K28 Trazodone and M-Chlorophenylpiperazine (m-CPP) Concentrations in Postmortem Blood

C. Richard Crooks, PhD, Aegis Sciences Corporation, 365 Great Circle Road, Nashville, TN 37228; David M. Schwope, PhD, Aegis Sciences Corporation, 365 Great Circle Road, Nashville, TN 37228; and Jana A. James, MS, 209 Hatfield Drive, Franklin, TN 37064*

After attending this presentation, attendees will be able to describe expected concentrations of trazodone and m-CPP, a metabolite of trazodone, in postmortem blood.

This presentation will impact the forensic science community by providing data that will assist forensic toxicologists in interpreting trazodone and m-CPP concentrations in postmortem casework.

Introduction: Trazodone has been used as an antidepressant for more than 30 years. Structurally, it is unique and unrelated to the tricyclic and tetracyclic antidepressants, as well as the newer SSRI and SNRI antidepressants. m-CPP is the major metabolite of trazodone; but is also considered a "designer" drug that can be abused by itself. Although postmortem trazodone blood concentrations have been documented, reports of postmortem m-CPP concentrations in blood are lacking.

Method: This study is a compilation of data obtained from 30 cases over a five-month period (femoral or heart blood). Trazodone samples were prepared by analysis using a dual Liquid-Liquid Extraction (LLE). Prior to extraction, each specimen was fortified with internal standards and pH adjusted using ammonium hydroxide. Solvent was evaporated to dryness and reconstituted in 150µL 10mM ammonium acetate, 0.1% formic acid High-Performance Liquid Chromatography (HPLC) water (mobile phase). Samples were analyzed via a Liquid Chromatography with Tandem Mass Spectrometry (LC/MS/MS) instrument comprised of a Shimadzu® HPLC and ABSciex™ API 3200 tandem mass spectrometer. Ionization was attained by electrospray (positive mode) with Multiple Reaction Monitoring (MRM) mode employed for detection and quantification. Gradient chromatographic separation starting at 20% B (0.1% formic acid in acetonitrile) was achieved using a C_{18} column (100 x 2.1mm, 3µm particle). Flow rate was 0.7mL/min with an overall run time of 3.0 minutes. Conservative Limits Of Quantification (LOQ) were 20ng/mL for both analytes. The assay was validated for linearity from 5ng/mL-250ng/mL trazodone and m-CPP (r^2>0.980 and concentrations within ±20% of target). Precision was characterized by CVs of 4.2% and 3.0% for trazodone and m-CPP, respectively, at 250ng/mL, and 6.3% and 7.9% at 20ng/mL. Accuracy was characterized by deviations of -3.2% and -3.0% for trazodone and m-CPP, respectively, at 250ng/mL, and 5.2% and -1.0% at 20ng/mL. No quantifiable carryover was observed at the method Upper Limit Of Quantification (ULOQ).

Results: Of 19 femoral blood specimens containing trazodone at >20ng/mL, m-CPP was not detected in five specimens (LOD 5ng/mL), detected at >LOD but <20ng/mL in six specimens, and quantified at >20ng/mL in eight specimens (trazodone mean of 596ng/mL, range 225ng/mL-1,383ng/mL, and m-CPP mean of 36.0ng/mL, range 21.4ng/mL-69.5ng/mL). Of 11 heart blood specimens containing trazodone at >20ng/mL, m-CPP was not detected in three specimens (LOD 5ng/mL), detected at >LOD but <20ng/mL in two specimens, and quantified at >20ng/mL in six specimens (trazodone mean of 836ng/mL, range 188ng/mL-2,145ng/mL, and m-CPP mean of 90.4ng/mL, range 26.6ng/mL-125ng/mL).

Conclusions: Trazodone and m-CPP concentrations are presented from 30 postmortem cases obtained over a six-month period. Trazodone concentrations were similar to literature values, with m-CPP detected > LOD in 22 of 30 cases. This data set will assist forensic toxicologists in casework where trazodone or m-CPP intake has occurred.

Trazodone, m-CPP, Postmortem Blood