The use of gas chromatography – high resolution mass spectrometry for suspect screening and non-targeted analysis of per- and polyfluoroalkyl substances (PFAS)

Seth Newton, Jonathan Casey

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The use of gas chromatography – high resolution mass spectrometry for suspect screening and non-targeted analysis of per- and polyfluoroalkyl substances

Jonathan S Casey[a], Stephen R Jackson[b], Jeff Ryan[b], Seth R Newton[b,*]

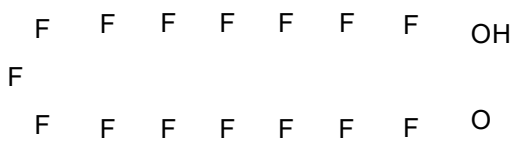
[a] ORISE, Office of Research & Development, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, United States
[b] Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, United States

- https://authors.elsevier.com/a/1gg014-ggU-4d

What Are PFAS?

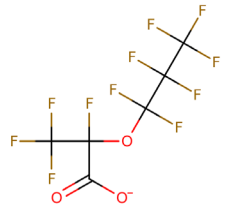
- Contain at least one perfluoroalkyl group (C_nF_{2n})
- There are > 9,000 known PFAS

Well known PFAS:



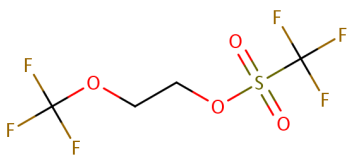
Perfluorooctanoic Acid

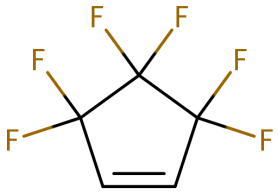
Perfluorooctane Sulfonic Acid

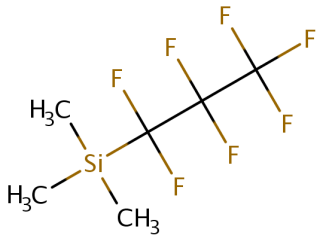


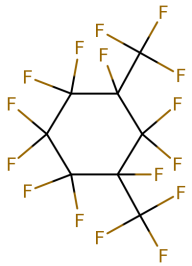
GenX

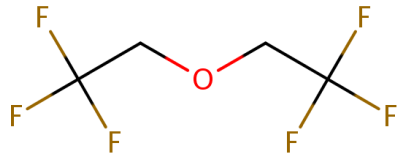
Lesser known PFAS:











PFAS Uses and Concerns

What are Polyfluorinated alkyl substances (PFAS) used for?

Toxicology of PFAS

- Increased cholesterol levels
- Changes in liver enzymes
- Decreased vaccine response in children
- Increased risk of high blood pressure or pre-eclampsia in pregnant women
- Small decreases in infant birth weights
- Increased risk of kidney or testicular cancer

https://ecology.wa.gov/Waste-Toxics/Reducing-toxic-chemicals/Addressing-priority-toxic-chemicals/PFAS

Why GC?

- Most Non-targeted analysis has been done using LC -> good for water, soil, etc.
- GC is needed for air
- We have been blind to emissions from:
  - Incineration (especially contaminated soils)
  - PFAS manufacturing emissions to air
  - Emission from PFAS applications (e.g., textile coating)

Goals

1. Construct a GC-HRMS spectral database of PFAS compounds
2. Develop a workflow for NTA using GC-HRMS
3. Evaluate the NTA workflow
4. Apply it to field samples

The Chemicals

- Not standards
- 150 diverse PFAS in ethanol
- Includes some legacy PFAS but mostly novel PFAS
- Analyzed in EI, PCI, and NCI -> all spectra added to custom database

Observed Functional Groups

PFAS Chemicals	EI	PCI	NCI	Any Mode	n
Acrylate	100	83	100	100	6
Alcohol	94	100	100	100	18
Alcohol/Amine	100	100	100	100	1
Alcohol/Sulfonamide	100	100	100	100	2
Aldehyde	100	100	100	100	2
Alkane	0	0	0	0	2
Alkene	0	0	0	0	6
Alkene/Carboxylic Acid	0	0	0	0	1
Amide	80	80	80	80	5
Amine/Carboxylic Acid	0	0	0	0	1
Amine/Halogen (I)/Sulfonamide	100	100	100	100	1
Amines	20	20	20	20	5
Carboxylic Acid	39	33	56	56	18
Cyclic	0	0	0	0	2
Cyclic /Acetone	0	0	0	0	1
Cyclic/Alkene	0	0	0	0	1
Cyclic/Amine/Ether	0	0	0	0	1
Epoxy	100	100	100	100	1
Ester	0	0	0	0	1
Ether	0	0	0	0	5
Ether/Alcohol	100	100	100	100	2
Ether/Alkene	0	0	0	0	2
Ether/Carboxylic Acid	33	0	33	44	9

PFAS Chemicals	EI	PCI	NCI	Any Mode	n
Ether/Carboxylic Acid/Amine	0	0	0	0	1
Ether/Ester/Alkene	100	100	100	100	1
Ether/Epoxy	100	100	100	100	1
Ether/Ketone	0	0	0	0	2
Ether/Sulfonate	0	0	0	0	1
Halogenated (Cl, Br, I)	43	29	29	43	7
Ketone	33	67	67	67	3
Ketone/Halogen (Cl)	0	0	0	0	1
Ketone/Thiol	100	100	100	100	1
Meta-acrylate	100	100	100	100	3
Methoxy	100	100	100	100	1
OCF	0	0	0	0	1
Phosphate	0	0	0	0	2
Silane	0	0	0	0	1
Silane/Halogen (Cl)	0	0	0	0	1
Silane/Methoxy	100	100	100	100	1
Sulfonamide	100	100	100	100	4
Sulfonamide/Amine	100	100	100	100	1
Sulfonate	11	0	11	11	9
Sulfonate/Potassium	0	0	0	0	3
Sulfonyl Chloride	0	0	100	100	1
Sulfonyl Fluoride	0	0	0	0	2
Thiol	100	100	100	100	1

Percent Observed

0% 50% 100%

Observation of Fragments and Molecular Ion

PFAS Alcohols	Mode Detected	CF_3 Fragment Detected in > 5% Relative Abundance	C_3F_5 Fragment Detected in > 5% Relative Abundance	C_7F_{13} Detected in > 0.8% Relative Abundance	C_8F_{15} Detected in > 0.8% Relative Abundance	Molecular Ion Detected
1-(Perfluorofluorooctyl)propane-2,3-diol	EI, PCI, NCI	EI	EI	EI, PCI, NCI	NF	EI, PCI
1H,1H,5H-Perfluoropentanol	EI, PCI, NCI	EI	EI	N/A	N/A	PCI, NCI
1H,1H,7H-Dodecafluoro-1-heptanol	EI, PCI, NCI	EI	EI	N/A	N/A	PCI, NCI
1H,1H-Heptafluorobutanol	EI, PCI, NCI	EI	EI	N/A	N/A	PCI, NCI
1-Pentafluoroethylethanol	EI, PCI, NCI	EI	NF	N/A	N/A	EI, PCI, NCI
3-(Perfluoro-2-butyl)propane-1,2-diol	EI, PCI, NCI	EI	EI	N/A	N/A	EI, PCI, NCI
3-(Perfluoropropyl)propanol	PCI, NCI	NF	NF	N/A	N/A	NF
3H-Perfluoro-2,2,4,4-tetrahydroxypentane	EI, PCI, NCI	EI	NF	N/A	N/A	NF
4:2 Fluorotelomer alcohol	EI, PCI, NCI	EI	EI	N/A	N/A	EI, PCI
4:4 Fluorotelomer alcohol	EI, PCI, NCI	EI	EI	N/A	N/A	EI, PCI
6:1 Fluorotelomer alcohol	EI, PCI, NCI	EI	EI	PCI	N/A	EI, PCI, NCI
6:2 Fluorotelomer alcohol	EI, PCI, NCI	EI	EI	NF	N/A	EI, PCI
7:3 Fluorotelomer alcohol	EI, PCI, NCI	EI	EI	NCI	NF	EI, PCI
8:2 Fluorotelomer alcohol	EI, PCI, NCI	EI	EI	EI	PCI	EI, PCI
10:1 Fluorotelomer alcohol	EI, PCI, NCI	EI, PCI	EI, PCI	EI, PCI, NCI	PCI, NCI	PCI
10:2 Fluorotelomer alcohol	EI, PCI, NCI	EI, PCI	EI, PCI	EI, PCI, NCI	PCI, NCI	EI, PCI
11:1 Fluorotelomer alcohol	EI, PCI, NCI	EI, PCI	EI, PCI	PCI, NCI	PCI, NCI	PCI, NCI
Hexafluoroamylene glycol	EI, PCI, NCI	EI	EI, NCI	N/A	N/A	PCI, NCI

Data Processing Workflow

Initial Filtering Criteria of Electron Ionization Database Matches

- Molecular formula contains at least one fluorine atom
- Reverse high resolution filtering (RHRF) ≥75
- Search index (SI) ≥ 400
- Reverse Search Index (RSI) ≥ 400
- Dot product ≥ 500
- Exclude features which are not more than 10x the peak area of solvent blank(s) and not more than 5x the peak area of the field blank(s)

↓

For Top 5 Non-Identical Candidates within each Feature

- Additional Measures:
  1) Examining EI, PCI, and NCI spectra for a molecular and/or psuedo-molecular ions
  2) Visually inspecting EI spectral matches for excessive noise and approximate ion ratios
  3) Eliminating candidates with extreme retention times based on structure
- Record RHRF, SI, RSI, retention index (RI), and other information (i.e., Molecular ion and/or pseudo-molecular ion) for top 5 candidates

Analysis of a Challenge Sample

Compound #	Compounds	Chemical Formula	Molecular Ion Present?	External Database	Custom Database EI entry
1	4:2 Fluorotelomer Alcohol	$C_6H_5F_9O$	EI: Yes PCI: Yes NCI: N/A	NIST20	Yes
2	6:2 Fluorotelomer Alcohol	$C_8H_5F_{13}O$	EI: Yes PCI: Yes NCI: N/A	NIST20 & Wiley 11	Yes
3	Perfluoro-2-methyl-3-oxahexanoic acid	$C_6HF_{11}O_3$	EI: Yes PCI: N/A NCI: N/A	N/A	Yes
4	1,1,1,2,2,3,3-Heptafluoro-3-(1,2,2,2-tetrafluoroethoxy)propane	$C_5HF_{11}O$	EI: No PCI: Yes NCI: No	NIST20 & Wiley 11	No
5	Perfluorohexanoic acid	$C_6HF_{11}O_2$		NIST20	No
6	1H,1H,2H-Perfluoro-1-decene	$C_{10}H_3F_{17}$		NIST20 & Wiley 11	No
7	1H,1H,2H-Perfluoro-1-hexene*	$C_6H_3F_9$		NIST20 & Wiley 11	No
8	1H-Perfluoroheptane	C_7HF_{15}		Wiley 11	No
9	1H,1H,2H-Perfluoro-1-octene	$C_8H_3F_{13}$		NIST20 & Wiley 11	No
10	1H,1H,2H-Perfluoro-1-dodecene	$C_{12}H_3F_{21}$		N/A	No

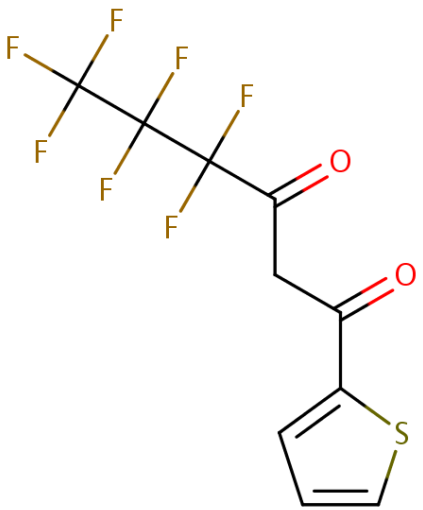
No signal from the instrument

*Scoring system by Koelmel et al (2022)

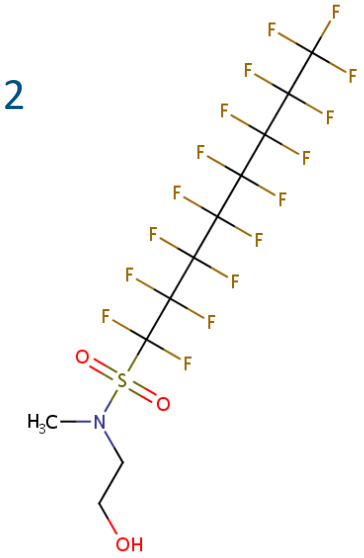
Incineration Samples Custom Database Matches

Compound #	Compounds	Molecular Ion Detected	Calculated RI from Incineration Extracts	RI from PFAS Chemicals	SI Score	Reverse SI Score	RHRF Score	Confidence Score
1	(Perfluorobutyryl)-2-thenoylmethane	No EI or NCI molecular ions detected	1007	1099	811	923	100	Level 3
2	N-Methyl-N-(2-hydroxyethyl) perfluorooctanesulfonamide	No EI or NCI molecular ions detected	1584	1685	647	779	89.5	Level 3

Compound 1



Compound 2



Incineration Samples NIST and Wiley Database Matches

Internal Standards

Compound #	Compound	Molecular Ion Detected	Calculated RI from Incineration Sample	Predicted RI, Estimated RI, NIST20 RI, or RI from In-House Commercial Std	SI score	Reverse SI Score	RHRF Score	Confidence Score
1	2-fluoro-1,1'-biphenyl*	EI, PCI	1368	1361	857	924	98.4	Level 1
2	2-fluorophenol*	EI, PCI, NCI	859	865	705	707	100	Level 1
3	5-Isopropyl-1-ϐ,D-ribofuranosyl)-4-(trifluoromethyl)-1H-pyrimidin-2-one	No	2121	2300	601	855	100	Level 3
4	(1,1-Difluoro-2-phenyl-1-(phenylsulfanyl)propan-2-yloxy)trimethylsilane	No	2241	1977	492	813	100	Level 4C
5	1-ethoxy-2-fluoro-benzene	PCI, NCI	826	944	739	772	100	Level 3
6	4-Butylbenzoic acid, pentafluorophenyl ester	PCI	2052	1944	556	892	90.7	Level 3
7	2,5-Di(trifluoromethyl)benzoic acid, 5-tridecyl ester	No	2323	2084	410	672	88.6	Level 4C
8	Acetamide, N-(1,5-dimethyl-6-oxo-4-hexenyl)-2,2,2-trifluoro-N-methyl-,(E)-(.+-.)	No	1368	1259	477	804	76	Level 4C

Conclusions

- Our data workflow can identify PFAS from the custom database and external databases like NIST and Wiley
- We wish there were more retention indices
- We can identify some compounds in incineration samples but maybe not the best matrix

Future Work

- Align EI and CI data better to utilize CI more
- De novo work on more PFAS enriched samples
- Retention time prediction
  - Follow up question: how valuable would it be to predict RIs for all compounds in the DSSTox database (1.2 million compounds)

Acknowledgements

- The NTA group at EPA
- EPA ORD and Oak Ridge Institute for Science and Education (ORISE)
- The Dashboard team

Contact Information:

Newton.Seth@epa.gov

Questions?