Targeted screening and semi-quantitation of drugs in plasma using high-resolution accurate-mass detection and online sample preparation

Sensitive and selective analytical methods are required in clinical research and forensic toxicology to properly identify a broad range of analytes in complex matrices. The existing methods need to be constantly updated as new compounds, such as designer drugs, become readily available to the illicit drug market. Liquid chromatography coupled to mass spectrometry (LC-MS) has been widely used in this area for years. So far, the preferred detection technology has been triple quadrupole MS for its selectivity in selected reaction monitoring (SRM) mode. However, this approach suffers from the limitation of being able to perform only targeted analysis, while not useful for unknown screening of new drugs. For this reason, the use of high resolution accurate mass (HRAM MS) instruments has gained in popularity, offering the possibility to perform screening in full-scan mode and identify new substances. The opportunity to screen a very large panel of compounds on a single injection from a low volume of sample is of high importance. Moreover, the use of multiple parameters for identification and confirmation provides additional confidence in the outcome of the screening analysis. We have developed a spectral library and compound database for the screening and semi-quantitation of more than 1500 compounds in plasma samples, and is applicable to other biological matrices. For each compound, the database includes the exact mass, chemical formula, retention time, and exact masses of its main fragments. A Thermo ScientificTM Q Exactive™ Focus Orbitrap high-resolution, accurate-mass spectrometer with a heated electrospray ionization source was used. The current work consisted of the injection of more than 1500 standard solutions to define a database and spectral library of compounds for forensic screening. Thermo ScientificTM TraceFinder 4.1 software was used for the processing of all these data.

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