

Note d'application

Extending PFAS Analytical Workflows with APGC-MS/MS Analysis: A Method for 35 GC-Amenable PFAS Compounds

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Abstract

An APGC-MS/MS method for the analysis of 35 GC-amenable per- and polyfluoroalkyl substances (PFAS) is presented, enabling labs to extend existing workflows to capture volatile and semi-volatile PFAS. The analysis includes fluorotelomer alcohols (FTOH), acrylates (FTAc), methacrylates (FTMAC), acetates (FTOAc), sulfonamides (PFSA) and sulfonamidoethanols (PFSE). Method development and optimization, including column and inlet liner selection, is discussed. The goal of the method is to allow for injection of samples pre-extracted for LC-MS/MS analysis that are mainly in methanol and water. Method lower limits of quantification (LLOQ) ranged from 0.005 – 5.0 ng/mL, with most compounds being below 0.10 ng/mL.

Benefits

- An APGC-MS/MS method for the analysis of 35 GC-amenable PFAS allowing for characterization of PFAS samples beyond the suite of commonly targeted LC-MS/MS compounds, for a more complete assessment of PFAS burden

- Injection of samples already extracted for LC-MS/MS analysis is possible without having to perform solvent exchange, saving time and labor
- Sensitive and robust analysis to detect trace levels of PFAS in samples

Introduction

Routine PFAS analysis most commonly utilizes liquid chromatography (LC) as the separation technique and is the basis for most standardized methods that are currently available. While this is a key technique in the analysis of PFAS, there are classes of volatile and semi-volatile PFAS that do not chromatograph well using LC and require the use of gas chromatography (GC) to be successfully analyzed. Classes of PFAS that favor GC analysis include, but are not limited to, fluorotelomer alcohols (FTOH), fluorotelomer acrylates (FTAc), fluorotelomer methacrylates (FTMAC), and fluorotelomer acetates (FTOAc). Additionally, there are classes that can be analyzed using both LC and GC techniques, including sulfonamides (PFSA) and sulfonamidoethanols (PFSE).

All of these compounds are considered precursor compounds that terminally transform into the most widely studied PFAS, perfluoroalkyl carboxylates (PFCA) and perfluoroalkyl sulfonates (PFSA). Not only are they precursors in the synthesis of PFCA and PFSA end products, they are also intentionally used in products such as food packaging and textiles to impart grease and water proofing qualities.

These precursor compounds are also discharged into the environment through similar routes as their end products (landfills, manufacturing waste, firefighting foams, etc), but also through volatilization, transport and deposition through the atmosphere either in the gas phase or bound to particulates. Like most PFAS, not much is known about the human toxicity of these particular PFAS, although some animal and *in vitro* studies do point to similar health effects as more commonly studied PFCAs and PFSA, including liver and kidney toxicity, endocrine disruption and negative immune effects.¹⁻⁴ Furthermore, their ability to transform in the environment to PFCAs and PFSA, which are known to have toxic health implications, make them of concern.

GC-MS/MS analysis for the volatile and semi-volatile GC amenable PFAS provides an additional tool in the workflow of PFAS sample analysis, increasing the comprehensiveness of sample characterization. In this application note, the development of an atmospheric pressure gas chromatography (APGC) coupled to tandem quadrupole mass spectrometry (MS/MS) method will be presented. Application of this method to authentic samples will be explored in a companion application note.

Experimental

Sample Preparation

Native PFAS standards were purchased from Wellington Laboratories and AccuStandard. Isotope labeled internal standards were purchased from Wellington Laboratories.

Calibration curves to assess method sensitivity were prepared from 0.01 to 50 ng/mL for all compounds, except the sulfonamides at 0.10 to 500 ng/mL due to lower sensitivity of this group of PFAS compounds. The concentration range for each compound used for quantitation is highlighted later in Table 1.

Proton transfer conditions were established in the APGC source using three vials of water in the source door tray. Each vial was capped with a small piece of capillary tubing pierced through the vial cap.

Isopropyl alcohol (IPA) and methanol were used as wash A and B, respectively, in the GC autosampler. Both pre and post injection washes were performed. IPA was found to help reduce carryover of the sulfonamide compounds.

GC Conditions

GC system:	Agilent 8890
Autosampler:	7693A ALS
Column:	Rtx-200 GC Capillary Column, 30 m x 0.25 mm ID, 0.50 µm
Inlet liner:	Siltek Deactivated Straight with Wool (4.0 x 6.5 x 78.5 mm)
Carrier gas:	Nitrogen
Flow rate:	2 mL/min

Injection:	Pulsed Split (40 psi until 0.6 minutes)
Split ratio:	10:1
Injection port temperature:	240 °C
Injection volume:	1 µL
Makeup gas:	Nitrogen at 300 mL/min
Transfer line temperature:	310 °C

Oven Program

Rate (°C/min)	Temperature (°C)	Hold (min)	Total Time (min)
Initial	40	1	1
12	200	0	14.3
50	310	3.5	20

MS Conditions

MS system:	Xevo™ TQ Absolute Mass Spectrometer
Ionization mode:	API+
Ionization mechanism:	Proton transfer (water)
Source temperature:	150 °C

Corona current:	1.0 μ A
Cone gas flow:	250 L/hr
Auxiliary gas flow:	150 L/hr
MRM method:	See Appendix for Full MRM Method details

MS Conditions for x:1 FTOH Compounds

Corona current:	3.0 μ A
Cone gas flow:	650 L/hr
Auxiliary gas flow:	250 L/hr

Data Management

Software:	waters_connect™ for Quantitation Software
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Results and Discussion

Advantage of APGC

APGC has an advantage over traditional electron ionization (EI) as it is a softer ionization technique, allowing the molecular ion to remain intact during the ionization process. A full scan APGC mass spectrum for 8:2 FTOH is shown in Figure 1, compared to an EI mass spectrum obtained from the NIST library. The molecular ion in EI mode should be present at m/z 364, but this compound is completely fragmented upon ionization, leaving only low mass fragments for use as the precursor mass for MRM transitions. In contrast, using APGC ionization, the $[M+H]^+$ molecular ion at m/z 365 is abundantly present, allowing much more selective and sensitive MRM

transitions for analysis. This improved selectivity and molecular ion preservation enables more confident compound identification, particularly in complex matrices.

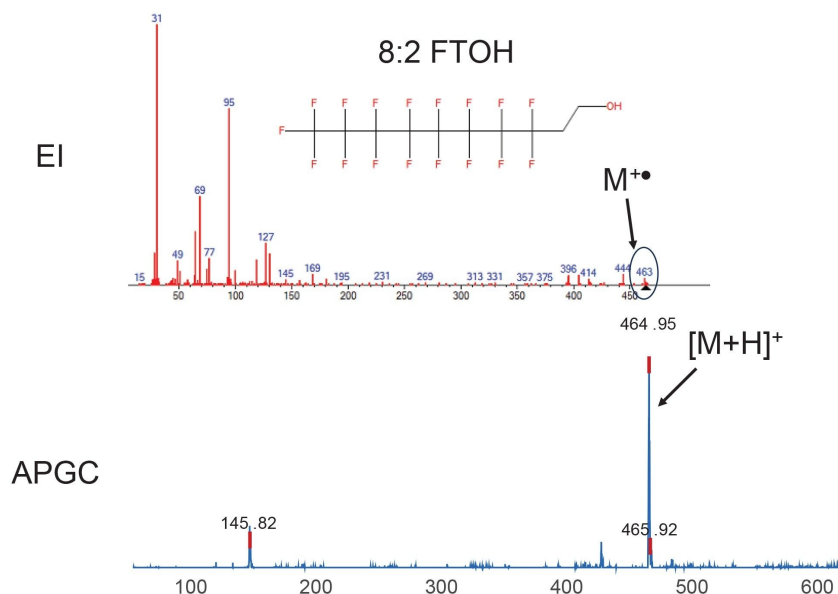


Figure 1. Comparison of mass spectra generated using (top) electron ionization (EI) and (bottom) APGC ionization for 8:2 FTOH.

Method Development

When developing the GC method, inlet liner choice was an important factor in achieving repeatable injections due to the reactivity of the sulfonamide compounds in the GC inlet. Initial injections were performed on a Restek topaz liner and the rapid degradation of the sulfonamides can be seen in Figure 2A. Changing inlet temperature and pressure did not resolve this issue. The inlet liner was changed to a siltek deactivated liner which proved to be more suitable for the reactive sulfonamide compounds, allowing them to be included in the method. Figure 2B demonstrates the stability of the sulfonamides using this inlet liner over more than 150 injections.

Typically, sample extracts that are prepared for LC-MS analysis are not considered to be in a GC friendly sample composition. Since the intention of this method was to be an additional tool in the PFAS analysis workflow, the goal was to be able to inject the same samples prepared for LC-MS analysis without a solvent exchange that could cause loss of the volatile compounds. For this method, the sample composition to be injected was

approximately 94% methanol, 4% water, 1% ammonium hydroxide and 0.6% acetic acid, following sample extraction using EPA Method 1633.⁵ Figure 3 demonstrates the improvement of peak shape by utilizing a split injection and a thicker film column. Figure 3A and 3B utilized a 20 m x 0.18 mm x 0.20 μ m with splitless and 10:1 split injections, respectively. In both cases, the peak shape was still broad and peaks were split, indicating the inefficient transfer onto the column and/or column overload. When the 10:1 split was performed on a longer and thicker film column (30 m x 0.25 mm x 0.50 μ m) the peak shape was corrected to sharp, gaussian peaks (Figure 3C), proving that the sample extract containing water and acetic acid can be injected onto a GC.

During source optimization for conditions like corona current, cone gas flow and auxiliary gas flow, all compounds optimized around the same conditions (standard conditions) except for the x:1 fluorotelomer alcohols (FTOHs). These compounds favored a higher corona current and higher gas flows. Under these conditions (alternative conditions), the response was increased for these compounds by about 10x. This is demonstrated in Figure 4A showing the overlay of calibration curves for 7:1 FTOH run using both sets of conditions. The source conditions optimal for the x:1 FTOH compounds were not suitable for the rest of the PFAS in the method, as demonstrated in Figure 4B, showing the peak response for 7:1 FTOH and 6:2 FTOH under both source methods. The set of standard conditions are recommended for general use of this APGC-MS/MS method, unless the x:1 FTOH compounds are of importance and/or maximum sensitivity is not required for all compounds.

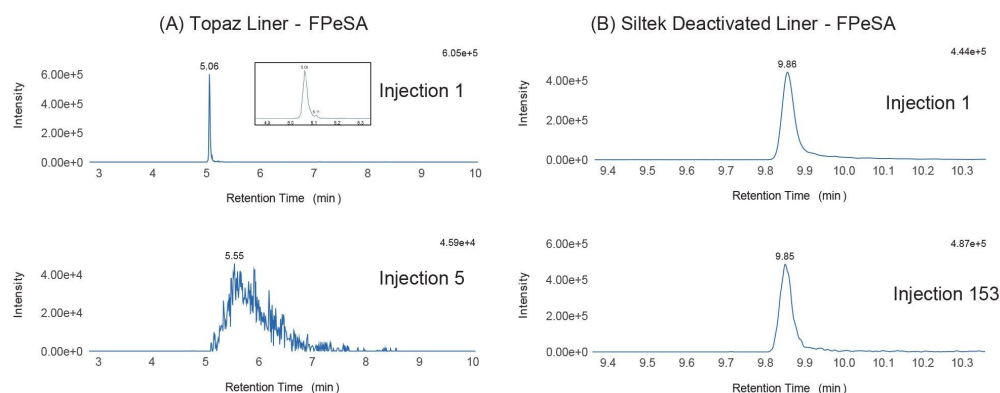


Figure 2. Comparison of the peak shape degradation over five injections of the sulfonamide compounds using a topaz inlet liner (A) compared to the stable peak shape over about 150 injections using a siltek deactivated inlet liner (B). The inset chromatogram in injection 1 of panel A is a zoom of the peak to compare peak shape to panel B time scale.

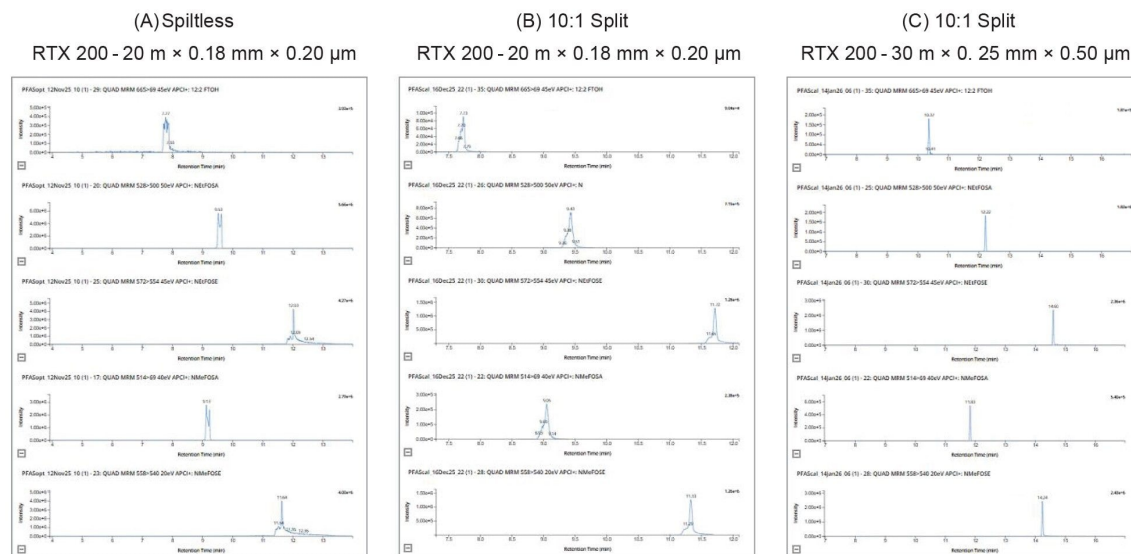


Figure 3. Peak shape examples of selected compounds using (A) splitless injection with a thinner film column, (B) 10:1 split on a thinner film column and (C) 10:1 split on a thicker film column.

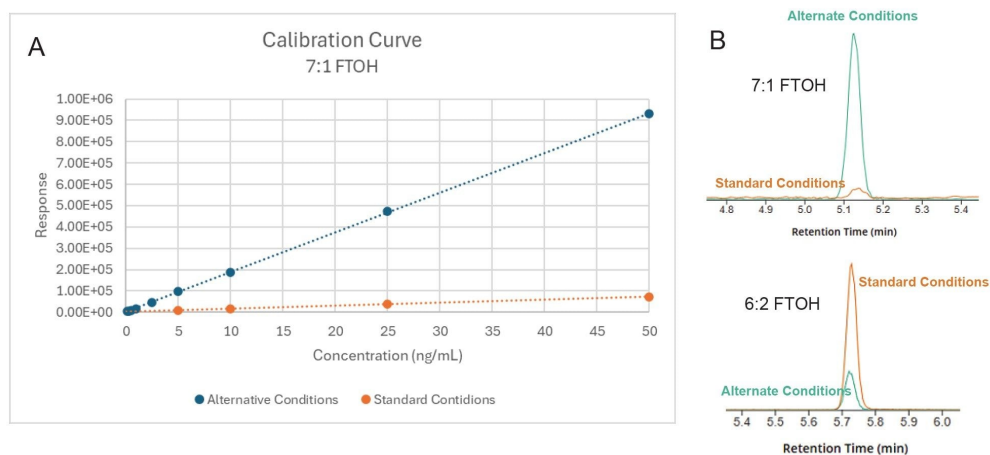


Figure 4. Comparison of the response between the two sets of source conditions where the standard conditions were optimal for all compounds but the x:1 FTOH compounds and the alternative conditions were optimal for only the x:1 FTOH compounds. (A) overlay of the calibration curve plot for 7:1 FTOH and (B) is peak overlay of examples of 7:1 FTOH and 6:2 FTOH demonstrating the response under each set of conditions.

Compound	LLOQ (ng/mL)	LLOQ S:N	Calibration Range (ng/mL)	R ²	Internal Standard Corrected
4:2 FTOH	0.10	64	0.1–50	0.998	Yes
6:2 FTOH	0.050	104	0.1–50	0.997	Yes
8:2 FTOH	0.050	182	0.05–50	0.995	Yes
10:2 FTOH	0.050	19	0.05–50	0.996	Yes
12:2 FTOH	0.10	49	0.1–50	0.998	Yes
6:3 FTOH	0.10	55	0.1–50	0.999	Yes
1:8:1 FTdiOH	1.0	30	1–50	0.993	No
9Me 8:2 FTOH	0.050	583	0.05–50	0.999	Yes
5:1 FTOH	10	27	N/A	N/A	No
5H 4:1 FTOH	2.5	18	2.5–50	0.997	No
7:1 FTOH	5.0	30	N/A	N/A	No
8:1 FTOH	5.0	16	2.5–50	0.997	No
N-MeFBSA	0.025	11	0.05–50	0.998	Yes
N-EtFBSA	0.005	26	0.05–50	0.998	Yes
NMeFOSA	0.010	20	0.05–50	0.998	Yes
NEtFOSA	0.010	45	0.05–50	0.998	Yes
N,N-Me2FOSA	0.50	409	0.5–50	0.998	Yes
N-EtFBSE	0.025	20	0.05–50	0.998	Yes
N-MeFOSE	0.010	34	0.05–50	0.998	Yes
N-EtFOSE	0.010	25	0.05–50	0.998	Yes
6:2 FTAcr	0.050	20	0.05–50	0.998	Yes
8:2 FTAcr	0.050	13	0.05–50	0.999	Yes
10:2 FTAcr	0.050	11	0.05–50	0.998	Yes
6:2 FTMAC	0.025	112	0.05–50	0.996	Yes
8:2 FTMAC	0.005	27	0.05–50	0.996	Yes
10:2 FTMAC	0.005	52	0.05–50	0.996	Yes
8:1 FTMAC	0.025	241	0.1–50	0.994	Yes
8:2 FTOAc	0.010	48	0.05–50	0.998	Yes
10:2 FTOAc	0.010	90	0.05–50	0.998	Yes
FBSA	5.0	23	5–500	0.997	No
FPeSA	1.0	31	1–500	0.994	No
FHxSA	1.0	90	1–500	0.996	No
FHpSA	1.0	42	1–500	0.997	No
FOSA	1.0	68	1–500	0.995	No
FDSA	2.5	318	2.5–500	0.998	No
5:1 FTOH*	2.5	44	2.5–50	0.998	No
5H 4:1 FTOH*	0.25	31	0.25–50	0.999	No
7:1 FTOH*	0.25	33	0.25–50	0.999	No
8:1 FTOH*	0.25	24	0.25–50	0.999	No

Table 1. LLOQ and calibration information for each compound in the method. () indicates the performance of these compounds under the alternative source conditions. N/A indicates not enough points were present to use for*

calibration.

Method Performance

An example chromatogram of the final optimized method can be seen in Figure 5 showing an overlay of all 35 PFAS compounds resolved over the GC temperature gradient.

Using this optimized method, a calibration curve was run. Selected calibration curves are shown in Figure 6, one compound from each class of PFAS represented is included. The linearity across the calibration range for every compound was excellent, regardless of whether internal standard correction or an external curve type were used, with all R^2 values > 0.993. The calibration range, linearity and whether or not an internal standard was used for quantitation are all listed in Table 1.

The LLOQ was determined to be the lowest level that the signal:noise (S:N) was ≥ 10 and both the quantitative and qualitative ions were present. The LLOQ value for every compound, along with the S:N value at that level, is listed in Table 1, with the LLOQ values provided for both the standard and alternative source conditions for the x:1 FTOH compounds. LLOQs ranged from 0.005 – 5.0 ng/mL, with most being below 0.10 ng/mL. Additionally, there are five PFAS that were included in the APGC-MS/MS method that are also included in most standard LC-MS/MS methods. Those five compounds are listed in Table 2, along with the LLOQ values determined in the LC-MS/MS analysis method.⁶ LLOQs are listed both as a ng/mL concentration, but also as fg on column (determined by injection volume and split value for GC analysis). In terms of fg on column sensitivity, APGC is actually 20 – 200 times more sensitive for N-MeFOSA, N-EtFOSA, N-MeFOSE and N-EtFOSE. For FOSA, APGC is 5 times less sensitive, meaning that LC-MS/MS may be a better option for that and similar sulfonamide compounds. Overall, the APGC-MS/MS method was demonstrated to be a very sensitive option for PFAS analysis.

Compound	APGC-MS/MS (ng/mL)	APGC-MS/MS (fg)	LC-MS/MS (ng/mL)	LC-MS/MS (fg)
NMeFOSA	0.01	1	0.01	20
NEtFOSA	0.01	1	0.01	20
N-MeFOSE	0.01	1	0.1	200
N-EtFOSE	0.01	1	0.1	200
FOSA	1.0	100	0.01	20

Table 2. Comparison of the LLOQ between the five compounds that cross over between LC and APMC analysis for EPA Method 1633 both as ng/mL and fg on column concentrations.

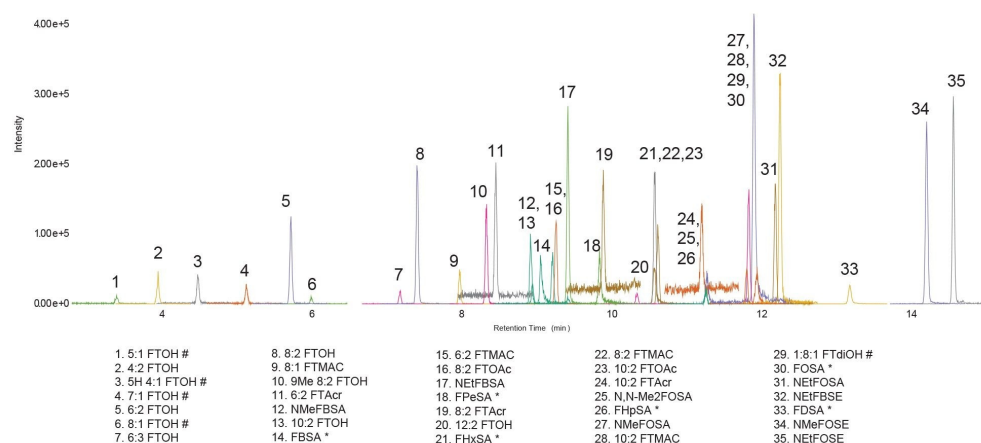


Figure 5. Solvent standard injection of all 35 PFAS compounds at 1 ng/mL, except for those indicated by (#) are 50 ng/mL and (*) are 25 ng/mL.

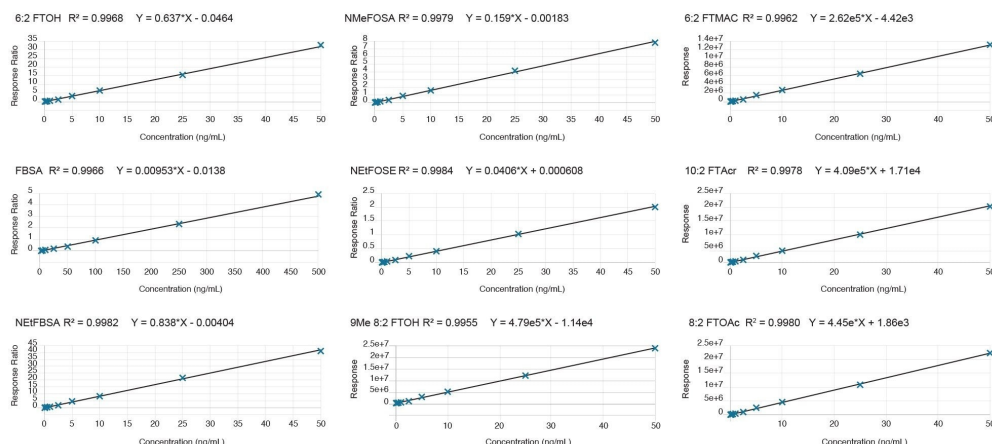


Figure 6. Example calibration curve plots for a compound from each different class of PFAS covered in the method.

Conclusion

An optimized APGC-MS/MS method for the analysis of 35 GC amenable PFAS has been presented, providing a practical way to extend existing workflows with sensitive and accurate analysis for fluorotelomer alcohols, acrylates, methacrylates, acetates, sulfonamides and sulfonamidoethanols. This approach could integrate seamlessly with existing LC-MS/MS workflows, allowing labs to extend compound coverage without requiring changes to established sample preparation protocols. Performance for all compounds was found to be optimal with the use of a siltek deactivated inlet liner and a 30 m x 0.25 mm ID, 0.50 μ m Rtx-200 column. This configuration allows for the injection of samples pre-extracted for LC-MS/MS analysis that are in mainly methanol and water, allowing labs to generate additional insights without increasing sample prep burden. Method LLOQs ranged from 0.005 – 5.0 ng/mL, with most compounds being below 0.10 ng/mL, delivering robust performance across compound classes, indicating the method can be used for trace level applications. Overall, APGC-MS/MS adds a complementary capability to LC-MS/MS methods, allowing labs to comprehensively assess PFAS contamination for better understanding and informed regulatory or product safety decisions. Further application notes will demonstrate the use of this method in environmental and food packaging samples, highlighting how labs can gain more complete PFAS insights while leveraging existing workflows.

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Appendix Table 1. APGC-MS/MS MRM Method Details

Compound	Precursor (m/z)	Product (m/z)	CV (V)	CE (V)	RT (min)
4:2 FTOH	265	181	15	20	3.88
		227	15	10	3.88
6:2 FTOH	365	281	20	20	5.71
		327	20	15	5.71
8:2 FTOH	465	69	30	40	7.41
		427	30	15	7.41
10:2 FTOH	565	69	35	30	8.96
		145	35	25	8.96
12:2 FTOH	665	69	45	45	10.36
		181	45	40	10.36
6:3 FTOH	379	295	5	20	7.18
		341	5	10	7.18
1:8:1 FTdiOH	463	403	10	20	11.93
		423	10	15	11.93
9Me 8:2 FTOH	515	76.9	35	25	8.34
		477	35	15	8.34
5:1 FTOH	301	281	30	10	3.3
	319	301	10	10	3.3
5H 4:1 FTOH	233	213	10	5	4.43
	251	233	20	5	4.43
7:1 FTOH	401	381	40	10	5.1
	419	401	5	10	5.1
8:1 FTOH	451	431	40	10	5.98
	469	431	5	15	5.98
NMeFBSA	314	69	25	25	8.94
	314	131	25	25	8.94
NEtFBSA	328	64	15	20	9.43
		300	15	10	9.43
NMeFOSA	514	69	25	40	11.82
		169	25	30	11.82
NEtFOSA	528	69	30	50	12.21
		500	30	15	12.21
NEtFBSE	372	71	25	20	12.27
		354	25	10	12.27
NMeFOSE	558	169	10	35	14.24
		540	10	15	14.24
NEtFOSE	572	462	20	30	14.6
		554	20	15	14.6
N,N-Me2FOSA	528	69	25	45	11.28
		92	25	40	11.28
6:2 FTAcr	419	54.9	25	20	8.46
		72.9	25	20	8.46
8:2 FTAcr	519	54.9	30	25	9.9
		72.9	30	20	9.9

Compound	Precursor (<i>m/z</i>)	Product (<i>m/z</i>)	CV (V)	CE (V)	RT (min)
10:2 FTACr	619	54.9	50	40	11.22
		73	50	20	11.22
6:2 FTMAC	433	59	35	40	9.22
		87	35	30	9.22
8:2 FTMAC	533	59	35	30	10.6
		87	35	20	10.6
10:2 FTMAC	633	59	35	30	11.85
		87	35	25	11.85
8:1 FTMAC	469	68.9	35	25	7.97
		441	35	20	7.97
8:2 FTOAc	507	61	20	20	9.27
		69	20	45	9.27
10:2 FTOAc	607	61	20	20	10.63
		69	20	40	10.63
FBSA	300	69	5	20	9.07
		216	5	15	9.07
FPeSA	350	69	5	20	9.86
		269	5	10	9.86
FHxSA	400	69	5	20	10.58
		336	5	10	10.58
FHpSA	450	69	5	40	11.29
		386	5	10	11.29
FOSA	500	69	25	50	11.97
		436	25	15	11.97
FDSA	600	69	35	35	13.2
		536	35	15	13.2
D4 4:2 FTOH	269	181	5	20	3.88
		230	5	10	3.88
13C2 6:2 FTOH	367	281	5	25	5.7
		329	5	15	5.7
13C2 8:2 FTOH	467	381	5	20	7.41
		429	5	10	7.41
D2 13C2 10:2 FTOH	569	481	35	25	8.96
		531	35	20	8.96
d3 NMeFOSA	517	169.6	10	25	11.82
		453	10	15	11.82
d5 NEtFOSA	533	65	10	20	12.21
		501	10	15	12.21
d7 NMeFOSE	565	64.3	10	30	14.25
		547	10	15	14.25
d9 NEtFOSE	581	467	10	25	14.6
		563	10	15	14.6

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