Studies on the metabolism and detectability of the phenethylamine-derived designer drug 2C-P in rat and human urine using GC-MS, LC-MS^n, and LC-HR-MS/MS

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Abstract

Aims: The aim of this present work was to study the phase I and II metabolism of the emerging phenethylamine-derived designer drug 2C-P (2,5-dimethoxy-4-propylphenethylamine) in rat and human urine and to show its detectability in our standard urine screening approaches (SUSA) using GC-MS and LC-MS^n. Finally, the involvement of human CYP isoenzymes in the initial metabolic steps should also be identified.

Methods: After application of 2C-P to male Wistar rats for toxicological diagnostic reasons (10 or 1 mg/kg BM for metabolism and toxicological detection studies, respectively), urine was collected over 24h. The phase I metabolites were extracted and analyzed directly or after enzymatic cleavage by SPE (HCX) followed by GC-MS (TF ISQ) after acetylation or trifluoroacetylation as well as underivatized by LC-high-resolution (HR)-MS/MS (TF Q-Exactive). The phase II metabolites were analyzed and identified after SPE (C18) or protein precipitation by LC-HR-MS/MS. For studies on the toxicological detection, the authors' GC-MS and LC-MS^n (TF LXQ) SUSAs were applied to rat and human urine samples submitted for toxicological analysis. Finally, CYP dependent metabolism was tested using the ten most important isoenzymes.

Results and Discussion: 2C-P metabolism was comparable to that of other 2Cs. The following metabolic steps could be proposed: various hydroxylations, bis-hydroxylation, deamination followed by oxidation, *O*-demethylation, bis-*O*-demethylation, and combinations. Phase II metabolism included glucuronidation, sulfation, and *N*-acetylation. In rat urine (low dose) as well as in human urine, 2C-P and/or its main metabolites were detectable by SUSA using the GC-MS or LC-MS^n. Finally CYP2D6 and CYP3A4 were shown to be capable of forming the hydroxy metabolites.

Conclusion: 2C-P was excreted in more or less metabolized form by rats and humans and could be screened for by both SUSAs.

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