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Widening exposome exploration by means of complementary HRMS analytical platforms: use case on pesticide exposure

Elodie Mirmont¹, Tarek Moufawad², Fatima-Zahra Alem³, Cécile Chevrier³, Nathalie Bonvalot³, Emmanuelle Kesse-Guyot⁴, Julia Baudry⁴, Emmanuelle Bichon², Ingrid Guiffard², Jean-Philippe Antignac², Arthur David³, Emilien Jamin¹, Laurent Debrauwer¹

¹TOXALIM – INRAE, INRAE UMR 1331, 180 chemin de Tournefeuille, BP 93173, 31027 Toulouse Cedex 3
²LABERCA – ONIRIS/INRAE, UMR 1329, Route de Gachet, La Chantrerie, CS 50707, 44307 Nantes
³Univ Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail), UMR_S 1085, Rennes, France
⁴CRESS – EREN – INRAE, EREN, Université Paris13 – Sorbonne Paris Nord, SMBH, 74 rue Marcel Cachin, 93017 Bobigny cedex

emilien.jamin@inrae.fr ; laurent.debrauwer@inrae.fr

Introduction

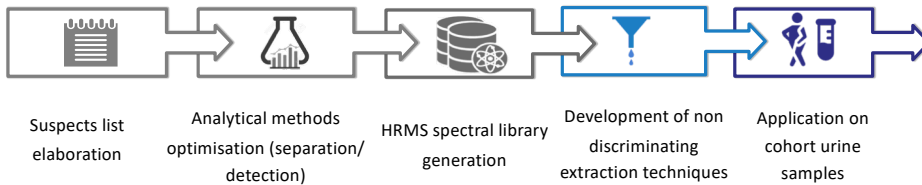
Human exposure to food and environmental contaminants (such as pesticides) is generally estimated by indirect methods. Targeted bio-monitoring is a way to assess the internal exposure on a limited number of substances, needing large sample amounts for analyses as rigorous and sensitive as possible. Thus, the human health risks associated with multi-exposure to complex mixtures currently remain under-explored. In this context, the SCREENPEST project aims at providing a unified methodology for large-scale characterisation of human internal exposure to pesticides, via a "suspect profiling" approach, using urine.



Objectives

- Develop and set-up an harmonised analytical workflow including sample preparation, instrumental measurement and data processing.
- Increase the coverage on human exposure to pesticides by a non-targeted multiplexed approach.
- Test the method developed through urine samples from cohorts to study possible links between exposure and adverse health effects.
- Provide extended information capabilities for early warning on emerging substances and help for decision making.

Developed workflow



PÉLAGIE

- Mother-child cohort (France, 2002-2006)
- Association between the exposure to pesticides of pregnant women and biometric data at birth
- Access to 168 samples



NutriNet-Santé

- General population (France, since 2009)
- Association between the exposure to pesticides and the onset of type 2 diabetes
- Access to 200 samples

Method development



Large list of standards (ca. 200 pesticides and phase I/II metabolites), covering a wide range of physicochemical properties (logKow: [-4.71;8.38], MM/g.mol⁻¹: [72;720]) for analytical developments. Standard selection: commercial availability, bibliography, pesticide use in France (2019), epidemiologists expertise and available data from the HMB4EU project (10.1021/acs.analchem.2c00061)

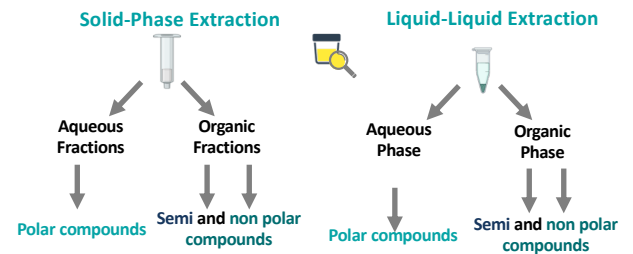


Optimisation of 3 HRMS techniques to get the best separation and detection of the suspects by both LC and GC. Characterisation of the suspects by HRMS

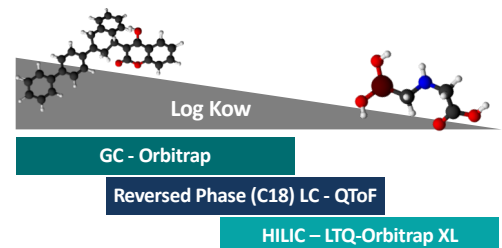
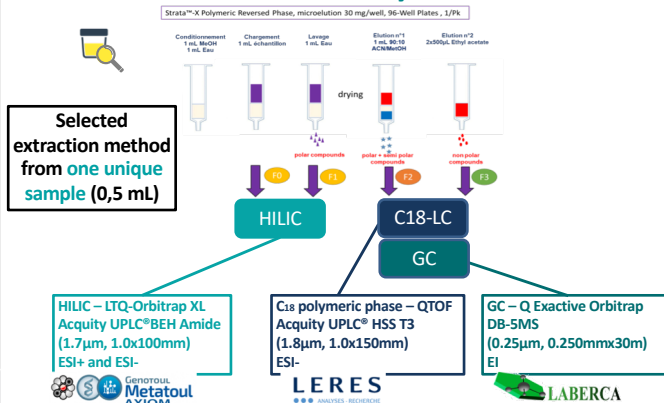


Optimisation of sample preparation: various concentration levels (20, 50 and 100 ng mL⁻¹) spiked in pooled urine (5 replicates).

Performance comparison of two non discriminating extraction techniques (recovery and matrix effect)



Extraction and HRMS analysis



Analytical challenges to cover a wide range of compounds with:

- Different physicochemical properties :
 - Mol. weight [72;720]
 - Polarity / Log Kow [-4.71;8.38]
- Poorly characterised biotransformation products
- Low levels concentration

Data treatment - Bioinformatic tools



Extended HRMS spectral library of reference pesticides and metabolites.



Complemented in house non-targeted and suspect screening chemo-informatics tools (XenoScreener / PeakForest / MetaboHUB W4M).



Improved annotation and identification capacities on a large range of pesticides



Statistical analysis and data interpretation (in progress)