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(Semi) quantification en l'absence de standards analytiques: développement de stratégies adaptées à l'analyse de traces de micropolluants dans des matrices complexes par GC-HRMS, LC-HRMS, LC-MS/MS

(Semi)quantitative assessment in the absence of analytical standards: development of analytical strategies for micropolluants trace analysis in complex matrices by GC-HRMS, LC-HRMS, LC-MS/MS

Keywords : mass spectrometry, semi-quantification, retrospective analysis, targeted and untargeted analyses, high and low mass resolution, LC-QTRAP, LC-QqQ, LC-QToF, GC-Orbitrap

Trace and ultra-trace analysis is an important driver of progress in analytical chemistry, particularly in the field of the environmental exposome. This requires constant innovation in analytical strategies in terms of sensitivity, identification, resolution, speed and reliability. The scientific advances made over the last fifteen years in terms of sensitivity and identification are mainly linked to technical advances in the coupling of chromatography and mass spectrometry, and to the improved resolution of the analysers.

However, the quantification of trace levels remains a real analytical challenge due to the complexity of the environmental matrices and to their low available amounts or volumes. Another major difficulty for scientists is the lack of analytical standards for many metabolites or transformation products (TPs), which escape environmental monitoring and for which no quantitative data are available.

Environmental risk assessment associated with aquatic or terrestrial contamination is mostly based on measured environmental concentrations of a limited list of chemicals in selected media or organisms. However, to get a more comprehensive picture of the exposure to harmful chemicals, non-targeted screening with reversed phase liquid chromatography electrospray ionization or gas chromatography coupled to high resolution mass spectrometry (LC/ESI/HRMS, GC-HRMS) are increasingly employed as an alternative to targeted analysis. Moreover, they offer the possibility of retrospective analysis of digitally stored HRMS data, if new questions or new knowledge emerge. This raises the issue of retrospective quantification of micropollutants that were not targeted at the time of data acquisition.

In this context, the objectives of this thesis are:

- In the perspective of non-targeted screening, the aim is to develop analytical workflows (LC-QqToF and GC-orbitrap couplings) that allow the unambiguous identification (i.e. limiting false

positives or negatives) then quantitative analyses to be carried out retrospectively to data acquisition.

- With the aim of semi-quantifying metabolites or TPs, the response factors of an analyte and its by-products from the main degradations (conjugation, carbon oxidation, heteroatom oxidation, dealkylation, hydrolysis) will be studied to evaluate the impact of adding or removing a functional group on the electrospray ionisation efficiency, electron impact response factor, and fragmentation patterns. Firstly compounds whose transformation products analytical standards are available will be used in order to establish QSPR (quantitative structure property relationship) models that will make it possible to predict the response factors in the absence of standards. Then, different methodologies will be developed and compared, such as the closest eluting compound approach, a structurally similar compound approach, the use of internal standard, ionisation efficiency of suspect compounds present (Kiefer et al., 2019; Liigand et al., 2021; Wiest et al., 2021).

- Finally, the proposed workflows could be applied to the semi-quantification of metabolites or TPs in the presence of environmental matrices. Various complex matrices will be considered in order to study the impact of the matrix on the semi-quantification.

The thesis will be carried out within the TRACES team of the Institute of Analytical Sciences, whose research activities focus on the development of analytical methods, based on mass spectrometric detection, to improve the characterisation of chemical pollution markers in environmental matrices, including sentinel species. The combination of targeted or global analytical strategies allows a better understanding of the Exposome and its consequences on the environment.

Contact : Emmanuelle VULLIET (emmanuelle.vulliet@isa-lyon.fr; +33(0)4 37 42 36 08)

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