An Extraordinarily High Bromazolam Concentration in a Clinical Case

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Case Description

A 42-year-old male presented at a medical facility following possible drug overdose after marijuana use or vaping with acute unwitnessed syncope. The patient was intubated for airway protection and blood samples were collected the following day. Toxicology testing was performed and targeted commonly encountered drugs and metabolites such as amphetamines, anticonvulsants, antidepressants, antihistamines, antipsychotics, benzodiazepines, central nervous system stimulants, hallucinogens, hypnosedatives, muscle relaxants, and non-steroidal anti-inflammatory agents, in addition to a number of novel psychoactive substances (NPS). Bromazolam was identified and quantitated as part of the confirmation testing in this case.

Analyte	Concentration (ng/mL)
11-Hydroxy Delta-9 THC	2.1
Delta-9 Carboxy THC	44
Delta-9 THC	7.5
Bromazolam	1400

Table 1. Positive findings for this case

Background

Bromazolam was first synthesized in 1976 but was never approved for use. Today it is frequently found in conjunction with opioids such as fentanyl and heroin, often in the form of clandestine or counterfeit tablets. It is an increasingly prevalent NPS, as evidenced by an increase in identifications in both seized drugs and toxicology samples. Bromazolam use is generally characterized by central nervous system depression and can be life-threatening; therefore, accurate identification and quantitation of bromazolam is critical for patient care. Toxicology screening via immunoassay is common and would likely yield a presumptive positive result for benzodiazepines as a drug class but would not allow for identification of the analyte of interest. The use of powerful mass spectral techniques like time-of-flight (TOF) coupled with a comprehensive and relevant scope of analysis make it possible to efficiently and effectively test for NPS in clinical samples.

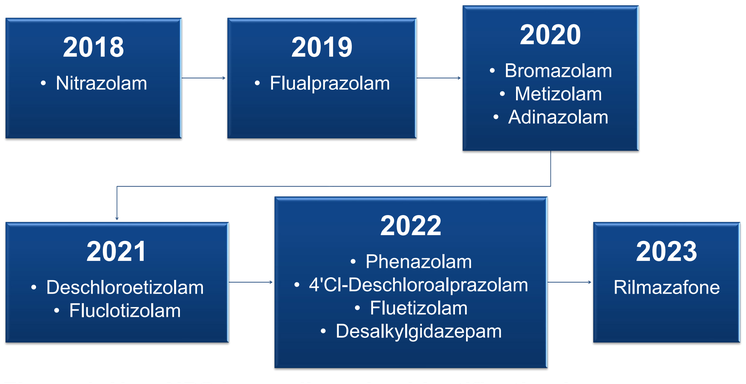


Figure 1. New NPS benzodiazepine identification by year through June 2023

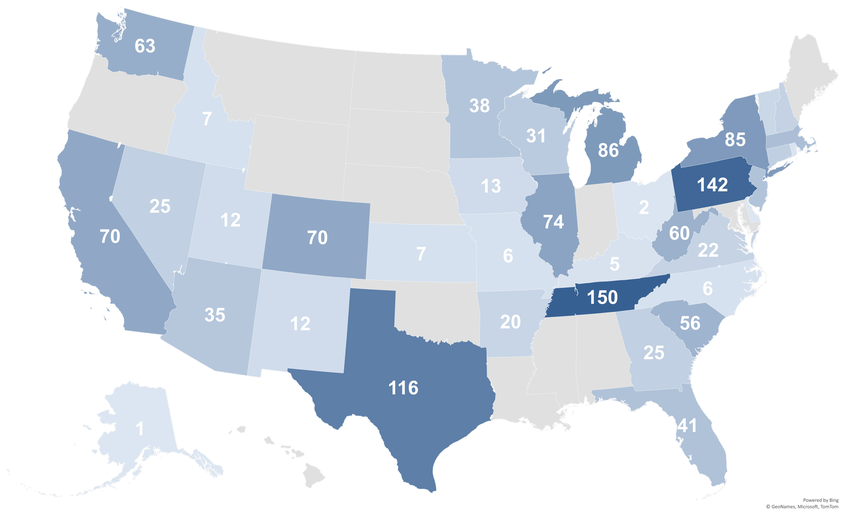


Figure 2. Frequency of bromazolam identifications in blood by state

Results reported from samples submitted to NMS Labs and in which bromazolam testing was added and confirmed positive from 2021 through 2023.

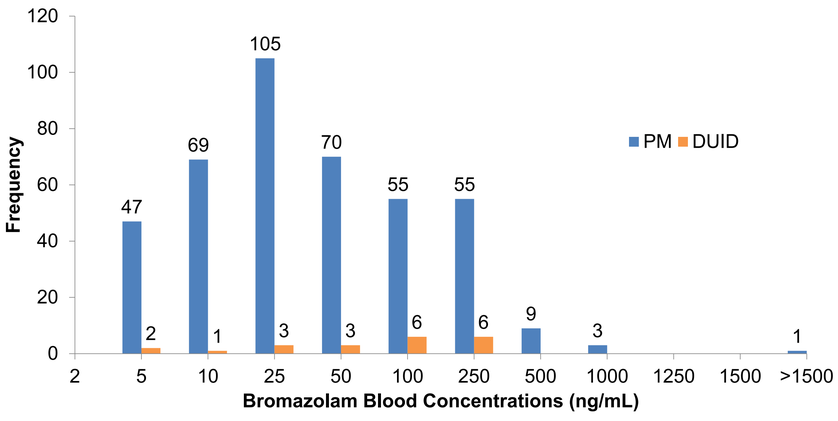
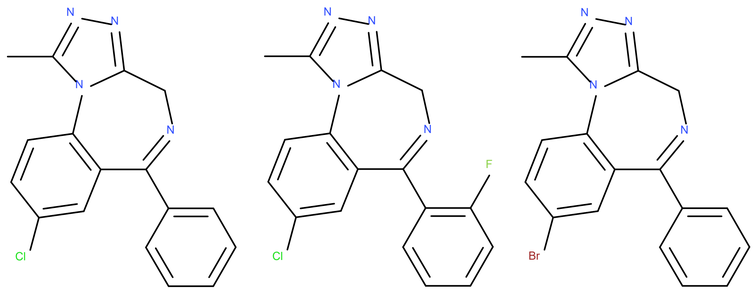


Figure 3. Frequency of bromazolam blood concentrations in driving under the influence (DUID) and postmortem (PM) samples

Results reported from samples submitted to NMS Labs and in which bromazolam testing was added and confirmed positive from 2021 through 2023.

Alprazolam **Flualprazolam** **Bromazolam**

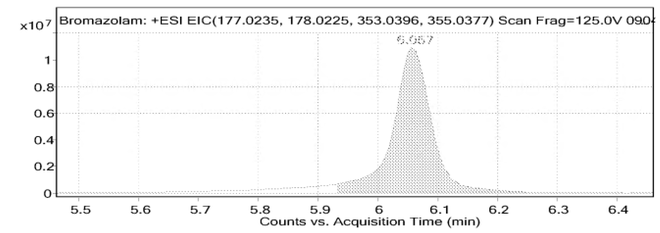


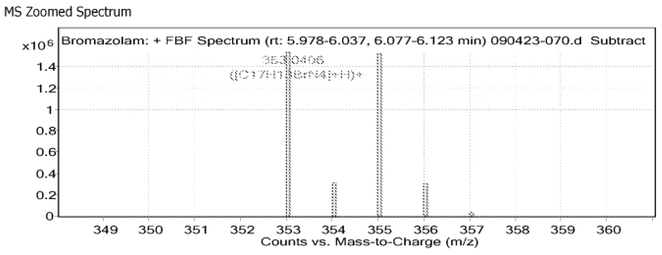
Disclaimer

The authors are paid employees of NMS Labs, a commercial provider of Toxicology and other forensic testing services.

MS Method and Results

Routine screening for THC, barbiturates, salicylates, and gabapentin was performed via immunoassay. For expanded screening, 0.5 mL of serum was buffered, extracted with organic solvent, and analyzed via LC-TOF-MS. Bromazolam confirmation testing utilized 0.5 mL of buffered serum in a liquid/liquid extraction. The reconstituted extract was separated using UPLC and analyzed with positive-ion electrospray tandem mass spectrometry for detection and quantitation. **The patient's serum bromazolam concentration was 1400 ng/mL.**





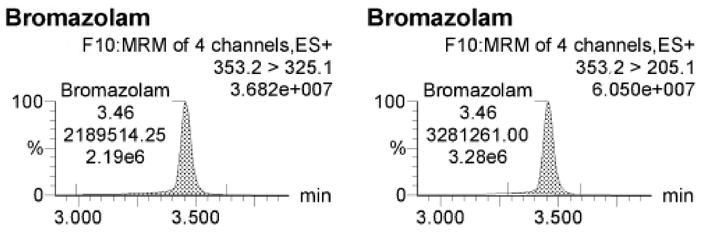


Figure 4. Mass spectral data from the TOF screen and LC-MS/MS confirmation testing in this clinical case

Discussion and Conclusion

Seizures, hyperthermia, and myocardial injury associated with bromazolam use were recently reported, and deaths attributed to bromazolam use are increasing. Bromazolam use can have serious and life-threating impacts on patient health, and its inclusion in clandestine or counterfeit tablets complicates patient care, as patients are often unaware of the true composition of these items. Previous reports of bromazolam-positive samples in the literature, including fatalities, were one to two orders of magnitude lower in concentration than the case reported herein.