to move S1 onto the sidewalk, and he noted that as he grabbed S1’s right elbow area, his muscles tensed and he became rigid. During normal witness interviews, W2 stated that she was stopped behind a tow truck that was blocking her lane.

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*Presented in part at the 66th Annual Meeting of the American Academy of Forensic Sciences, February 17–22, 2014, in Seattle, WA.

Received 17 June 2013; and in revised form 24 Sept. 2013; accepted 13 Oct. 2013.
of travel and that while stopped, the truck S1 was driving collided with the rear of her vehicle. W2 also stated that the truck S1 was driving continued to slowly drive away after the collision but that she exited her vehicle and walked up to the truck S1 was driving continued to slowly drive away after the collision. During his roadside interview, S1 admitted that he was the one driving the truck and stated that he was unaware of anything being mechanically wrong with his vehicle. When asked, he also stated that he was not diabetic or epileptic. S1 responded "Yes" when asked "where were you stopped?" and stated that he had not been drinking alcohol. S1’s speech was described as “mellow” and his voice as “barely audible above the ambient street noise.” His bodily movements at the roadside were described as “slow,” and the investigating officer felt that S1 was “under the influence of a depressant or narcotic.” S1 said to the investigating officer that he was trying to switch lanes and accidentally hit the vehicle in front of him. Because of the high suspicion that he was under the influence of a substance while operating his vehicle, S1 was placed under arrest at 1305 h and his evaluation by a police officer certified as drug recognition expert (DRE) was requested.

Evaluation by Drug Recognition Expert and Field Sobriety Test Performance

The DRE evaluation of S1 started 105 minutes after the traffic collision at 1430 h after he was transported to a local police station. The standardized DRE Evaluation Interview Questions/Answers and Physical Evaluation and Field Sobriety Test Results of this driver are presented in Table 1. During his interview, S1 stated that he had not smoked “real marijuana for almost a month” but that had recently used “blueberry spice.”

Blood Specimen, Analytical Protocol, and Toxicologic Findings

Whole blood was collected by venipuncture under vacuum in three sterile blood collection glass tubes (BD Vacutainer® by Becton Dickinson and Company, Franklin Lakes, FL) after S1’s arm was cleaned using a new benzalkonium chloride antiseptic and germicide towelette (PSS World Medical, Inc., Jacksonville, FL) Each test tube contained 100 mg sodium fluoride as preservative and 20 mg potassium oxalate as anticoagulant and was inverted a few times after the blood collection for mixing purposes. The biological evidence was transported to the Forensic Laboratory Division of the San Francisco Office of the Chief Medical Examiner under Chain of Custody and was first tested for forensic alcohol analysis under Title 17 of the Code of Regulations of the State of California but produced negative results. The blood was then subjected to the standard drug screening protocol for driving under the influence of drugs (DUID) cases employing commercially available screening techniques including enzyme-linked immunosorbent assay (ELISA) and full-scan gas chromatography—mass spectrometry (GC-MS) for amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, methadone, phencyclidine, opiates/opioids and over one hundred other drugs and metabolites. All in-house toxicologic screens produced negative results, and a portion of the blood specimen was then transported under Chain of Custody to an accredited commercial reference analytical laboratory (NMS Labs, Willow Grove, PA) for synthetic cannabinoid receptor agonist and bath salt screening by LC-MS/MS. Specifically, the synthetic cannabinoid receptor agonist screen was undertaken on an ACQUITY® ultra-performance liquid chromatographic (UPLC) system coupled with a tandem quadrupole mass spectrometric detector (TQD) by Waters Corporation (Milford, MA). The analytical column utilized was the ACQUITY® UPLC BEH C18 reversed-phase column (1.7 µm, 2.1 x 100 mm) which has a very wide usable pH range (pH 1–12) and is suitable for UPLC separations due to its trifunctionally bonded ethylene-bridged hybrid (BEH) particles. The mobile phase was a mixture of 0.1% formic acid in deionized water and 0.1% formic acid in methanol. The injection volume was 20 µL. Data analysis was performed on the MassLynx™ MS Software platform by Waters Corporation. Target compounds included A-796260, AM-1248, AM-2201, AM-2233, AM-694, JWH-018 5-chloropentyl, JWH-018, JWH-019, JWH-022, JWH-073, JWH-081, JWH-122, JWH-200, JWH-203, JWH-210, JWH-250, RCS-4, RCS-8, UR-144, and XLR-11. All target compounds had a limit of detection of 0.10 ng/mL except...
JWH-022 whose limit of detection was 0.20 ng/mL. The deuterated internal standards JWH-200-d₄, AM-694-d₄, AM-2201-d₅, RCS-4-d₅, JWH-073-d₆, JWH-250-d₇, JWH-203-d₁₁, JWH-018-d₁₀, JWH-081-d₁₀, JWH-122-d₁₀, JWH-019-d₁₃, and JWH-210-d₉ were used. The MS/MS ion transitions monitored were 330.3→125.2 and 330.3→232.3 for synthetic cannabinoid receptor agonist XLR-11. Calibration curves (similar to the one shown in Fig. 1) were made by spiking drug-free blood at 0.10, 0.20, 1.0, 4.0, 10.0, and 20.0 ng/mL. MRM chromatograms of a typical blank, a positive quality control spiked with XLR-11 and this driver’s whole blood specimen, are shown in Fig. 2. Synthetic cannabinoid receptor agonist XLR-11 was identified in the biological specimen of this driver and later quantified in a second blood aliquot at a concentration of 1.34 ng/mL.

Discussion and Conclusion

Synthetic cannabinoid receptor agonist XLR-11 (also known as 5-fluoro-UR-144) has the chemical name (1-(5-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone and is a “spice” compound recently encountered on the worldwide designer street drug market. It is a white powder with a molecular weight of 329, a melting point of 73°C and the mass spectrum shown in Fig. 3 (5). In the United States of America, it is controlled under the Federal Controlled Substances Act (Schedule I). Its chemical structure shows great similarities to other federally scheduled substances such as JWH-018, AM-2201, and UR-144 (Fig. 4). Synthetic cannabinoid receptor agonist XLR-11 is believed to cause similar pharmacologic effects as JWH-018, that is, it lowers body temperature, produces analgesia, decreases overall activity, and precipitates catalepsy, that is, a state of trance or seizure-like with loss of sensation and consciousness and rigidity or stiffness of the body (6). In the present case report, the police officers were presented with a young Caucasian driver who appeared really “high on weed,” was cooperative, had a blank stare, was slow in responding to questions, and who appeared to have comprehension difficulties. He was found to be rigid with robotic movements and poor balance and needed to use his arms to maintain his balance. The officers also detected an unusual odor which they described as “unknown burnt smokey smell.” A DRE evaluation of the driver found, among other signs, low body temperature, rigid muscle tone, normal pulse, lack of HGN, lack of VGN, nonconvergence of the eyes, dilated pupil size, and normal papillary reaction to light. Standard ethanol and drug screens were negative but testing by a commercial reference analytical laboratory detected XLR-11 by LC-MS/MS as the only psychoactive compound in the whole blood specimen of the driver who was involved in a motor vehicular accident. During the DRE evaluation, driver S1 mentioned that he had previously used “blueberry spice” but did not state exactly when that use had occurred. His whole blood was found to contain XLR-11 at a concentration of 1.34 ng/mL approximately 214 min after the traffic accident. Such low blood concentrations necessitate early collection of blood evidence, and police officers should be aware of this limitation. Additionally, agencies and toxicology laboratories involved in the investigation of alleged DUI cases can no longer just rely on past analytical protocols that involve alcohol and those drugs traditionally encountered in such cases but they should, instead, consider including screening techniques for the new synthetic drugs

FIG. 1—Calibration curve for synthetic cannabinoid receptor agonist XLR-11 ranging from 0.10 to 20.0 ng/mL.

![FIG. 1](image)

<table>
<thead>
<tr>
<th>Compound name: XLR11 Qual A</th>
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<tr>
<td>Coefficient of Determination: R² = 0.999815</td>
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<tr>
<td>Calibration curve: 134.98 * x^2 + 30228 * x + 384.361</td>
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<tr>
<td>Response type: External Std, Area</td>
</tr>
<tr>
<td>Curve type: 2nd Order, Origin: Exclude, Weighting: 1/x, Axis trans: None</td>
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![FIG. 2](image)

**FIG. 2**—MRM XLR-11 chromatograms of (A) blank, (B) positive quality control, and (C) driver S1’s whole blood specimen.
now seen in the designer street drug market, especially after reading the police report and familiarizing themselves with the driver’s symptoms and signs observed at the roadside. This case clearly demonstrates that had it not been for the contracted analytical capabilities of a commercial laboratory such as NMS Labs that is able to screen for synthetic cannabinoid receptor agonists and metabolites, and this case would have erroneously been treated by the toxicologists, police, prosecutors, and defenders as a toxicologically negative case when in fact it was positive for the synthetic cannabinoid receptor agonist XLR-11. Although the Forensic Laboratory Division of the San Francisco Office of the Chief Medical Examiner has previously encountered the presence of synthetic cannabinoid receptor agonists in other types of cases including drug-facilitated sexual assaults and postmortem toxicology cases (7), this is the first documented case involving a driver who was driving under the influence of the synthetic cannabinoid receptor agonist XLR-11 in San Francisco or anywhere else. This case report will function as a reference and educational tool for toxicologists, police officers, attorneys, and legislators as, for the first time, it includes details of the driving pattern, demeanor, and behavior, as well as performance on field sobriety tests, objective signs of intoxication, forensic toxicologic findings, and whole blood concentration of XLR-11 approximately 214 min after driving.

Acknowledgments

The employees of the Forensic Laboratory Division of the Office of the Chief Medical Examiner of the City and County of San Francisco are hereby acknowledged for the performance of accurate and timely toxicologic testing in this case per existing work orders with the San Francisco Police Department. The San Francisco Police Department’s invaluable assistance is also acknowledged in the release of (i) the case incident report, (ii) the driving under the influence arrest investigation report, (iii) the traffic collision report, and (iv) the drug recognition evaluation. NMS Labs in Willow Grove, PA, is hereby acknowledged for (i) the performance of ordered analytical work and (ii) the provision of the associated analytical data support package. NMS Labs received remuneration in accordance with agreed fees as an approved vendor for the provision of unusual or infrequent toxicologic analyses for the City and County of San Francisco’s Office of the Chief Medical Examiner.

References


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