Wastewater-based epidemiology of illicit drugs and pharmaceuticals: analytical challenges and recent developments

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Wastewater-based epidemiology (WBE) relies on the analysis of illicit drugs, pharmaceuticals and their human metabolic excretion products (biomarkers) in urban wastewater and has received much scientific attention in the last decade. The concentrations measured can be used as a new non-intrusive tool to provide evidence-based and real-time estimates of community-wide drug consumption. Moreover, WBE allows monitoring patterns and spatial and temporal trends of drug use. The use of advanced analytical techniques, commonly based on liquid chromatography coupled to (tandem) mass spectrometry (LC-MS/MS), is mandatory because the low analyte concentration (ng/L range) and the complexity of the raw wastewater samples make quantification and identification/confirmation of relevant biomarkers challenging.

Nowadays, LC-MS/MS has wide recognition and acceptance for accurate quantification of target drug residues in wastewater. LC-MS/MS allows simultaneous quantification and identification of the target compounds in complex matrices due to its excellent sensitivity and selectivity. In this case, the determination is directed towards specific compounds that have been previously selected, and is therefore limited to those substances for which the method has been developed. Consequently, other compounds different than target compounds may be ignored in the analyses. However, high resolution mass spectrometry (HRMS) opens new perspectives in this analytical field due to the powerful information provided (e.g. accurate-mass full-spectrum mass data). LC-HRMS transcends the limitations of LC-MS/MS and shows strong potential for suspect and non-target screening of large number of compounds, such as new psychoactive substances (NPS). Investigation of (bio)transformation products that can be formed in wastewater is also one of the main possibilities offered by this technique. LC-HRMS is commonly limited to qualitative screening, i.e. detection and identification, but recent improvements promoted its use for quantification too.

To produce reliable and comparable results, it is important to perform inter-laboratory exercises and to analyze appropriate quality controls. Other crucial steps in WBE, such as sample collection and sample pre-treatment, such as solid-phase extraction, are also highlighted. Enantiomeric profiling of drugs in wastewater by chiral chromatography coupled with mass spectrometry is presented as a viable option to make a distinction between consumption and direct disposal of unused drugs to wastewater.

Finally, a best-practice protocol is presented to 1) produce homogeneous and comparable data at different sites and 2) provide the most reliable estimates of drug use to consistently complement existing epidemiological studies.