SOFT 2022
Abstract Submission Form

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*****Do not exceed 600 words including tables and charts.*****

TITLE: Quantitation of the New Synthetic Cathinone *N,N*-Dimethylpentylone in a Post-Mortem Case Series

AUTHOR(S) AND AFFILIATION(S): *Indicate the presenting author with an asterisk and bold font. Author names should be separated by a comma and be in the format of First Name Last Name, e.g. John Doe. Affiliations should include affiliation name, city, state, and country (if not USA).*

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ABSTRACT: *Structure the abstract using the following headers.*

Background/Introduction: Synthetic cathinones emerged over ten years ago onto the novel psychoactive substances (NPS) drug market as substitutes for "ecstasy," "Molly", and "MDMA". Following similar patterns of other subclasses of NPS, these drugs have exhibited rapid turnover in positivity post-scheduling of specific drugs at the international level. The most recent example is the decline in eutylone positivity after the recommendation of international control in September 2021, which subsequently led to the emergence of *N,N*-dimethylpentylone. *N,N*-Dimethylpentylone, an isomer of *N*-ethyl pentylone, is a new synthetic cathinone not previously identified in the recreational drug supply; therefore, toxicology labs lacked the ability to detect and quantify this drug.

Objectives: The purpose of this presentation is to describe an analytical method capable of chromatographically resolving the isomeric beta-keto methylenedioxyamphetamines (bk-MDAs) related to *N,N*-dimethylpentylone and showcase the concentrations of *N,N*-dimethylpentylone found in authentic forensic toxicology specimens.

Methods:
The following analytes were included in this method: isomers *N,N*-dimethylpentylone, *N*-ethyl pentylone, diethylone, hexylone, and tertylone, and isomers pentylone, and eutylone. Biological specimens (0.5 mL) were extracted using a basic (pH 10.4) liquid-liquid extraction. Samples were diluted, as necessary, to fit into the calibration range based on previous analyses (e.g., screen via LC-QTOF-MS).

Quantitative analysis was performed using a Waters Xevo TQ-S Micro tandem mass spectrometer coupled with a Waters Acquity UPLC® (Milford, MA). Chromatographic separation was achieved using an Agilent Poroshell EC C-18 column (3.0 mm x 100 mm, 2.7 µm) (Santa Clara, CA) heated to 60°C with a flow rate of 0.4 mL/min. The mobile phases were 5 mM ammonium formate in water, pH 3 (A) and 0.1% formic acid in acetonitrile (B) used in the following 7 min gradient: 90A:10B, increasing over 5.5 mins to 65A:35B, increasing again to 95%B over 0.5 mins, and at 6.1 mins returning to initial conditions with a 0.9-minute hold.

Authentic specimens were initially quantified via standard addition (up-spikes at 0, 1, 10, and 100 ng/mL) to determine the appropriate concentration range for method validation. As the number of submitted cases increased, a fit-for-purpose method validation was performed evaluating the following criteria: accuracy, intra- and inter-precision, linearity, limit of detection, limit of quantitation, and matrix and commonly encountered interferences. Dilution integrity was performed in blood at 1:2 and 1:10 and in urine at 1:10 and 1:50.

Results:

All bk-MDAs met acceptability criteria during the validation experiments. All calibration curves were calculated using a quadratic fit with 1/x weighting regression and a resulting calibration range of 10-1000 ng/mL. All drugs met acceptability requirements of accuracy (<±20% from target) and intra- and inter-precision (coefficient of variation <±15%).

Forensic investigations suspected to involve *N,N*-dimethylpentylone were submitted to our laboratory starting in September 2021, primarily from Florida or New York. To date, *N,N*-dimethylpentylone has been quantitated in 18 postmortem cases with a resulting concentration range of 3.3 to 970 ng/mL (median: 145 ng/mL, mean 277±283 ng/mL). Pentylone, a suspected metabolite of *N,N*-dimethylpentylone, was detected in all cases (range: 1.3-420 ng/mL, median: 31 ng/mL, and mean: 88±127 ng/mL). *N,N*-Dimethylpentylone was found in combination with fentanyl (n=7), eutylone (n=6), and methamphetamine/amphetamine (n=5). An additional 62 cases are pending analysis as the prevalence of *N,N*-dimethylpentylone continues to increase.

Conclusion/Discussion:

Blood concentrations reported for *N,N*-dimethylpentylone follow similar trends of previously reported synthetic cathinones (e.g., eutylone). In all cases, the concentration of pentylone was less than *N,N*-dimethylpentylone, further supporting that pentylone is a metabolite, however, co-ingestion cannot be ruled out. With this sudden increase in identifications of *N,N*-dimethylpentylone, if forensic toxicologists find samples positive for pentylone it is recommended that they be further investigated for *N,N*-dimethylpentylone at this time with methodology that separates N,N-dimethylpentylone from its isomer *N*-ethyl pentylone.