K48 Postmortem Tissue Distribution of Synthetic Cathinones

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After attending this presentation, attendees will better understand tissue distributions and the potential for some synthetic cathinones to exhibit significant Postmortem Redistribution (PMR).

This presentation will impact the forensic science community by increasing the fundamental understanding of synthetic cathinone distribution in postmortem toxicological samples and the influence of PMR.

Postmortem toxicology results can provide crucial information in death investigations regarding the cause and manner of death; however, postmortem drug concentrations may not always reflect antemortem concentrations. Drugs may also undergo PMR, resulting in significant differences between central and peripheral blood. To assess PMR, Central to Peripheral (C/P) blood ratios can be calculated. PMR can be somewhat predicted using drug properties, including volume of distribution, lipophilicity, and p*Ka*. Blood and tissue distributions have been studied for many common illicit drugs, but this information is still limited for synthetic cathinones, a class of designer drugs that has been increasing in popularity over the past decade. In this presentation, postmortem tissue distributions and C/P ratios for select synthetic cathinones from cathinone-positive fatalities will be presented.

Postmortem samples from 60 cathinone-positive cases were included in the study. A total of 210 specimens were evaluated, including liver, urine, vitreous humor, and blood collected from the aorta, inferior vena cava, iliac, subclavian, and femoral vessels. Quantitative analysis was performed using blood or urine calibrators with matrix-matched controls. Samples were analyzed using a previously published and validated procedure for the determination of 22 synthetic cathinones in urine and blood using Liquid Chromatography/quadrupole Time-Of-Flight/Mass Spectrometry (LC/qTOF/MS). A total of nine isotopically labelled internal standards were used. The principal compounds of interest were methcathinone, 3-fFuoromethcathinone (3-FMC), 4-Fluoromethcathinone (4-FMC), ethcathinone, ethylone, methedrone, buphedrone, butylone, mephedrone, eutylone, 4-Methylethcathinone (4-MEC), 3,4-Methylenedioxy-α-Pyrrolidinobutyrophenone (MDPBP), pentedrone, pentylone, 3,4-Dimethylmethcathinone (3,4-DMMC), α-Pyrrolidinopentiophenone (α-PVP), 4-Ethylmethcathinone (4-EMC), 4-Methyl-α-Pyrrolidinobutiophenone (MPBP), Methylenedioxypyrovalerone (MDPV), pyrovalerone, and naphyrone.

Of the 22 cathinones in the assay, 9 were identified in at least one case: α-PVP (*n*=18), methylone (*n*=17), ethylone (*n*=15), MDPV (*n*=6), pentylone (*n*=3), methedrone (*n*=2), 4-MEC (*n*=1), butylone (*n*=1), and MDPBP (*n*=1). Concentration ranges in blood, urine, and liver, respectively, were <2 to 1,090ng/mL, 33 to 7,580ng/mL, and 14 to 663ng/g for α-PVP; <2 to 202 ng/mL, 2 to 38,064ng/mL, and 28 to 5,731ng/g for methylone; <2 to 2,743ng/mL, 32 to >20,000ng/mL, and 10 to 18,893ng/g for ethylone; 3 to 80ng/mL, 4 to 5,210ng/mL, and 64 to 840ng/g for MDPV; <5 to 322ng/mL in blood and 122 to >5,000 in urine for pentylone. Where possible, average C/P ratios were determined as follows: methylone (4.0, range 2.39-6.0, *n*=4), ethylone (2.9, range 0.5-9.2, *n*=6), pentylone (2.0, *n*=1), α-PVP (1.2, range 0.5-1.9, *n*=8), methedrone (1.1, *n*=1), MDPV (1.0, *n*=1), and butylone (0.7, *n*=1). Although C/P ratios were highly variable, some cathinones appeared to have significant potential for redistribution. Generally, the highest C/P ratios were observed in methyenedioxy-type cathinones bearing secondary amines. Although the pyrrolidine-type cathinones are less polar and subsequently more lipophilic, they are less basic than their secondary amine counterparts. Vitreous humor was only available in a small number of cases, but concentrations in vitreous were comparable to peripheral blood within this limited population. Although the concentration range of forensic interest was wide, the results also highlight the need for low limits of detection and quantification.

Tissue distributions and C/P ratios are presented and compared with existing literature. Variability of C/P ratios and the potential for cathinones to degrade *in situ* and during storage significantly complicates their interpretation. Of the 60 cases submitted, 50 cases had at least one specimen test positive for a synthetic cathinone. The results highlight the potential for some cathinones to exhibit PMR, the importance of collecting multiple specimens, and the interpretation of results within the full context of investigative information.

Synthetic Cathinones, Postmortem Redistribution, LC/qTOF/MS

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