Method validation and preliminary pharmacokinetic studies on the new designer stimulant 3-fluorophenmetrazine (3-FPM)

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Pharmaceutical research not only provides the basis for the development of new medicinal products but also for the synthesis of new drugs of abuse. 3-Fluorophenmetrazine (3-FPM), a fluorinated derivative of the anorectic phenmetrazine, was first patented in 2011 and appeared on the drug market in 2014. Though invented for potential medical purposes, pharmacokinetic data on this compound, crucial for interpreting forensic as well as clinical cases, are not available. Therefore, a liquid chromatography-electrospray ionization-tandem mass spectrometry (LC-ESI-MS/MS) method for the detection of 3-FPM in serum, urine and oral fluid was developed, validated for urine and serum, and used to quantify 3-FPM in samples obtained during a controlled self-experiment. The method proved to be linear, selective and sufficiently sensitive. The limits of detection (LOD) were 0.1 ng/mL, 0.2 ng/mL, and 0.05 ng/mL in serum, urine, and oral fluid. Inter-day precision and intra-day precision (RSD) in serum samples were below 6.3% and below 8.5%, respectively. The highest serum concentration (cmax) of 210 ng/mL was reached 2.5 h (tmax) after ingestion. The elimination half-life and the volume of distribution were calculated to be approx. 8.8 h and 4.0 L (0.053 L/kg). 3-FPM could be detected in serum and urine up to 82 h and 116 h, respectively. It was still detected in the last oral fluid sample taken 55 h after ingestion. 3-FPM was mainly excreted unchanged. Main metabolic reactions were aryl-hydroxylation and N-hydroxylation. Interestingly, the product of oxidative ring opening (2-amino-1-(3-fluorophenyl)propan-1-ol) showed the largest window of detection in the self-experiment.

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