Poster

[P26-10] P26-10: Assay of toxicants

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[P26-10-6] New psychoactive substances 1P-LSD &1P-ETH-LAD: metabolism and detectability studied by GC-MS, LC-MSn, and LC-HR-MS/MS

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Background

New psychoactive substances (NPS) are sold as alternatives to controlled drugs of abuse and often provide similar chemical structures. In this study, the in vivo and vitro metabolic fate of the LSD analogs 1-propionyl-lysergic acid diethylamide (1P-LSD) and 1-propionyl-*N*^{6}-ethyl-6-norlysergic acid diethylamide (1P-ETH-LAD) were investigated for urine screening purposes, as no comprehensive metabolism data are published so far. The detectability in standard urine screening approaches (SUSAs) using GC-MS, LC-MS^n, and LC-HR-MS/MS was also evaluated. Furthermore, CYP isoenzymes involved in the initial steps were identified.

Methods

After application of 1P-LSD or 1P-ETH-LAD to male Wistar rats for toxicological diagnostic reasons (10 and 0.01 mg/kg BW for metabolism and toxicological detection studies, respectively), urine was collected over 24h. The phase I metabolites were identified after simple urine precipitation or after enzymatic cleavage and SPE (HCX) followed by LC-HR-MS/MS (TF Q-Exactive Plus). The phase II metabolites were identified after urine precipitation and LC-HR-MS/MS. For the detectability studies, SUSAs by GC-MS (TF ISQ), LC-MS^n (TF LXQ), and LC-HR-MS/MS (TF Q-Exactive) were applied to rat urine collected after recreational doses. Finally, a CYP activity screening was performed to identify CYP isoenzymes involved in the initial metabolic steps.

Results

1P-LSD and 1P-ETH-LAD were mainly metabolized by elimination of the propionyl moiety, *N*-dealkylation, hydroxylation, and their combinations as well as by glucuronidation of the main phase I metabolites. 1P-LSD and 1P-ETH-LAD and their metabolites at recreational doses were not detectable by the SUSAs. CYP3A4 was involved in all main steps, with exception of the depropionylation. The latter was identified as NADPH independent reaction and thus not exclusively catalyzed by CYP enzymes.

Conclusions

The presented study demonstrated that the LSD analogs were metabolized by various steps, mainly under involvement of a single CYP enzyme. Due to the low concentrations after recreational dose, the SUSAs were not suitable to detect an intake. However, sample preparations such as SPE might be an alternative to allow detection even after low doses.