K17 GC/MS Method Development for the Quantitation of Quetiapine in Various Biological Specimens

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After attending this presentation, attendees will be aware of a GC- MS method that can be used to detect and quantitate the presence of quetiapine in biological specimens using chemicals and instrumentation that is widely available in most laboratories.

This presentation will impact the forensic community by providing a new method for the detection of quetiapine.

Quetiapine ($C_{21}H_{25}N_3O_2S$) is classified as a dibenzothiazepine derivative and is used clinically as an antipsychotic for the treatment of schizophrenia and bipolar disorder. In the body, quetiapine acts as an antagonist, targeting the serotonin and dopamine receptors. Quetiapine is metabolized in the liver, with 73% eliminated through the urine. Less than 1% of the parent drug is eliminated unchanged. Quetiapine is known to be 83% plasma protein bound and have a volume of distribution of 10 ± 4 L/kg. It is administered orally as a fumarate salt in 25mg, 100mg, 200mg, 300mg, and 400mg tablets. The fumarate salt is comprised of two quetiapine molecules per one fumarate molecule (MW = 883.1). The drug is structurally similar to the antipsychotic drug clozapine.

The Montgomery County Coroner's Office (MCCO) encountered quetiapine in 47 cases in 2007. Incidents of quetiapine in casework are increasing and as MCCO did not possess a method for the quantitation of quetiapine, specimens had to be analyzed by an outside laboratory. A study was completed identifying an extraction and instrumental procedure for the detection and quantitation of quetiapine in order to diminish the cost of outside testing. The postmortem specimens analyzed were blood, brain, liver, cerebral spinal fluid, bile, vitreous fluid, and urine. The internal standard was Smith Kline French-525A (SKF-525A). Calibrators were prepared from a quetiapine stock standard solution at concentrations of 0.01, 0.05, 0.1, 0.25, 0.5, 0.75, 1.0, 1.5, and 2.0µg/mL. Liquid and powder forms of quetiapine were prepared for controls. The analysis was completed by following an in- house liquid-liquid extraction for basic drugs. Quetiapine was extracted with hexane/isoamyl alcohol (99/1). Back extraction was completed by the addition of hydrochloric acid. The drug was re-extracted into methylene chloride, which was then evaporated to dryness. Derivatization was completed by reconstituting with BSTFA + 1% TMCS and heating for 20 minutes at 75ºC. One microliter was injected on an Agilent 5973 Series gas chromatograph mass spectrometer (GC- MS) with a DB-5MS (30m x 0.25mm x 0.25µm) column. The temperature program has an initial temperature of 100ºC with an increase of 20ºC per minute to a final temperature of 285ºC. Single ionization mode (SIM) was used with the quetiapine target quantitation ion 210 and the qualifier ions 239 and 321. The target quantitation ion for the internal standard was 86. The assay was linear from 0.01 - 2.0µg/mL.

Quetiapine was identified to have a retention time of 22.64 minutes. Linear regression analysis indicated an R^2 value of 0.9952 over the entire calibration range. The concentration range of quetiapine in twelve blood specimens was 0.16 – 1.75µg/mL. The postmortem distribution of quetiapine in all other specimens were as follows: brain 0.10-1.90µg/mL (6 cases), liver 0.14-1.69µg/mL (6 cases), cerebral spinal fluid 0.10-0.18µg/mL (3 cases), bile 0.10-0.64µg/mL (3 cases), vitreous fluid 0.12- 1.42µg/mL (4 cases), and urine 0.01-0.77µg/mL (7 cases).The completion of this study identifies a method that MCCO can utilize to detect and quantitate quetiapine.

Quetiapine, Postmortem Toxicology, Gas Chromatograph Mass Spectrometry

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