Poster

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

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[P26-10-2] Is a linear triple quadrupole efficient enough to characterize designer benzodiazepines and their metabolites?

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Background

Designer benzodiazepines (DBZD) have become of particular importance in the past few years. The metabolites monitoring of DBZD in biological fluids could be of great interest in clinical and forensic toxicology. However, DBZD metabolites are not known or not commercially available. The identification of some DBZD metabolites has been mostly explored by self administration studies or by in vitro studies followed by high resolution mass spectrometry. The question arose whether a unit resolution instrument could be efficient enough to allow the identification of DBZD metabolites.

Methods

We used an in vitro experiment where 8 DBZD were incubated with human liver microsomes (HLM): diclazepam, flubromazepam, etizolam, deschloroetizolam, flubromazolam, nifoxipam, meclonazepam and clonazolam. Then the metabolites identification was carried out by using a UHPLC (LC-20ADxr pumping system; Shimadzu, France) coupled to a QTRAP triple quadrupole linear iontrap tandem mass spectrometer system (3200 QTRAP; Sciex, France). Two approaches were applied: (i) a general unknown screening (GUS) (i.e. a non-target analysis) and (ii) a multi-target screening (MTS) focusing on transitions of parent and product ions of putative and previously reported metabolites.

Results

We identified 26 phase I metabolites from the 8 DBZD. Among them, 3 had not been reported yet: Desmethyl-clonazolam (m/z 340), denitro-nifoxipam (m/z 270) and a monohydroxylated flubromazolam. The 1.4 benzodiazepines (diclazepam and flubromazepam) mimicked the metabolism of diazepam. The 1.4 triazolo-benzodiazepines (etizolam, deschloroetizolam and flubromazolam) were metabolized in the same way as brotizolam. The nitro-benzodiazepines (clonazolam, nifoxipam and meclonazepam) mimicked the metabolism of flunitrazepam. All metabolites were denitro-, mono- or di-hydroxylated and desmethyl derivatives.

Conclusions

This supports that LC coupled to a simple QTRAP could be used by laboratories to identify not-known/not-commercialized DBZD metabolites.