Analysis of the novel PFOA-replacement compound, GenX, by high resolution and triple quadrupole mass spectrometry

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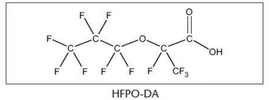
ABSTRACT

Gen-X is an emerging per- and polyfluorinated alkyl substance (PFAS) and the objective of this study was to add the main component of Gen-X to a multi-components PFAS method. GenX and several PFOS-replacement compounds (e.g. DONA) were optimized on the SCIEX X500R QTOF system and the SCIEX Triple Quad™ 4500. The X500R system was optimized for MRM^{HR} acquisition mode. An MDL study showed that quantitation of Gen-X can be achieved at approximately 50 ng/L in water samples in a method along with other PFAS.

INTRODUCTION

Per- and polyfluorinated alkyl substances (PFAS) are widespread environmental contaminants found in soil, air, biota, and water. Over the past few years, interest has increased from a small group of PFAS including PFOA and PFOS to a broad number of compounds representing multiple classes. Most recently, public attention has shifted towards several new classes of PFAS compounds found in drinking water in North Carolina. One of these commercial mixtures is known as GEN-X and it's main component is the dimer acid of hexafluoroprolyene oxide (HFPO-DA). Because HFPO-DA exhibits similar chemical characteristics to other PFAS, the goal of this method was to analyze HFPO-DA in a multi-residue method along with 24 other common PFAS.



HFPO-DA

MATERIALS AND METHODS

Sample Preparation:
All standards including HFPO-DA and its stable isotope labelled surrogate 13C3-HFPO-DA were purchased from Wellington Laboratories (Guelph, Ontario). 200 mL water samples were extracted using Strata-XL-AW weak anion exchange SPE cartridges following the conditions in the ISO Method (cited in PFAS app note). Samples were also passed through activated carbon following the requirements of DOD QSM 5.1 (cite). The final volume of the SPE eluent was 8 mL. Final extracts consisted of 80% methanol and 20% water.

HPLC Conditions:
An Agilent 1100 LC system with a Phenomenex Gemini C18, 100x3,0mm, 3µm column at 40° C with a gradient of eluent A water + 20mM ammonium acetate and eluent B methanol at a flow rate of 500µL/min and injection volume of 10 µL. A delay column was placed between the autosampler and LC system to retain system PFAS contamination away from analytical peaks; this has become a standard configuration for LC-MS/MS PFAS analysis.

MS/MS Conditions, SCIEX Triple Quad™ 4500 system:
A SCIEX Triple Quad™ 4500 LC/MS/MS systemsystem with Turbo V™ source and negative mode electrospray ionization (ESI) probe was used for analysis. *Scheduled* MRM™ algorithm was used for best accuracy and reproducibility.

MS/MS Conditions, SCIEX X500R QTOF system:
The system also utilized the Turbo V^{TM} source operated in negative ion mode. The TOF MS range was monitored from 100-1000*m/z*and individual MRM^{HR} transitions were defined for the suite of GenX compounds. Each transition was monitored using an optimized declustering potential (DP) and collision energy (CE) for maximum sensitivity.

Table 1. Analytical column and delay column used for Gen-X a diverse group of PFAS

Column	Name	Dimensions
Delay column	Phenomenex Luna C18(2)	5 µm; 30 x 3 mm
Analytical column	Phenomenex Gemini C18	3 µm; 50 x 2.1 mm

RESULTS: SCIEX Triple Quad^{TM} 4500 system

HFPA-DA, commonly known as Gen-X, eluted between PFBS and PFHxS in our gradient chromatography method using the Phenomenex Gemini C18 HPLC column. Several multiple reaction monitoring (MRM) transitions were determined for Gen-X, and based on the sensitivity of these transitions, two were used as the quantification and qualifier ions as shown in Table 2. Calibration was linear over a range of concentrations from 50-10,000 ng/L (Figure 2).

In a validation study method detection limit (MDL) study, nine replicate injections of a water sample spiked at 50 ng/L were extracted and analyzed. The variability among the replicates was 10.4% as shown in Figure 4. This variability represents the variability in the spiking of the water samples, the sample extraction, the autosampler, and the variability of ionization in the mass spectrometer. The percent recover of the MDL injections is shown in Figure 5.

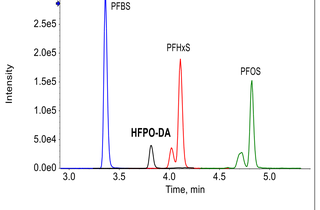


Figure 1. Chromatography of HFPO-DA in a mixture of PFAS.

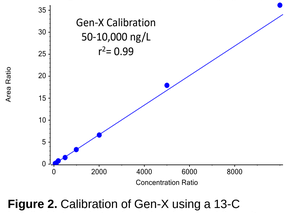


Figure 2. Calibration of Gen-X using a 13-C labelled internal standard showing good linearity over a calibration ranged of 50-10,000 ng/L.

Table 2. MRM transitions for HFPO-DA determined using a SCIEX 4500 Triple Quadrupole Mass Spectrometer

Compound	Q1	Q3	RT	DP	CE
HFPO-DA (Quant)	329	185	3.7	-30	-32
HFPO-DA (Qual)	329	169	3.7	-30	-18
$^{13}C_3$-HFPO-DA	332	185	3.7	-30	-32

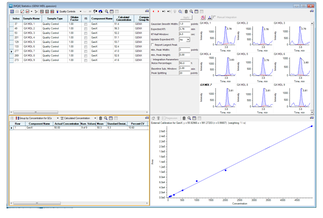


Figure 4. MDL study showing Multiquant™ quantitation batch with peak review (top right), curve (bottom right), statistics (bottom left), and results table (top left).

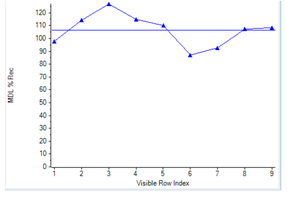


Figure 5. Variability of 9 MDL replicates.

RESULTS: SCIEX X500R QTOF system

Analyte	TOF MS ~LLOQ, ng/mL (S/N > 10)	TOF MS S/N at 1 ng/mL	TOF MS Cal Range (ng/mL)	MRM^{HR} ~LLOQ, ng/mL (S/N > 10)	MRM^{HR} S/N at 1 ng/mL	MRM^{HR} Cal Range (ng/mL)
HFPO-DA	0.05	550	0.05 - 20	< 0.05	2100	0.05 - 20
DONA	< 0.05	1700	0.05 - 20	< 0.05	16,000	0.05 - 20
9Cl-PF$_3$ONS	< 0.05	32,000	0.05 - 20	< 0.05	600,000	0.05 - 20
11Cl-PF$_3$OUdS	< 0.05	120,000	0.05 - 20	< 0.05	7,000	0.05 - 20

Figure 6. TOF MS vs. MRM^{HR} Quant Comparison. Both scans happen simultaneously in a single injection, and processing can utilize either or both. Sensitivity to <50 ppt was demonstrated using QTOF and MRM^{HR} for a suite of GEN X PFAS.

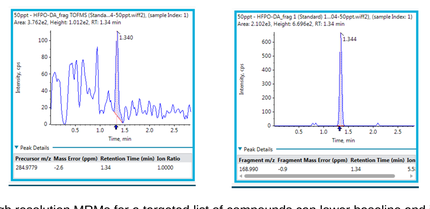


Figure 7. High resolution MRMs for a targeted list of compounds can lower baseline and increase specificity/sensitivity for GENX PFAS. TOF MS quantitation can be used when increased signal is needed.

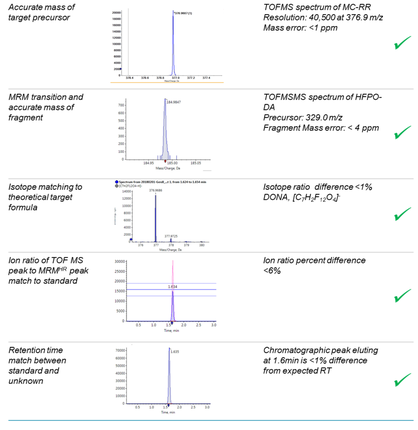


Figure 8. Five points of confirmation demonstrated for ID confidence using MRM^{HR}. High confidence in compound detection and identification is extremely desirable given the controversial and toxic nature of GenX compounds. Utilizing the SCIEX X500R QTOF system allows for the confirmation of compound ID by using accurate mass of the extracted MS1 ion, the accurate mass of the product ion (MRM transition), the isotope pattern match, the ion ratio match, and the retention time match.

CONCLUSIONS

GenX is an emerging contaminant, and analysis of GenX along with other PFAS is vital for proper risk assessment of contaminated water and soil and human exposure. These results show that GEN-X can be included in a method along with 24 other PFAS to be analyzed simultaneously in a single injection. The selectivity and sensitivity of the SCIEX 4500 Triple Quadrupole MS along with the chromatography provided by the Phenomenex Gemini C18 HPLC column allow this method to achieve sub-ppt reporting limits without a concentration step. Sensitivity to <50 ppt was demonstrated using QTOF and MRM^{HR} for a suite of GenX PFAS on the SCIEX X500R QTOF system. High resolution MRMs for a targeted list of compounds can lower baseline and increase specificity/sensitivity for GenX PFAS. Highly confident compound identification can be achieved by taking advantage of the data acquired using MRM^{HR} scan type on the SCIEX X500R QTOF system.

TRADEMARKS/LICENSING

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