

Metabolism and toxicological detection of the new pyrrolidino-phenone designer drug 3',4'-methylenedioxy-alpha-pyrrolidino-butyrophenone (MDPBP) in rat and human urine using GC-MS and LC-MSⁿ

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Abstract

Aims: The aim of the presented study was to identify the phase I and II metabolites of the new designer drug MDPBP in rat and human urine and to show its detectability in our standard urine screening approaches (SUSA) using GC-MS and LC-MSⁿ. In addition, the cytochrome P450 isoenzymes (CYP) involved in the main metabolic step should be identified.

Methods: After application (20 or 1 mg/kg BM for metabolism and toxicological detection studies, respectively) of MDPBP to male Wistar rats for toxicological diagnostic reasons, urine was collected over 24h. The phase I metabolites were extracted and analyzed directly or after enzymatic cleavage by solid phase extraction (HCX or C18) followed by GC-MS (AT GC-MSD) and LC-MSⁿ (TF LXQ). For studies on the toxicological detection, the authors' GC-MS and LC-MSⁿ SUSAs were applied to rat and human urine samples submitted for toxicological analysis. Finally, general involvement of CYP enzymes in the initial metabolic step(s) was checked using incubation with ten recombinant human CYPs.

Results and Discussion: 17 phase I and 7 phase II metabolites could be identified so that the following pathways could be proposed: demethylenation followed by partial methylation of one hydroxy group, side chain hydroxylation, pyrrolidine oxidation, oxidative deamination, combinations of them, and partial conjugation. In rat urine (low dose) and in authentic human urine, several metabolites could be detected by both SUSAs. CYP2C19, CYP2D6 were the most relevant enzymes in the formation of the demethylenyl metabolite.

Conclusion: The presented study demonstrates that MDPBP is extensively metabolized and that its intake can be monitored by both SUSAs.