Studies on the Metabolism and Toxicological Detection of the Designer Drug DOI in Rat Urine Using GC-MS Techniques

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Abstract

The designer drug 2,5-dimethoxy-4-iodoamphetamine (DOI) is becoming increasingly important on the illicit drug market. The aim of this study was to identify its metabolites in rat urine and to study their detectability within our systematic toxicological analysis (STA) procedure. Urine samples from rats treated with DOI collect over 24h were used.. The following metabolic steps could be observed besides small amounts of unchanged DOI: *O*-demethylation in position 2 or 5 of the aromatic ring and *O,O*-bis-demethylation. Using our STA, DOI and its metabolites could be detected in rat urine after a common dose. Assuming similar metabolism in humans, the STA should be suitable for proof of an intake of DOI in human urine.

1. Introduction

4-Iodo-2,5-dimethoxy-amphetamine (DOI) is a non-scheduled hallucinogenic drug that was synthesized by A. Shulgin who also gave qualitative and quantitative comments on its effects [11, 12]. Structure-activity relationship studies revealed that the highest hallucinogen-like activity was caused by the primary amine functionality separated from the phenyl ring by two carbon atoms, the presence of methoxy groups in position 2 and 5, and a hydrophobic 4-substituent [8, 9]. Several seizures in clandestine laboratories in some countries lead to the assumption that DOI is abused as designer drug but so far no intoxications have been reported. Further evidence about its popularity among drug abusers can be found on internet web sites (http//:www.erowid.org, http//:www.lycaeum.org; March 2007) where experience reports and descriptions of DOI intake have been published.

The metabolism of DOI has not been studied systematically so far. Therefore, the first aim of this study was to identify the main metabolites of DOI to be screened for, besides other about 2000 compounds, by the authors' systematic toxicological analysis (STA) procedure in urine by GC-MS [1, 2, 4-6, 13-16]. The second aim was to investigate the detectability of DOI and its major metabolites as target analytes within the authors' STA procedure.

2. Experimental

2.1. Chemicals and reagents

DOI was provided by Hessisches Landeskriminalamt (Wiesbaden, Germany) for research purposes. All chemicals and biochemicals were obtained from Merck (Darmstadt, Germany) and were of analytical grade.

2.2. Urine samples

The investigations were performed using urine of male Wistar rats (about one year old and 400 g body mass (BM), Ch. River, Sulzfleck, Germany) for toxicological diagnostic reasons according to the corresponding German law. They were administered a single 5.0 or 0.05 mg/kg BM dose for metabolism studies or the STA study, respectively, in aqueous suspension by gastric intubation (n = 2).

2.3. Sample preparation

The urine samples were worked up as described for DOB and MDOB [1].

2.4. GC-MS apparatus

A Hewlett Packard (Agilent, Waldbronn, Germany) 5890 Series II gas chromatograph combined with a HP 5989B MS Engine mass spectrometer was used for the metabolism study and a Hewlett Packard (Agilent, Waldbronn, Germany) 5890 Series II gas chromatograph combined with a HP 5972A MSD for the STA study under the conditions described for DOB and MDOB [1].

2.5. GC-MS procedure for identification of metabolites and STA

DOI and its metabolites were separated by GC and identified by MS in acetylated urine extracts. For toxicological detection of DOI and its metabolites, mass chromatography with the selected ions m/z 86, 290, 332, 349, and 391 was used. The identity of the peaks in the mass chromatograms was confirmed by computerized comparison of the mass spectra underlying the peaks (after background subtraction) with reference spectra recorded during this study [6, 7].

3. Results and discussion

Besides DOI, two *O*-demethyl metabolites and a *O,O*-bisdemethyl metabolite could be identified in urine. All metabolites were partly excreted as glucuronides or sulfates. In contrast to the other 2,5-dimethoxy-amphetamines DOB or TMA-2, only *O*-demethylation was observed. This may be explained by the fact that DOI was described to be a potent monamineoxidase (MAO) A inhibitor [10], so that the common side-chain degradation was impossible.

Using the STA procedure, the two isomers of *O*-demethyl DOI were found to be suitable as target analytes. The EI mass spectra, the retention indices (RI), the structures and the predominant fragmentation patterns of DOI and its metabolites can be found in ref. [3].

4. Conclusions

DOI undergoes single and double *O*-demethylation to three metabolites. The authors' STA procedure allowed proving an intake of a common drug users' dose of DOI in rat urine by detection of its major metabolites. Earlier studies and the authors' experience in metabolism and analytical studies on rats and humans support the assumption that the metabolites found in rat urine should also be present in human urine. Therefore, it can be concluded that the procedure should also be applicable for human urine screening for DOI in clinical or forensic toxicology.

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6. References

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