



K60 Postmortem Tissue Distribution of U-47700 Following Lethal Intoxication and Novel Scheduling in the State of Ohio

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After attending this presentation, attendees will better understand the synthetic opioid U-47700, a Novel Psychoactive Substance (NPS), and its concentration in postmortem cases involving single and multiple drug intoxications.

This presentation will impact the forensic science community by informing forensic professionals on abuse trends for opioid NPS designer drugs. This presentation adds to the small amount of published data concerning the potential toxicity of these opioid NPS designer drugs and provides an approach for the analysis of these substances.

3,4-dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methyl-benzamide, also known as U-47700, is structurally categorized as an opioid and is an isomer of AH-7921. U-47700 was produced by the Upjohn Company in 1978 as a synthetic alternative to morphine. U-47700 exerts its pharmacologic effects as a μ -opioid receptor agonist and has approximately 7.5 times the potency of morphine. Opioid NPS drugs are popular recreational substitutes for heroin, fentanyl, or morphine. NPS drugs can be taken orally, intravenously, or rectally or can be smoked or snorted. They are sold on the internet as "legal highs" and are often mixed with heroin or other psychoactive substances. There have been more than 60 deaths in the United States and European countries involving U-47700.

The effects of U-47700 are similar to other opioids and include analgesia, sedation, and mild euphoria. U-47700 toxicities should be similar to the opiate toxidrome and include respiratory depression, altered mental states, pulmonary edema, coma, bradycardia, hypotension, hypothermia, nausea, and vomiting.

Due to drug scheduling research initiated by the Ohio Attorney General's Bureau of Criminal Investigation (BCI), a swift and unanimous vote by the State of Ohio Board of Pharmacy classified U-47700 as a Schedule I opium derivative under rule 4729-11-02 of the Ohio Administrative Code. The next day, Ohio Governor John Kasich signed an executive order authorizing the Board to take emergency action and subjected U-47700 to criminal drug



penalties as of May 4, 2016. U-47700 is also scheduled in the states of Wyoming and Georgia and the countries of Finland and Sweden.

Case 1: A 35-year-old White male with a history of heroin abuse was found unresponsive, seated on a couch. Autopsy findings were unremarkable, except for moderate pulmonary vascular congestion and pulmonary edema (right lung 950g, left lung 710g).

Case 2: A 49-year-old White male was found at home, prone on the bathroom floor. The decedent's past medical history included back and neck pain, sleep apnea, arthritis, and migraines. Autopsy findings were remarkable for moderate coronary artery disease, a 540g heart, fatty liver/cirrhosis, moderate pulmonary vascular congestion, and pulmonary edema (right lung 840g, left lung 1,060g).

Case 3: A 29-year-old White male was found on the bedroom floor. The case was reported to the Lake County Sheriff's Office as an accidental overdose. This was the first confirmed U-47700 death in Ohio. No autopsy was performed.

No apparent foul play or trauma was noted in any of these cases. The decedents in all of the cases purchased U-47700 from the internet.

Standard comprehensive toxicology and drug chemistry analyses were performed on multiple specimens/drug exhibits using Gas Chromatography/Mass Spectrometry (GC/MS). U-47700 detection in tissues was accomplished using GC/MS, Ultra High-Performance Liquid Chromatography/Tandem Mass Spectrometry (UHPLC-MS/MS) after Solid-Phase Extraction (SPE) and liquid-liquid extraction and in hair using HPLC-MS/MS after SPE.

U-47700 concentrations:

Specimen (ng/mL)	Femoral Blood	Heart Blood	Urine	Gastric	Vitreous	Bile	Liver (ng/g)	Kidney (ng/g)	Brain (ng/g)	Hair
Case 1	456	137	Present	Present	55.2	360	605	NTDN	NTDN	Present*
Case 2	90.1	116	Present	Present	117	1070	561	253	123	Present**
Case 3	242	NTDN	NTDN	NTDN	NTDN	NTDN	NTDN	NTDN	NTDN	NTDN

NTDN=No testing performed.

Case 1: No other drugs, including synthetic cannabinoids, fentanyl analogs, novel opioids, or other NPS drugs, were found to be present in the femoral blood, except cotinine. Consecutive 30-day hair segments from the root end contained U-47700 at 10,619, 12,391, and 13,185pg/mg*.

Case 2: Femoral blood contained 0.016mg/L alprazolam, 3.2mg/L topiramate, 0.091mg/L diphenhydramine, and 0.155mg/L bupropion. Cotinine was present. Fentanyl analogs, novel opioids and other NPS drugs were negative in the femoral blood. The unsegmented 0-90-day hair segment contained U-47700 at 12,536pg/mg.**

Case 3: Femoral blood contained 5.3ng/mL delta-9-carboxy THC with presumptive positive benzodiazepines and cannabinoids in the urine. U-50488 and furanyl fentanyl were negative.

Drug chemistry exhibits found near the decedents contained U-47700 in all three cases.

The cause of death in Case 1 was ruled a drug intoxication by U-47700. The cause of death in Case 2 was ruled an intoxication by the combined effects of U-47700, alprazolam, topiramate, diphenhydramine, and bupropion. The cause of death in Case 3 was ruled an acute intoxication by U-47700. The manner of death for all



Toxicology - 2017

three postmortem cases was accidental. Tissue and fluids associated with detoxification had higher concentrations of U-47700.

Based on the U-47700 concentrations in Cases 1 and 2, there appears to be postmortem redistribution.

U-47700, Postmortem Drug Distribution, Scheduling of NPS Drug