



### K22 Death Due to Ingestion of Tramadol in London, UK

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Attendance at this presentation will enable the participant to study an unusual toxicological case in London involving tramadol. The presentation will also enable the participant to learn how such cases are processed by the Forensic Toxicology Service in London, UK.

This presentation is important to the toxicological and analytical community as it is the first such case in London, UK involving the highest reported level of tramadol in addition to a concentration of enalapril consistent with therapy. Considering the lack of any other significant autopsy findings, the results of our toxicological analyses are consistent with the assumption of a fatal overdose of tramadol producing a high concentration of the drug, exceeding any noted in the UK before.

The Forensic Toxicology Service offers a screening and quantification toxicology service to most of Her Majesty's Coroners and Forensic Pathologists in London as well as various Police Forces and one branch of the Armed Forces. As a result, we are required to screen for a large number of prescribed and illicit drugs in post-mortem specimens followed by quantification of those detected. All analyses must be completed and our final report must be submitted to the Courts within 15 business days of the arrival of the case at the Service. This case was presented to the Service in May 2003 and involved a 79-year-old Caucasian female with a history of pain related health problems, which required prescription of various analgesics, including tramadol. At the home of the deceased officers discovered empty boxes of tramadol and zopiclone as well as boxes of co-codamol (preparation of codeine and paracetamol), Duragesic® patches (fentanyl) and paracetamol. We were requested to subject the unpreserved post-mortem blood and urine specimens of the deceased to our standard alcohol and general drug screen in order to facilitate HM Coroner in his Inquest into this death.

The case blood and urine specimens were screened for alcohol and determined negative. Similarly, paracetamol (i.e., acetaminophen) and salicylates were not detected. Our benzodiazepine screen by HPLC-MSMS on the blood specimen did not detect any benzodiazepines or metabolites. Enalapril was detected by HPLC-MS-MS and, when quantified in blood, it measured 0.02 mg/L, which fell well within low levels observed in therapy. Using our standard liquid-liquid drug extraction scheme for basic (i.e. alkaline) drugs followed by gas chromatography – mass spectrometry (GC-MS), we were able to identify tramadol in both the blood and urine case specimens. The urine specimen also showed a spot under UV illumination following thin layer chromatography. When the TLC plate was sprayed with FPN reagent (ferric chloride; perchloric acid; nitric acid), the spot showed a strong purple color. When quantified by GC-MS using appropriate calibrators and controls, tramadol measured 10.3 mg/L in blood. Urine tramadol was not quantified.

Tramadol is prescribed in the United Kingdom as an opioid analgesic to treat moderate to severe pain as non-proprietary 50-mg capsules or 50mg/mL injection, or under various trade names including Zamadol® and Zydol® capsules and Dromadol® and Zydol® XL modified release tablets. Enalapril is prescribed in the UK to treat hypertension and also to alleviate symptomatic heart failure. It is available as non-proprietary tablets (2.5, 5, 10 or 20 mg) as well as under the trade names of Innovace® and Innozide®.

After reviewing the scientific literature on tramadol related fatalities, it was noted that published post-mortem blood levels in such cases ranged from 3.7mg/L (Loughrey et. al., 2003) to 9.6mg/L (Musshoff and Madea, 2001). Tramadol-related deaths and non-fatal intoxications have previously been studied and tramadol levels ranged from 0.03 to 22.59 mg/L (Goeringer et. al., 1997; Levine et. al., 1997). Our case is important to the toxicological and analytical community as it is the first such case in London, UK involving the highest reported level of tramadol in addition to a concentration of enalapril consistent with therapy. Considering the lack of any other significant autopsy findings, the results of our toxicological analyses are consistent with the assumption of a fatal overdose of tramadol producing a high concentration of the drug, exceeding any noted in the UK before.

#### **Tramadol, GC?MS, Fatality**