Characterising Neonicotinoid Insecticide Exposures Among the Irish Population Using Human Biomonitoring

Darragh Doherty¹, Sonja A. Wrobel², Holger M. Koch², Daniel Bury², Heiko-Udo Käfferlein², Craig Slattery³, **Alison Connolly**¹

¹UCD Centre for Safety and Health at Work; School of Public Health, Physiotherapy, and Sports Science, University College Dublin, D04 V1W8, Dublin, Ireland ²Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr-Universität, Bochum (IPA), Bochum, Germany. ³UCD Centre for Toxicology, Conway Institute; University College Dublin, D04 V1W8, Dublin, Ireland



Key Findings:

1. NNIs detected in 76% of urine samples from the general Irish population 2. All exposures were less than 0.1% of the Acceptable Daily Intake (ADI)

Introduction:

Neonicotinoid and neonicotinoid-like insecticides (NNIs) are a major class of pesticides that can be used as plant protection products, flea treatments, or indoor fly treatments (Figure 1) [1]. In 2018, NNIs were the most widely used class of insecticide in the world, with a market value of almost \$5 billion [2].

Results:

NNIs were detected in 76% of 227 urine samples from the Irish population, indicating a potential for widespread exposure. Exposure to all investigated NNIs was confirmed (*Figure 4*).





Figure 1: The main NNIs that have been used in Ireland and the EU are imidacloprid (IMI), thiacloprid (THIAC), thiamethoxam (THIAM), acetamiprid (ACE), sulfoxaflor (SULF), flupyradifurone (FLUP), and clothianidin (CLO) [3].

Many NNIs have had their use restricted as plant protection products (Figure 2). As of 2024, only FLUP and ACE are still fully approved for use as plant protection products, while IMI is approved for use as a flea treatment for pets [3, 4].

Figure 2: CLO, IMI, THIAM, and SULF have had their use restricted [5-8] due to adverse effects on pollinators. THIAC was restricted due to potential carcinogenicity of its metabolites [9].

Human biomonitoring (HBM) assesses chemical exposures by analysing biological matrices, such as urine or blood (*Figure 3*) [10]. In Ireland, there has been no HBM study of NNIs conducted.

Figure 4: Frequencies of samples with concentrations above the LOQ (Detects) and samples with concentrations below the LOQ (Non-Detects) in the study population. DME-ACE and IMI-Olefin, metabolites of ACE and IMI respectively were the two most widely detected analytes.

Max combined concentration of parent compounds and specific metabolites were a small fraction of ADIs (Table 2), indicating low exposure among the study population.

Table 2: The max combined concentration of NNIs is shown along with how this relates to the ADI.

NNI	Children		Adults	
	Max Conc. (ug L ⁻¹)	%ADI	Max Conc. (ug L ⁻¹)	% ADI
ACE	15.44	0.0595	14	0.0384
IMI	9.6	0.0063	12.63	0.0072
FLUP	3.95	0.0015	7.44	0.0044
SULF	1.85	0.0027	0.97	0.0014
THIAM	1.46	0.0061	2.69	0.0069
THIAC	1.08	0.0235	0.83	0.0084
CLO	1.37	0.0009	0.99	0.0004

Aim:

The EIRE 'nEonicotinoid Insecticide exposuREs' project aims to conduct the first HBM study of NNIs in Ireland. Urine samples from the general Irish population were analysed for NNIs using a previously published method [11].

Methods:

Figure 3: Principle of HBM in the EIRE study. HBM was used to assess exposure to NNIs from all exposure routes by analysing urine samples for NNIs.

Maximum combined concentrations compounds Of parent metabolites were compared with Acceptable Daily Intakes (ADIs) [3, 12, 13].

Urine samples (n=227) were collected from farm and non-farm families in Ireland to investigate glyphosate exposures from 2019 to 2020 [12].

These samples were analysed for selected NNIs and their metabolites (*Table 1*).

and

Table 1: The method used in the EIRE study.

NNI	LOQ	LOQ Metabolite(s)
	(ug L ⁻¹)	(ug L ⁻¹)
ACE	0.06	0.15 (<i>DME-ACE</i>)
MI	0.19	0.24 (IMI-Olefin)
		1 (<i>4/5 OH-IMI)</i>
ΓΗΙΑC	0.11	0.12 (40H- THIAC)
ΓΗΙΑΜ	0.3	0.18 (<i>DME-THIAM</i>)

Discussion:

1 St

• Largest HBM study of NNIs in the EU • Similar levels to previous studies [11,14,15]

• First HBM study of NNIs in Ireland First time quantifying FLUP in an EU population

Future Studies

Future HBM studies of NNIs should focus on quantifying exposures among users and subgroups susceptible to higher exposures of NNIs including gardeners, pet shelter workers, and families with pets that use NNIs

CLO	0.83	1.2 (DME-CLO)
FLUP	0.07	0.17 (<i>50H-FLUP</i>)
		0.2 (<i>DFE- FLUP</i>)
SULF	0.26	No metabolites in method

References

- Simon-Delso, N., et al., Systemic insecticides (neonicotinoids and fipronil): trends, uses, mode of action and metabolites. Environ Sci Pollut Res Int, 2015. 22(1): p. 5-34.
- Sparks, T.C., et al., Insecticides, biologics and nematicides: Updates to IRAC's mode of action classification-a tool for resistance management. Pesticide Biochemistry and Physiology, 2020. 167: p. 104587.
- The European Commission. EU Pesticide Database. Accessed 24 January 2022.
- European Medicines Agency. Advocate. Accessed 14 April 2023.
- The European Commission, Commission Implementing Regulation (EU) 2022/686 of 28 April 2022 amending Implementing Regulations (EU) 2015/1295 and (EU) No 540/2011 as regards the conditions of approval of the active substance sulfoxaflor. 2022: OJ L 126.
- The European Commission, Commission Implementing Regulation (EU) 2018/785 of 29 May 2018 amending Implementing Regulation (EU) No 540/2011 as regards the 6. conditions of approval of the active substance thiamethoxam. 2018: OJ L 132.
- The European Commission, Commission Implementing Regulation (EU) 2018/784 of 29 May 2018 amending Implementing Regulation (EU) No 540/2011 as regards the conditions of approval of the active substance clothianidin 2018: OJ L 132.
- The European Commission, Commission Implementing Regulation (EU) 2018/783 of 29 May 2018 amending Implementing Regulation (EU) No 540/2011 as regards the conditions of approval of the active substance imidacloprid. 2018: OJ L 132,.
- The European Commission, Commission Implementing Regulation (EU) 2020/23 of 13 January 2020 concerning the non-renewal of the approval of the active substance thiacloprid, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. 2020: OJ L 8.
- 10. Angerer, J., U. Ewers, and M. Wilhelm, Human biomonitoring: state of the art. Int J Hyg Environ Health, 2007. 210(3-4): p. 201-28.
- 11. Wrobel, S.A., et al., Rapid quantification of seven major neonicotinoids and neonicotinoid-like compounds and their key metabolites in human urine. Analytica Chimica Acta, 2022: p. 340680.
- 12. Connolly, A., et al., A Human Biomonitoring Study Assessing Glyphosate and Aminomethylphosphonic Acid (AMPA) Exposures among Farm and Non-Farm Families. Toxics, 2022. **10**(11): p. 690.
- 13. Wrobel, S.A., et al., Quantitative Metabolism and Urinary Elimination Kinetics of Seven Neonicotinoids and Neonicotinoid-Like Compounds in Humans. Environmental Science & Technology, 2023.
- 14. Li, A.J. and K. Kannan, Profiles of urinary neonicotinoids and dialkylphosphates in populations in nine countries. Environ Int, 2020. 145: p. 106120.
- 15. López-García, M., et al., Semiautomated determination of neonicotinoids and characteristic metabolite in urine samples using TurboFlow™ coupled to ultra high performance liquid chromatography coupled to Orbitrap analyzer. J Pharm Biomed Anal, 2017. 146: p. 378-386.

Funding: This project has been funded by the Science Foundation Ireland (SFI) Pathway Programme, Proposal ID: 21/PATH-S/9441

