Poster

[P25-11] P25-11: Clinical toxicology (1)

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[P25-11-4] New psychoactive substances: in vitro metabolism studies using human liver preparations compared to primary human hepatocytes and human urine

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Background

Metabolites have often to be used as targets for toxicological screening procedures in clinical and forensic toxicology. In case of new psychoactive substances (NPS), human samples (from controlled studies) are often not available; therefore in vitro alternatives have to be used such as primary human hepatocytes, but high costs, limited availability, and high variability of metabolizing enzymes limit their applicability. Therefore, the aim was to exemplarily investigate the metabolism of selected NPS from different drug classes using pooled human liver preparations without these limitations in comparison to primary human hepatocytes and human urine samples in order to find the most suitable model for the given purpose.

Methods

Metabolism of AB-PINACA, 25-I-NBOMe, and 4-methoxy-α-PVP at 10 M was investigated using pooled S9 fraction, or pooled human liver microsomes (pHLM) combined with cytosol (pHLC). Both systems were incubated for 15, 30, 60,120,180, 240, 360, 480 min after addition of all co-substrates necessary for common phase I and II reactions. Reactions were initiated by addition of substrate and stopped by acetonitrile. Samples were analyzed using LC-high resolution-MS/MS. Results were compared to each other and to published data after incubating primary hepatocytes and analyzing human urine samples.

Results

Various phase I and II metabolites were detected in both systems. The metabolites formed by pS9 or pHLM/pHLC were comparable in number and abundance. Using pS9, 12, 10, and 6 metabolites and using pHLM/pHLC, 15, 10, and 5 metabolites were detected for AB-PINACA , 25-I-NBOMe, and 4-methoxy-α-PVP, respectively. For primary human hepatocytes, 23, 14, and 11 metabolites were described, respectively. The most abundant metabolites described in primary human hepatocytes and human urine, which were probably the most suitable targets for urine screening procedures, were also detected in pS9 and pHLM/pHLC incubations.

Conclusions

Pooled human liver preparations, pS9 or pHLM/pHLC, seem to be a suitable alternative to primary human hepatocytes and authentic human samples if all relevant co-substrates were added, at least for prediction of suitable targets for urine screening of NPS.