Methoxetamine: metabolism and detectability of a novel ketamine analog – studied by GC-MS, LC-MS^n, and LC-HR-MS^n

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Abstract

Aims: Methoxetamine (MXE) was reported to be among the top-five of new psychoactive substances offered for sale in online shops in 2011 and 2012 (EMCDDA, Annual Report 2012). Therefore, the aim of the presented work was to study its phase I and II metabolism and to show its detectability in our standard urine screening approaches (SUSA) using GC-MS and LC-MS^n.

Methods: After application of MXE to male Wistar rats for toxicological diagnostic reasons (20 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 and LC-HR-MS^n (TF Orbitrap Velos). The phase II metabolites were analyzed and identified after protein precipitation by LC-HR-MS^n. 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 enzyme kinetic studies were conducted using the product formation as well as the substrate depletion approach.

Results and Discussion: MXE is mainly metabolized by N-deethylation, O-demethylation and aryl-hydroxylation as well as by glucuronidation and sulfation of its phase I metabolites. Intake of MXE was detectable by GC-MS and LC-MS^n screening approaches in rat and human urine samples. Concerning enzyme kinetic studies, CYP2B6 and CYP3A4 were identified to catalyze the formation of initial metabolites.

Conclusion: The presented study demonstrates that MXE is extensively metabolized and can be analyzed by both SUSAs. Since CYP2B6 and CYP3A4 are involved in initial metabolic steps, interactions should be likely to occur in certain constellations.

In the meantime, this study was published as original paper: