



K36 Clinical Manifestations of U-47700 and Flubromazepam Intoxication

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After attending this presentation, attendees will be able to describe the pharmacological effects observed in two individuals exposed to opioid and benzodiazepine Novel Psychoactive Substances (NPS).

This presentation will impact the forensic science community by comparing behavioral and toxicological findings in two NPS intoxication cases. This information is useful in directing efforts toward additional screening when an investigation indicates drug use, but initial tests are unremarkable.

Pharmaceutical companies and academic researchers continue to develop new alternatives to traditional licit and illicit drugs. These advances led to the creation of compounds now sold as designer drugs or NPS. NPS, such as synthetic cannabinoids, cathinones, phenethylamines, tryptamines, opioids, and benzodiazepines, may be pursued as “legal highs” for individuals attempting to evade legal repercussions.

This presentation reports two non-fatal cases of NPS intoxication. The first involved a 21-year-old male exhibiting flushed skin, nausea, confusion, and unpredictable behavior. On several occasions during the incident, he became combative with others and would lose consciousness once seated. He was transported to the hospital, administered resuscitation measures, and responded positively to naloxone. The initial clinical laboratory urine toxicology screen was positive for benzodiazepines only. Additional hospital urine toxicology found chlorpheniramine, dextromethorphan, dextropropion, and diphenhydramine. Investigation of his belongings revealed syringes, estrogen blockers, and supplements. He admitted to using synthetic cannabinoids and to purchasing several vials of U-47700 from the internet for back pain. After release from the hospital, he was observed sleeping for 19 to 24 hours. The second case involved a 21-year-old male with a history of cocaine use who was shaking and acting erratically and reported using pre-workout supplements.

Venous blood and urine from both cases were submitted for routine toxicological analysis. Positive findings are reported in Table 1.



Table 1. Toxicology Results

Case 1	Blood	Urine
Case 1	36ng/mL U-47700 450ng/mL Flubromazepam 120ng/mL Dextromethorphan	U-47700 Flubromazepam Dextromethorphan Chlorpheniramine
Case 2	20ng/mL U-47700 50ng/mL Flubromazepam	U-47700 Flubromazepam Diphenhydramine

Two NPS, U-47700 and flubromazepam, were detected in both cases, with low U-47700 concentrations quantified in the blood. U-47700 is an N-substituted cyclohexyl benzamide synthetic μ -opioid receptor agonist with 7.5 times the potency of morphine. AH-7921, a structurally similar yet less active opioid analgesic, first appeared four years ago. This signals a progression toward the use of stronger alternatives to prescription opioids and heroin. Patents that describe this atypical opioid class also contain derivatives expected to possess similar activity as U-47700 at μ -opioid receptors.

Flubromazepam is a designer benzodiazepine reported to have an extended duration of action and induce excessive sedation and fatigue. Higher flubromazepam concentrations were found in Case 1, in which prolonged sleep was indicated by case history. Although flubromazepam and U-47700 have not been well-characterized in human subjects, opioids and benzodiazepines in combination may elicit profound Central Nervous System (CNS) depression and require medical intervention, as observed in Case 1. Published fatalities describe U-47700 in combination with fentanyl, antidepressants, antipsychotics, and other NPS. Reported here is the first non-fatal multi-drug intoxication cases of U-47700 in combination with flubromazepam and U-47700 is highlighted as a potent opioid difficult to detect by routine toxicological analysis.

U-47700, Flubromazepam, NPS