



HAL
open science

Untargeted identification of pesticides metabolites to study their effects on metabolic and Parkinson diseases

Emilien Jamin, Romain Vuillaume, Carla Orlandi, Nicolas Loiseau, Anne Fougerat, Clémence Rives, Laurence Gamet-Payrastre

► **To cite this version:**

Emilien Jamin, Romain Vuillaume, Carla Orlandi, Nicolas Loiseau, Anne Fougerat, et al.. Untargeted identification of pesticides metabolites to study their effects on metabolic and Parkinson diseases. 73rd Conference on Mass Spectrometry and Allied Topics, Jun 2025, Baltimore (MD), United States. <hal-05091181>

HAL Id: hal-05091181

<https://hal.science/hal-05091181v1>

Submitted on 31 May 2025

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



HAL Authorization

Untargeted identification of pesticides metabolites to study their effects on metabolic and Parkinson diseases

Emilien Jamin^{1,2}, Romain Vuillaume^{1,2}, Carla Orlandi^{1,2}, Nicolas Loiseau^{1,3}, Anne Fougerat^{1,3}, Clemence Rives^{1,3}, Laurence Gamet-Payrastrre^{1,3}

1- Toxalim, Toulouse University, INRAE, ENVT, EI-Purpan, Toulouse, France 2- MetaboHUB-MetaToul, National Infrastructure of Metabolomics and Fluxomics, Toulouse, France
3- Toxicology and Integrative Metabolism, Toxalim, Toulouse University, INRAE, ENVT, EI-Purpan, Toulouse, France

Overview

- Two preclinical studies of correlation of pesticides and metabolic and Parkinson diseases
- Mice exposed to pesticides mixtures at admissible daily intake (ADI)
- UHPLC-HRMS analyses of urine samples, using MS/MS and ion mobility
- Identification and quantification of pesticides metabolites with/without standards

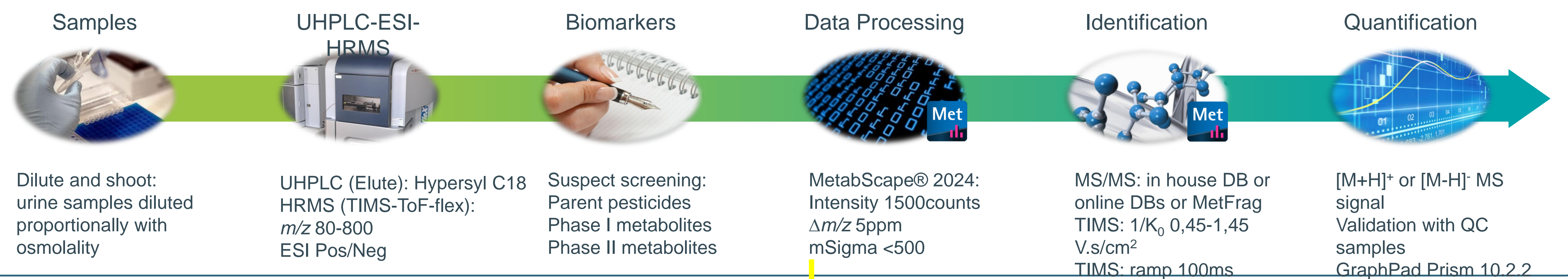
Experimental Designs

- Study of pesticides metabolism with metabolic diseases [1]:**
Cocktail effect of 4 pesticides: **boscalid**, **cyhalothrin**, **imazalil** & **thiabendazole**
2 diets: Western Diet (WD) enriched with fat and sugar vs Chow Diet (CD)
Mice unexposed or exposed to the ADI or 10 times ADI of each pesticide in each diet
Collection of urine after 20 weeks of exposure
- Study of pesticides metabolism with Parkinson disease [2]:**
Cocktail effect of 6 pesticides: **boscalid**, **captan**, **chlorpyrifos**, **thiacloprid**, **thiophanate methyl** & **ziram**
Mouse model (M83) expressing human alphasynuclein (M53T -/-) that recapitulates neuronal lesions
Mice unexposed or exposed to the ADI of each pesticide in each diet
Collection of urine after 27 weeks of exposure

Introduction

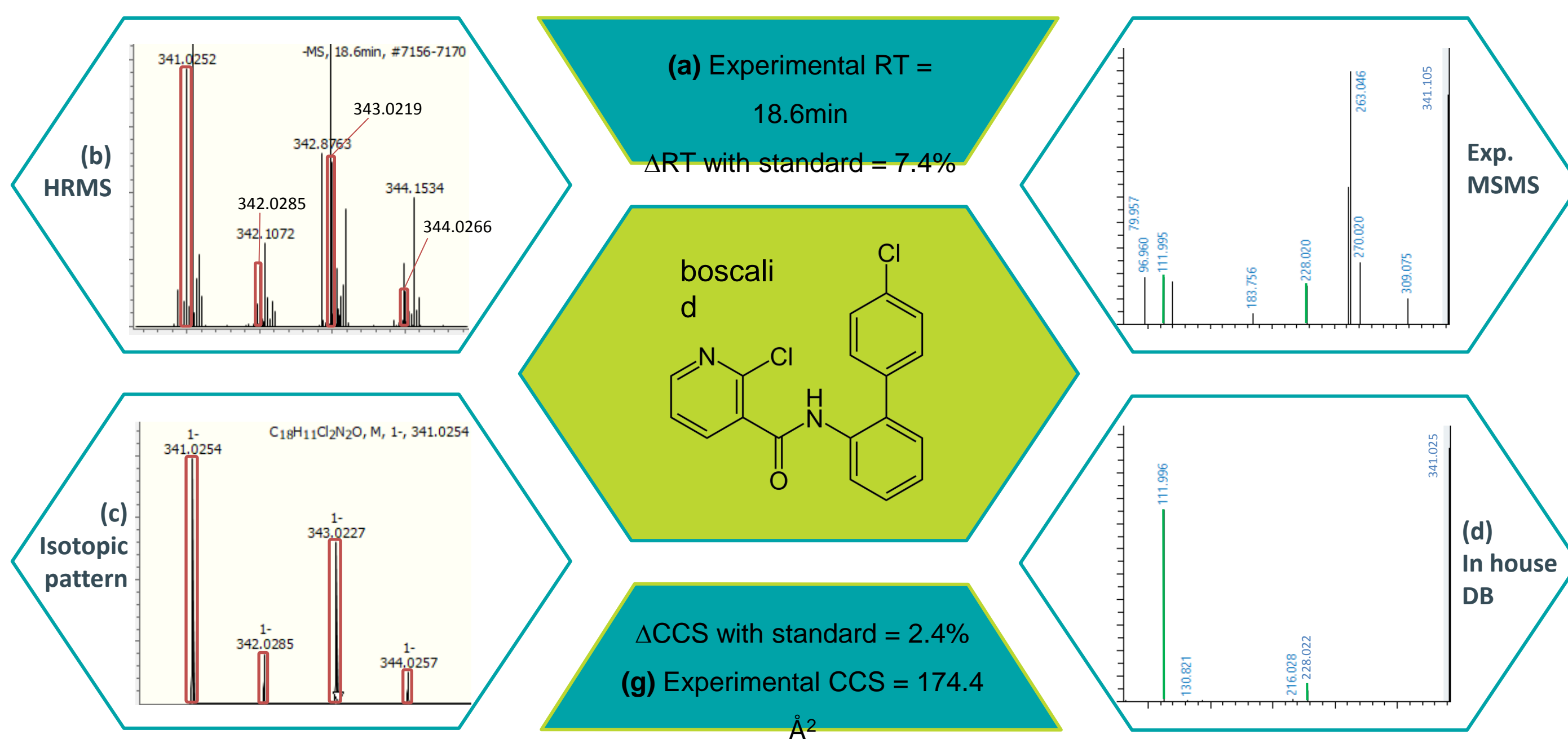
The exposome concept has led to the toxicological assessment of pollutant mixtures. To understand consequences of chronic dietary exposure to pesticide cocktails on Parkinson and metabolic diseases, 2 preclinical studies were performed with mice exposed to the individual admissible daily intake (ADI) of different pesticides in mixture for 20 or 27 weeks. The impact of pesticides may depend on the biotransformation of each one that could be altered when pesticides are in combination. Thus, the characterization of residues (active substance and its metabolites) would not only support exposure but also provide a better insight of the observed effects. However, in a context of low-dose exposure and in the absence of commercial standards, detecting, identifying, and quantifying metabolites is challenging.

Material and Method

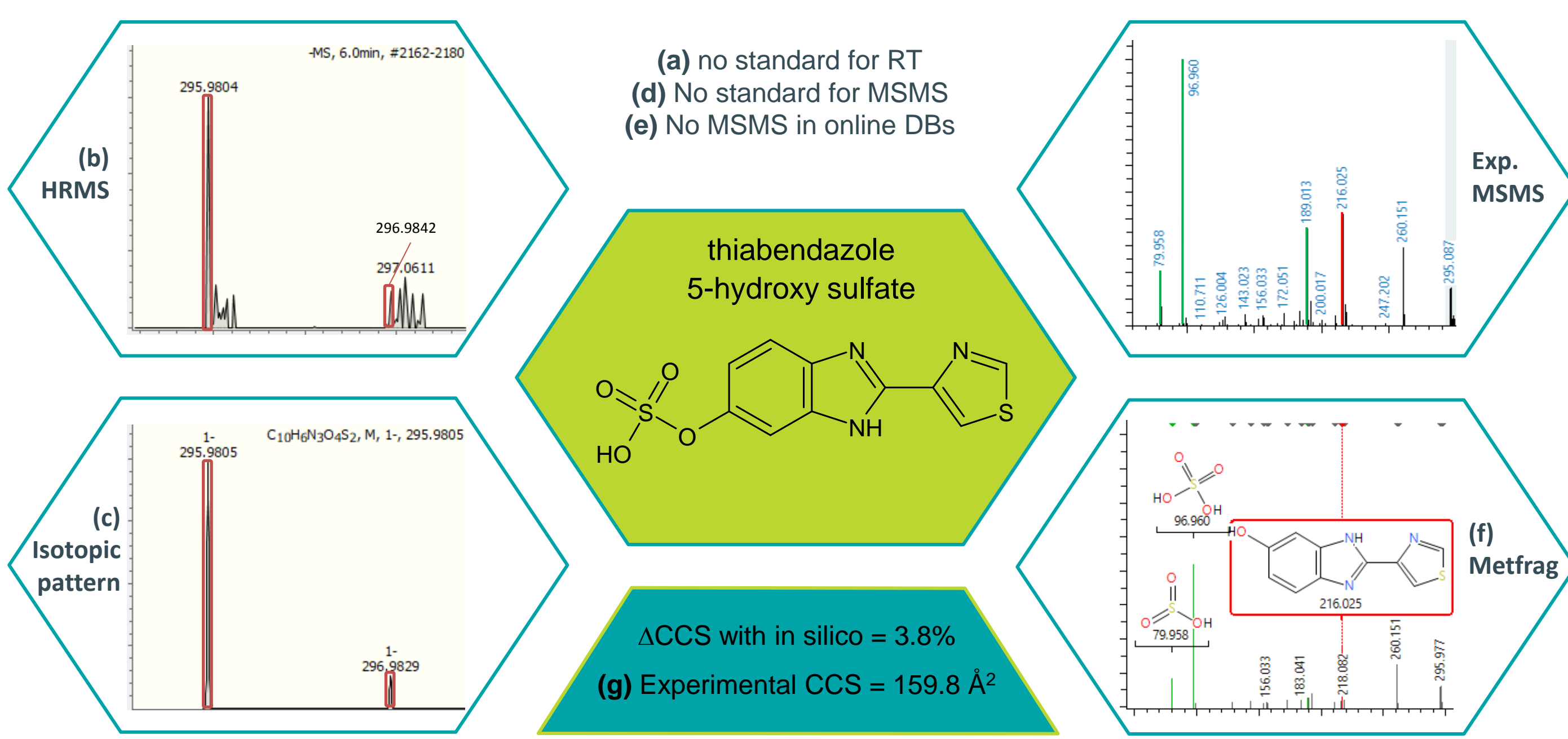


Metabolites Annotation & Identification

- Example of level 1 identification:



- Example of level 2 annotation:



Results

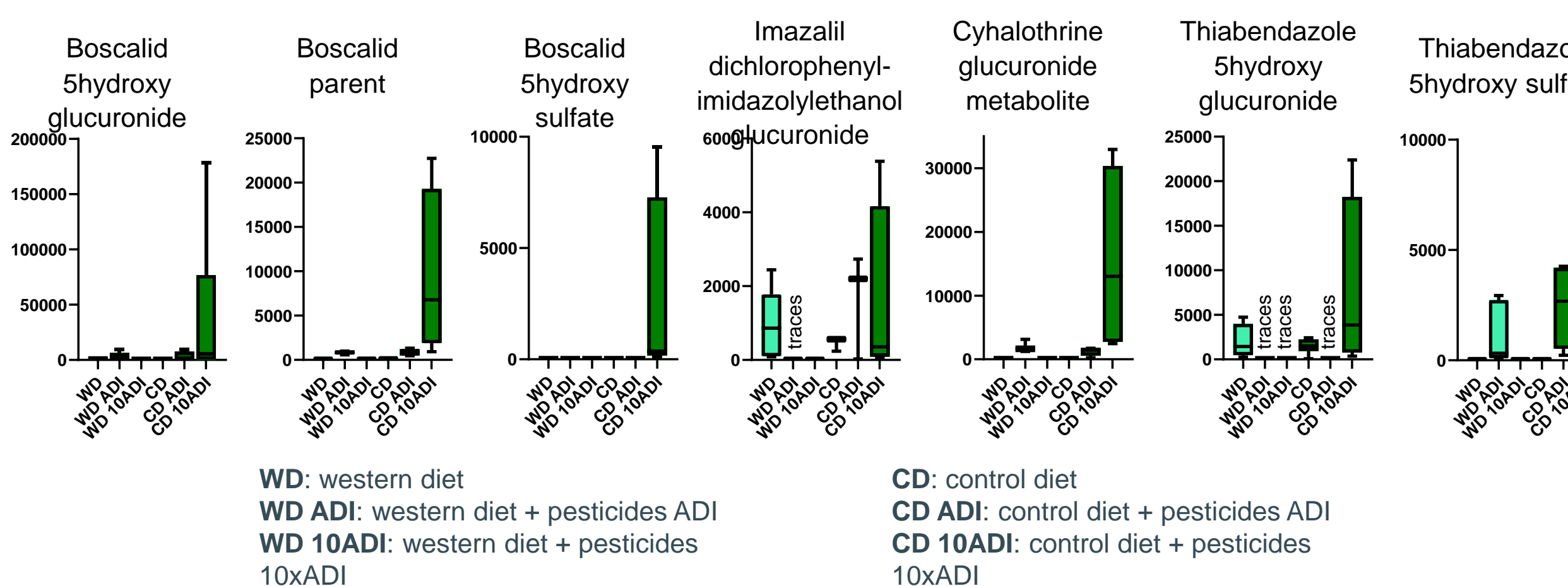
Study of pesticides metabolism high/low fat diet:

- Annotated exposure biomarkers

Name	Identification level	Annotation parameters	Structure
Boscalid 5-hydroxy glucuronide	1	a,b,c,d,g	
Boscalid-5-hydroxy sulfate	1	a,b,c,d,g	
Boscalid parent	1	a,b,c,d,g	
Cyhalothrine Chlorotrifluoropropenyldim ethylcyclopropane carboxylic acid glucuronide	2	b,c,f,g	
Imazalil dichlorophenylimidazolylethanol glucuronide	3	b,c	
Thiabendazole 5-hydroxy glucuronide	2	b,c,f,g	
Thiabendazole 5hydroxy + sulfate	2	b,c,f,g	

a: RT = standard
b: m/z = theory
c: isotopic pattern = theory
d: MS/MS = standard
e: MS/MS = online DBs
f: MS/MS = MetFrag and expert interpretation
g: CCS = standard or in silico

- Quantification of exposure biomarkers



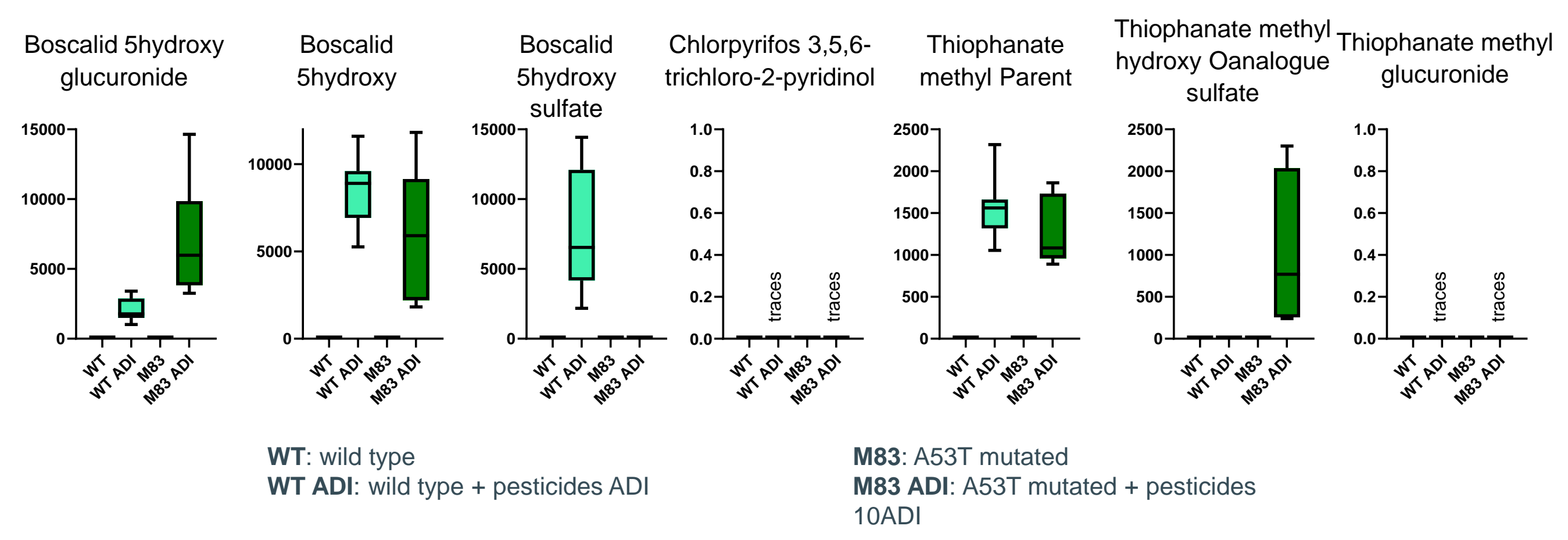
Study of pesticides metabolism with/without neuronal lesions:

- Annotated exposure biomarkers

Name	Identification level	Annotation parameters	Structure
Boscalid 5-hydroxy glucuronide	1	a,b,c,d,g	
Boscalid-5-hydroxy sulfate	1	a,b,c,d,g	
Boscalid 5-hydroxy	1	a,b,c,d,g	
Chlorpyrifos 3,5,6-trichloro-2-pyridinol	1	a,b,c,d,g	
Thiophanate methyl Parent	1	a,b,c,d,g	
Thiophanate methyl glucuronide	2	b,c,f,g	
Thiophanate methyl sulfate	3	b,c,f,g	

a: RT = standard
b: m/z = theory
c: isotopic pattern = theory
d: MS/MS = standard
e: MS/MS = online DBs
f: MS/MS = MetFrag and expert interpretation
g: CCS = standard or in silico

- Quantification of exposure biomarkers



Conclusions

UHPLC-ESI-TIMS-ToF analyses allowed the detection and quantification of pesticides metabolites at admissible daily intake exposure doses. Identifications were enhanced by the use of ion mobility. Each pesticide of the high/low fat diet has at least one detected exposure biomarker. They all displayed a diet effect on the amounts of exposure biomarkers. Interestingly, metabolites and parent compounds were found higher with control diet than western diet. Captan, thiacloprid and ziram exposure biomarkers were not detected in urines of mouse mutated or not on A53T gene to recapitulate neuronal lesions of the Parkinson disease. Other exposure biomarkers of boscalid and thiophanate methyl didn't displayed clear concentration differences between the two animal models at this stage of the study.

Acknowledgments:

These works were supported by Fondation pour la Recherche Medicale (Equipe FRM EQU202303016327), and ANSES (DEEP project). LCMS analyses were achieved in the French national infrastructure MetaboHUB (MetaboHUB-ANR-11-INBS-0010).