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BUILDING A FORENSIC GC-MS/MS MRM DATABASE

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BACKGROUND

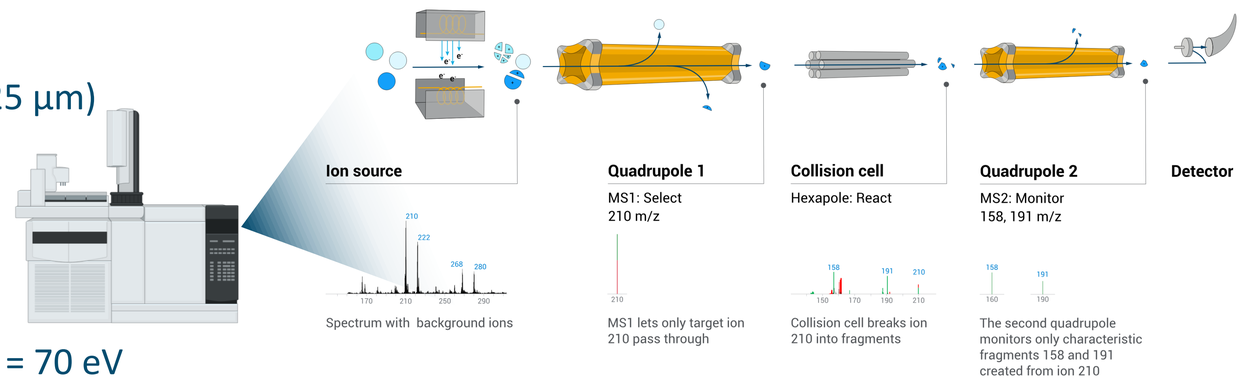
- An ever growing and changing toxicant landscape makes it impossible to obtain analytical standards for every (novel) chemical.
- Labs are looking for robust & pragmatic methods for confirmation of the presence of a toxicant.
- Gas chromatography coupled to mass spectrometry (GC-MS) is an easily optimizable technique available in many forensic labs, that generates uniform & comparable results between instruments and labs.
- The use of tandem mass spectrometry (MS/MS) can improve selectivity & sensitivity.

OBJECTIVES

- Building a database of readily available MRM transitions for (forensic) toxicologically relevant chemicals that are compatible with GC.
- Developing a workflow for practical and straightforward addition of more (new) toxicants.

METHODOLOGY

- Instrument: Agilent 7890B GC coupled to a 7000D triple quadrupole MS
- Stationary phase: Agilent DB-5MS capillary column (30 m x 0.25 mm x 0.25 µm)
- Carrier gas: He
- Injection: pulsed splitless mode – V = 2 µL
- Retention time locking to cocaine to 12.26 min
- Electron impact ionisation: source temperature = 230 °C, electron energy = 70 eV



MRM CURATION WORKFLOW

Full scan acquisition
- Underivatized
- Acetylated
- Trimethylsilylated

Analyte identification
- Deconvolution MS
- Libraries search

MRM optimisation
- Acquisition, selection & curation of precursor ions
- Acquisition, selection & curation of product ions
- Collision energy optimisation

Favouring molecular ions as precursors, larger *m/z* values, product ions overlapping between collision energies

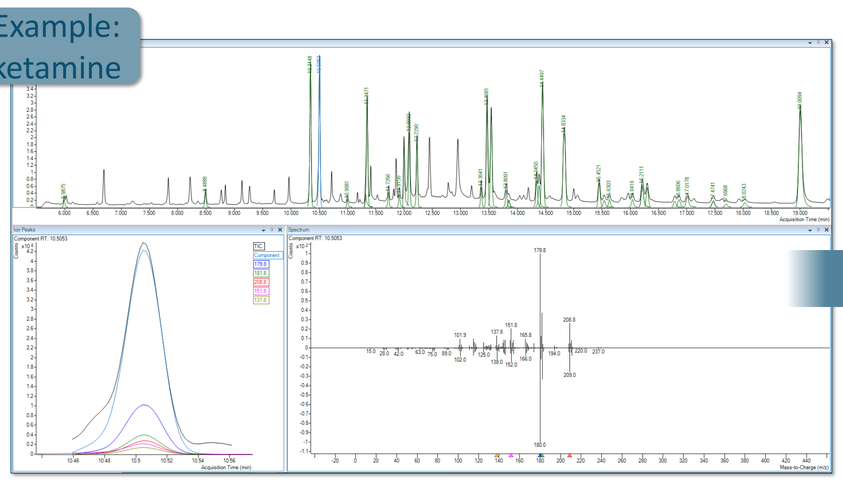
Output

Library/CSV file
- 176 entries in total
- Retention time
- 3 - 12 transitions per compound
- Relative abundance
- Collision energy

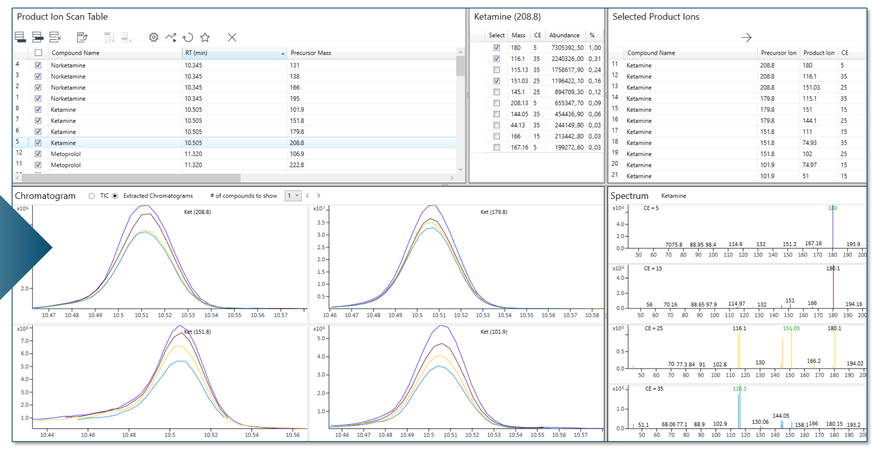
154 unique compounds
- 124 underivatised entries
- 34 trimethyl-silylated entries
- 18 acetylated entries

Agilent Unknowns Analysis

Example: ketamine

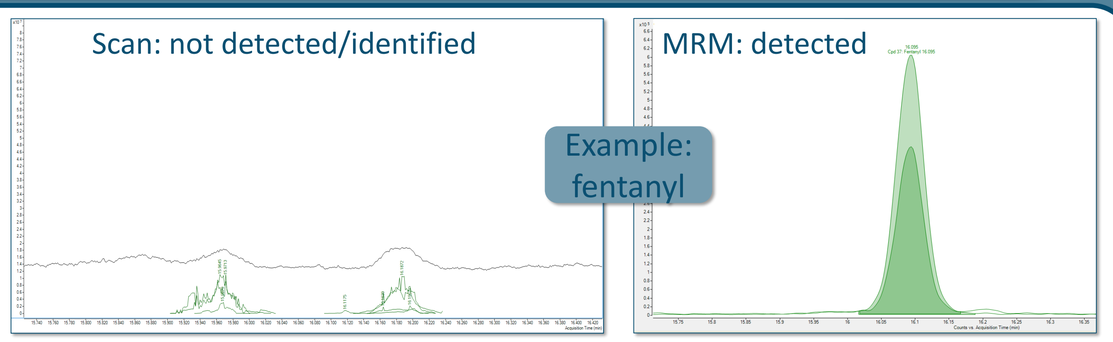


MassHunter Optimizer for GC/TQ
Mass Spectral Library of Drugs, Poisons, Pesticides, Pollutants and their Metabolites[A]



APPLICATION

- Proof of concept: application to archived post-mortem blood samples (n = 25)
- Comparison full scan only with MRM
- All compounds found with MRM approach, not with full scan only
- E.g. fentanyl in therapeutic concentration range (1.7 ng/mL)



CONCLUSIONS

- A database of readily available MRM transitions for relevant toxicants was established and successfully applied to authentic samples.
- The developed MRM database can be tested and used with any GC-MS/MS instrument, simplifying the development of screening and quantitation methods in forensic labs.
- The developed MRM curation workflow showed the potential to continuously add new chemicals to the database in a uniform and practical way.

FUTURE PERSPECTIVES

- Addition of more novel toxicants & their metabolites to the database, sharing library and crowd-sourcing.
- Continued authentic samples analyses: tablets, powders, urine, vitreous humour, tissues (e.g. kidney, liver), …
- Implementation in routine screening methods.

References
- [A] Maurer, H. H., Pfleger, K. & Weber, A. A. Mass Spectral Library of Drugs, Poisons, Pesticides, Pollutants, and Their Metabolites, 2007 (3rd Edition).