

Determination and distribution of clotiapine (Entumine®) in human plasma, postmortem blood and tissue samples from clotiapine treated patients and from autopsy cases

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Despite that the antipsychotic drug clotiapine (Entumine®) has been marketed for more than 35 years now, only few data have been published on therapeutic and toxic levels of this drug. To fill this gap, two rapid and sensitive methods were developed for the determination of clotiapine, (2-chloro-11-(4-methyl-1-piperazinyl)dibenzo-[b,f][1,4]-thiazepine), in human plasma and postmortem blood and tissue samples. After simple liquid-liquid extraction at pH 9.5 with n-hexane/dichloromethane (85/15, v/v), clotiapine was quantitated by liquid chromatography diode-array detection (HPLC-DAD) and by gas chromatography with nitrogen-phosphorous detection (GC-NPD). The calibration curve was linear between 10 and 1000 µg/l. The limit of detection (LOD) and the limit of quantification (LOQ) were found to be 2 and 6 µg/l for the GC-NPD method and 5 and 15 µg/l for the HPLC method, respectively. These methods were applied to twelve plasma samples from patients treated with clotiapine, to seven autopsy cases and to one case of driving under the influence of drugs (DUID). Concentrations ranged for the clotiapine treated patients between 6 and 155 µg/l (mean 46 µg/l), and for the autopsy cases between 22 and 341 µg/l (mean 123 µg/l). The HPLC-DAD method allows tentative identification of clotiapine, while the GC-NPD method is more sensitive.

KEYWORDS: *Clotiapine; Antipsychotic; Blood level; Postmortem distribution*

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