



K26 The Detection and Quantification of Tianeptine in Postmortem Blood and Urine

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Learning Overview: After attending this presentation, attendees will be familiar with the toxic and lethal effects of tianeptine and a method for its toxicological analysis.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by relaying information about the toxicity of tianeptine, an atypical tricyclic drug.

Proposition Statement: The presented postmortem concentrations of tianeptine are consistent with a fatal overdose.

Background/Introduction: Tianeptine is an atypical tricyclic drug approved for use in Europe, Asia, and Latin America. In the United States, tianeptine is not approved by the United States Food and Drug Administration (FDA), but is sold on websites as an unscheduled pharmaceutical agent, a nootropic or smart drug/cognitive enhancer. Tianeptine use in the United States has increased in the last several years. The National Poison Data System received a total of 11 tianeptine exposure calls between 2000 and 2013. The total number of tianeptine exposure calls increased from 5 in 2014 to 38 in 2015, 83 in 2016, and 81 in 2017. The dual activation of the mu and delta opioid receptors is believed to be responsible for causing many of the known acute and chronic effects of tianeptine, including its antidepressant and anxiety actions. The major metabolic pathway is β -oxidation and the principal metabolites are propanoic acid (inactive) and pentanoic acid (active) metabolites. Less than 3% of the dose is excreted unchanged in urine. There are limited published case reports of tianeptine fatal overdoses with blood concentrations ($n=5$) ranging from 2–18mg/L and free tianeptine in urine ($n=2$) at 2.0 and 3.2mg/L.¹⁻⁴

Case: Presented are the femoral blood and urine results from a 31-year-old White male found at home by his girlfriend approximately four hours after he was last seen. Needles, syringes, and a glass pipe were also found at the scene. Initial screening of the blood and urine samples revealed amphetamine, methamphetamine, and tianeptine.

Method: A High-Performance Liquid Chromatography/Tandem Mass Spectrometry (HPLC/MS/MS) method was used for the detection and quantitation of tianeptine in blood and urine. A seven-point matched matrix calibration curve ranging from 0.001–0.100mg/L, blood and urine quality control specimens (0.001, 0.003, 0.030, and 0.075mg/L), and the samples were analyzed. Method was assessed for bias, precision, carryover, matrix effects, and dilution integrity. The linear regression coefficients of determination (r^2) for calibration curves were 0.9996 or greater. Controls were assessed over three days in triplicate. Accuracy/bias of the quality control specimens was determined to be within $\pm 20\%$ of the target concentrations for both blood and urine. The precision did not exceed a coefficient of variation of 15%. Validation criteria for carryover, specificity, matrix effects, and dilution integrity were also acceptable. Blood samples were deprotonated with methanol prior to extraction. To prepare the samples, 0.200mg/L protriptyline Internal Standard (ISTD) was added to 200 μ L aliquots of the calibrators, controls, and samples followed by the addition of 200 μ L of 50:50 acetonitrile: water. Samples were briefly mixed and transferred to Clean Screen FAST[®]SPE columns and rapidly eluted into auto-sampler vials. Analysis was performed using a Waters[®] ACQUITY[®] Xevo Tandem Quadrupole Detection (TQD) HPLC/MS/MS with ESI ionization in positive ion mode.

Results: The determined blood and urine concentrations were 11mg/L and 0.66mg/L, respectively.

Conclusion: The blood and urine tianeptine concentrations determined by the presented HPLC/MS/MS method were consistent with the limited published tianeptine fatal overdose concentrations. The blood concentration of 11mg/L was within the range of published blood tianeptine concentrations. The urine concentration of 0.66mg/L was lower than that of the two published urine postmortem tianeptine concentrations.

This project was supported by the National Institute of Health (NIH) Center for Drug Abuse.

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Tianeptine, Postmortem, HPLC-MS/MS