

## Studies on the metabolism and detectability of xylazine in rat and human urine using GC-MS, LC-MS<sup>n</sup>, and LC-HR-MS<sup>n</sup>

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### Abstract

**Aims:** Xylazine,  $\alpha$ -2-agonist, is used in veterinary medicine for sedation, anesthesia, and analgesia. As abuse of this drug was also reported, the aim of this study was to identify the phase I and II metabolites and to test its detectability in our standard urine screening approaches (SUSA) using GC-MS and LC-MS<sup>n</sup>.

**Methods:** Rat urine samples were collected over a 24 h period from male Wistar rats, which had been administered for toxicological diagnostic reasons a 10 (metabolism study) or 2 (detectability studies) mg/kg BW dose of xylazine. Metabolites were identified directly or after enzymatic cleavage, solid-phase extraction, and acetylation by GC-MS (AT MSD) or after protein precipitation by LC-high resolution-MS<sup>n</sup> (TF Orbitrap Velos). For toxicological detection, rat and human urine samples (submitted for toxicological analysis) were analyzed by the following SUSAs: 1) GC-MS after acidic hydrolysis, liquid-liquid extraction (LLE), and acetylation, 2) LC-MS<sup>n</sup> (TF LXQ) after protein precipitation.

**Results and Discussion:** Xylazine was metabolized to eight phase I metabolites, which allowed to propose the following main pathways: *N*-dealkylation to dimethylaniline, *N*- and *S*-dealkylation of the thiazine ring, aromatic hydroxylation, oxidation of the thiazine ring and combinations. The aromatic hydroxy metabolites were partly excreted as glucuronides and/or sulfates. Intake of xylazine was detectable by both SUSAs in rat and human urine samples with the hydroxy metabolites as major targets.

**Conclusion:** Xylazine was extensively metabolized and its intake could be monitored with both SUSAs.

**The case report was recently published:** Meyer GMJ, Meyer MR, Mischo B, Schofer O, Maurer HH. Case report of accidental poisoning with the tranquilizer xylazine and the anesthetic ketamine confirmed by qualitative and quantitative toxicological analysis using GC-MS and LC-MS<sup>n</sup>. Drug Test. Anal. 2013; DOI 10.1002/dta.1475

**The metabolism study will be published soon:** Meyer GMJ, Maurer HH. Studies on the metabolism and toxicological detection of xylazine, a veterinary tranquilizer and drug of abuse, in rat and human urine using GC-MS, LC-MS<sup>n</sup>, and LC-HR-MS<sup>n</sup>, submitted for publication.