Ultrafast detection of drugs and metabolites in urine by Flow Injection Analysis (FIA) coupled to Magnetic Resonance Mass Spectrometry (MRMS)

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1. Introduction

Detection of metabolites and drugs in body fluids such as plasma or urine by LCMS is a routine method in metabolomics and doping analysis. Routine UPLC-MS measurements are performed typically in 15 min. Therefore, the number of analyzed samples is highly limited. In this work, a fast method for detection of drugs and their metabolites in urine using FIA-MRMS is presented. Roughly 250 samples can be measured in 24h using this technique.

2. Approach

Six pooled urine samples were purified by SPE using Merck LiChrolutEN SPE cartridges. Samples were extracted with methanol from SPE cartridges and diluted 1 to 100 for FIA. Each samples was analyzed in 5 minutes by FIA-MRMS using a solariX 2xR (Bruker Daltonik, Bremen) in ESI using positive and negative ion mode. Analysis of data was performed with MetaboScape 3.0 (Bruker Daltonik, Bremen).

3. Results

The data of the ESI(+) and ESI(-) were combined for feature analysis. More than 2100 features have been found for the pooled urine samples. More than 90% of the detected features could be assigned with a molecular formula. 300 drug candidates have been detected in the urine samples using a HMDB urine database [1] with a mass error tolerance of only 0.5 ppm. The detected drugs have been compared with the medication of the patients. Several drugs have been found only in one or a few pooled urine samples. By comparing the relative abundances of features of all samples, possible metabolites of drugs could be identified.

Figure 1. Schematic MRMS aXelerate workflow:
a) FIA-MRMS acquisition using a scimaX MRMS,
b) Data processing and evaluation using T-ReX 2D in MetaboScape 4.0,
c) Generate list of molecular formula annotations including annotation qualities,
d) Putative metabolite annotations using AnalyteList of known and expected compounds,
e) Statistical analysis to identify features of interest,
f) Optional export for advanced statistical analyses

4. Discussion

Drugs and their metabolites can be detected by FIA-MRMS in a few minutes. This workflow is much fast than the conventional workflow using UPLC-MS. This method could even be used for quantification when internal drug standards are added. Due to the complexity of the samples ultra-high mass resolution as well as very accurate mass detection is a prerequisite for this workflow.

References

1. D.S. Wishart, Y.D. Feunang, A. Marcu, A.C. Guo, K. Liang, et al., HMDB 4.0 — The Human Metabolome Database for 2018. Nucleic Acids Res. 2018. Jan 4;46(D1):D608-17