B138 Differentiation and Identification of U-47700, U-51754, and U-49900 Using Gas Chromatography/Mass Spectrometry (GC/MS) and Nuclear Magnetic Resonance (NMR) Spectroscopy

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Learning Overview: After attending this presentation, attendees will understand methods to differentiate and identify emerging synthetic opioids U-47700, U-51754 and U-49900 using gas chromatography/mass spectrometry (GC/MS) and nuclear magnetic resonance (NMR) spectroscopy, including the influence of salt forms and solubility.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by demonstrating methods to rapidly analyze emerging synthetic opioid new psychoactive substances (NPS) "legal high" compounds.

U-47700 (*trans*-3,4-dichloro-*N*-[2-(dimethylamino)cyclohexyl]-*N*-methyl-benzamide, 329.3 g/mol), also known as “Pink”, “Pinky”, or “U4”, is a synthetic opioid known to be 7.5 times the potency of morphine and binds the mu opioid receptor. It has been documented in cases to cause adverse effects such as respiratory depression, cyanosis, pinpoint eyes, and tachycardia. U-47700, which gained popularity in U.S. forensic laboratories in 2015, was placed into a 24-month emergency action Schedule I by the Drug Enforcement Administration (DEA) in 2016 after a surge of deaths were confirmed as linked to it. Surrounding this scheduling, two structural analogs of U-47700 appeared in the drug market, U-51754 (*trans*-3,4-dichloro-*N*-[2- (dimethylamino)cyclohexyl]-*N*-methyl- benzeneacetamide, 343.3 g/mol) and U-49900 (*trans*-3,4-dichloro-*N*-[2-(diethylamino) cyclohexyl]-*N*-methyl-benzamide, 357.3 g/mol). These newer synthetic opioids have not been scheduled and very little literature or data is available. U-51754 is described by users as more dysphoric and dissociating than U-47700. However, key information is missing about both U-51754 and U-49900 including GC retention times, MS fragmentation patterns and NMR spectra. While current methods primarily focus on the detection of traditional opioids in drug-related overdoses the ever-adapting drug market makes it imperative for an increase in optimal methods that will detect, differentiate, and identify the emerging synthetic opioids.

1D and 2D NMR spectra for U-49900 are available in a recent publication.[1] H NMR spectra (32 scans) were collected on a 400 MHz JEOL SS NMR spectrometer for each synthetic opioid (5 mg commercial standard) dissolved in 0.7 mL of deuterated chloroform. A mixture of U-49900 and U-51574 was created using 0.150 mL and 0.300 mL, respectively, of the above samples. U-51754 and U-49900 differ in structure: U-51754 has a dimethyl substituent group on the cyclohexylamine and U-49900 has a diethyl substituent group in that position. U-51754 also has a methylene separating the chlorinated benzene ring from the amide bond than can be used to differentiate it from U-47700. These differences are reflected in the NMR spectra and can be used to identify the components of the mixture: U-51754 exhibited a singlet at 1.7 ppm attributed to its cyclohexylamine dimethyl groups and U-49900 exhibited a quadruplet at 2.65 ppm and 3.4 ppm attributed to the CH_2 in its diethyl groups and a triplet at 1.0 ppm corresponding to the CH_3 of the cyclohexylamine ethyl group. GC/MS spectra of each substance and separation of a mixture of the three synthetic opioids will also be presented. UV-Vis and ATR FT-IR spectra of the three compounds will also be presented.

Reference(s):

1. Fabregat-Safont D, Carbón X, Ventura M, Fornís I, Guillamón E, Sancho J. V, Hernández F, Ibáñez M. “Updating the list of known opioids through identification and characterization of the new opioid derivative 3,4-dichloro-N-(2-(diethylamino)cyclohexyl)-N-methylbenzamide (U-49900),” *Scientific Reports 7* (July 2017): 6338, https://www.nature.com/articles/s41598-017-06778-9.

U-47700, U-51754, U-49900