응용 자료

Analysis of Per- and Polyfluoroalkyl Substances in Groundwater by Direct Injection Using the Benchtop Multi-Reflecting Time-of-Flight Xevo™ MRT Mass Spectrometer

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Abstract

The increasing regulatory scrutiny and scientific interest in per- and polyfluoroalkyl substances (PFAS) are driving a shift in analytical workflows from traditional tandem quadrupole (TQ) methods toward high-resolution mass spectrometry (HRMS) platforms. While TQ systems are the preferred choice for absolute quantification, they are restricted by the availability of commercialized standards and the limited number of compounds that can be identified and quantified within a single method. In contrast, HRMS enables both absolute quantification and non-targeted screening (NTS) workflows simultaneously, offering a more holistic understanding of PFAS profiles in complex environmental matrices.

To demonstrate the capabilities of HRMS, the Xevo MRT Mass Spectrometer was evaluated for sensitivity and dynamic range by direct injection of groundwater samples and standards. 30 PFAS compounds were detected

across a broad concentration range, with root-mean-square (RMS) mass measurement accuracy maintained below 0.5 ppm (RMS ≤ 0.5 ppm).

Benefits

- Exceptional mass measurement accuracy: Xevo MRT Mass Spectrometer achieves RMS mass accuracy consistently ≤ 0.5 ppm, effectively reducing the number of candidate compounds for identification.
- Broad PFAS Profiling: Identification and quantification of 30 PFAS compounds, including linear and branched isomers, was acheived with high confidence using HRMS and data-independent acquisition (MS^E).
- High sensitivity and wide dynamic range: Low limits of detection of ≤ 5 ng/L for 24 out of 30 PFAS compounds and a dynamic range spanning four orders of magnitude (1 ng/L to 10,000 ng/L) were achieved.
- Absolute quantitation using direct injection of water samples: Similar to TQ systems, the Xevo MRT Mass Spectrometer provides sufficient sensitivity to support absolute quantification of PFAS via direct injection of a 10 µL sample.
- Integrated screening and quantification platform: The waters_connect™ Software Platform, including the UNIFI™ Application, supports non-targeted screening and absolute quantification within a unified platform, enhancing productivity, and data traceability.

Introduction

Sample preparation methods such as solid phase extraction (SPE) are commonly recommended prior to analysis to concentrate the analytes and facilitate sample cleanup. However, SPE can introduce bias by favoring compounds with strong adsorption affinity to the cartridges. Additionally, many PFAS-related compounds are either proprietary or result from biotransformation processes and may therefore be absent in existing databases.[2,3,4] Comprehensive identification of these compounds without reference standards would require complementary techniques like nuclear magnetic resonance (NMR)[5], which poses challenges due to its need for large sample volumes and high analyte concentrations. In contrast, liquid chromatography coupled with HRMS (LC-HRMS) direct injection methods offer an unbiased approach to sample interrogation, enabling putative identification through accurate mass measurements, isotopic patterns, fragment ion data, and mass defect filtering.[6,7] HRMS, particularly when coupled with NTS workflows, offers a powerful solution for comprehensive PFAS analysis. The Xevo MRT Mass Spectrometer employs multi-reflecting time-of-flight technology to deliver high mass accuracy and sensitivity, thereby enabling the direct injection analysis of environmental samples, eliminating the need for SPE sample preparation.

This study evaluates the performance of the Xevo MRT Mass Spectrometer for non-target screening and quantification of PFAS compounds in groundwater from the Channel Islands, demonstrating the instrument's sensitivity, mass accuracy, and suitability for both quantitative and NTS workflows. 5 PFAS compounds were confidently identified and quantified, including perfluorobutane sulfonate (PFBS), perfluoroheptanesulfonic acid (PFHpS), perfluoropentanesulfonic acid (PFPeS), and both linear and branched isomers of perfluorooctanesulfonic acid (PFOS) and perfluorohexane sulfonate (PFHxS). Detected concentrations ranged from 13 ng/L to 1,000 ng/L. All 5 compounds are among the EU's PFAS watch list. The amount of total PFAS quantified in the sample exceeds the European Commission proposed Environmental Quality Standards (EC-EQS) and the UK guidance thresholds for groundwater.[8,9] These results highlight the value of a sensitive HRMS platform like Xevo MRT Mass Spectrometer in delivering both non-target screening and quantitative analysis, supporting the transition from legacy TQ targeted methods to a more holistic view of the PFAS content.

Experimental

A PFAC30PAR standard mix containing 30 PFAS compounds including perfluoroalkylcarboxylic acids (C4–C14), perfluoroalkylsulfonates (linear and branched), sulfonamides, fluorotelomer sulfonates (FTS), and emerging PFAS such as HFPO-DA and NaDONA, was obtained from Wellington Laboratories. A stock solution at 100 ng/mL in methanol was prepared and then serially diluted with methanol:water containing 0.1% formic acid to generate the calibration standards. Groundwater samples collected from the Channel Islands were diluted 1:1 with methanol containing 0.2% formic acid prior to direct injection analysis.

LC Conditions

System:	ACQUITY™ Premier LC System modified with PFAS Kit (p/n: 205000588, 205000589)
Analytical column:	ACQUITY Premier BEH C_{18} Column, 1.7 µm, 2.1 × 100 mm, 90 Å (p/n: 186009453)

Isolator column:	Atlantis™ Premier BEH C_{18} AX Column, 2.1 × 50 mm, 5 µm (p/n: 186009407)
Vials:	Polypropylene autosampler vials (p/n: 186005219) with pre-slit caps (p/n: 186000305)
Column temperature:	35 °C
Sample temperature:	20 °C
Injection volume:	10 µL
Flow rate:	0.3 mL/min
Mobile phase A:	95:5 water:methanol with 2 mM ammonium acetate
Mobile phase B:	Methanol with 2 mM ammonium acetate

LC Gradient Table

Time (min)	Flow rate (mL/min)	%A	%B	Curve
0	0.3	100	0	Initial
1	0.3	80	20	6
6	0.3	55	45	6
13	0.3	20	80	6
14	0.3	5	95	6
17	0.3	5	95	6
18	0.3	100	0	1
22	0.3	100	0	1

MS Conditions

MS system:	Xevo MRT Mass Spectrometer System
Ionization mode:	ESI-
Mass range:	m/z 50–1200
Acquisition mode:	MS^E a data independent acquisition method
Acquisition rate:	10 Hz
Lock mass:	Dual point lock mass using Leucine enkephalin (*m/z* 554.26202 and 130.08735)
Capillary voltage:	0.5 kV
Cone voltage:	10 V
Source temperature:	100 °C
Desolvation temperature:	250 °C
Cone gas:	100 L/h
Desolvation gas:	600 L/h
Source offset:	30 V
Low collision energy:	6 V
High collision energy:	ramp 20 – 70 V
StepWave RF voltage:	100 V

Body gradient: 5 V

Software Tools

Data acquisition and processing were performed using the waters_connect Software Platform with the UNIFI Application, supporting both targeted quantification and non-targeted screening workflows.

Results and Discussion

Instrument Performance – Mass Accuracy

The Xevo MRT Mass Spectrometer demonstrated exceptional mass accuracy across a broad concentration range. A total of 535 measurements were obtained from the analysis of 30 PFAS standards at concentrations from 200 ng/L to 10,000 ng/L (Figure 1A). Across all measurements, mass accuracy values ranged from -1.2 ppm to 1.6 ppm, with an RMS equal to 0.496 ppm.

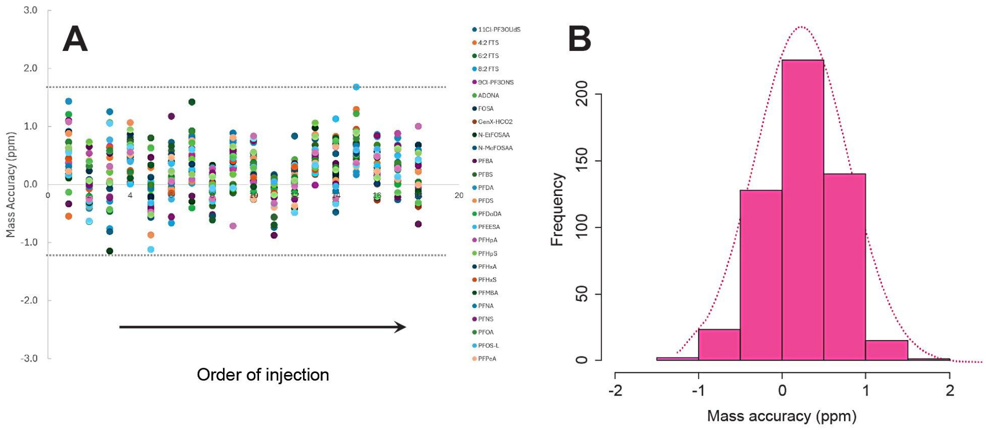

Figure 1A. Mass accuracies of 30 PFAS standards at six levels of concentration as a function of the order of injection. A total of 535 measurements were recorded. The RMS of the 535 measurements is < 0.5 ppm. Figure 1B: Frequency plot of the 535 mass accuracy values. The dotted line corresponds to the normal distribution fit.

A frequency distribution analysis revealed a symmetrical, bell-shaped curve centered around zero, indicating minimal bias and excellent reproducibility. The frequency plot contained eight bins, each representing a 0.5 ppm interval, covering the range from -2.0 ppm to 2.0 ppm (Figure 1B). The distribution appears relatively symmetrical with a bell-shaped curve (dotted lines) that follows a normal distribution. Over 68% of the measurements fall between -0.5 ppm and 0.5 ppm, centered around zero. The plot also shows that there is a very little spread or variability in the measurements with a slight tendency to the positive. (Figure 1B).

Instrument Performance – Sensitivity and Dynamic Range

The sensitivity and the dynamic range for each of the compounds were assessed. Serial dilutions of the 30 PFAS standards were prepared with concentrations varying from 1 ng/L to 10,000 ng/L. The standards were analyzed in triplicate, and the data was processed using the UNIFI Application within the waters_connect Software Platform. Calibration curves were obtained by plotting the response of each identified analyte from the low-energy scan versus its corresponding concentration and fitted by linear regression with 1/X weighting. The instrument LOD for a compound was set with a signal-to-noise value above 3, calculated using the peak-to-peak method, without peak smoothing.

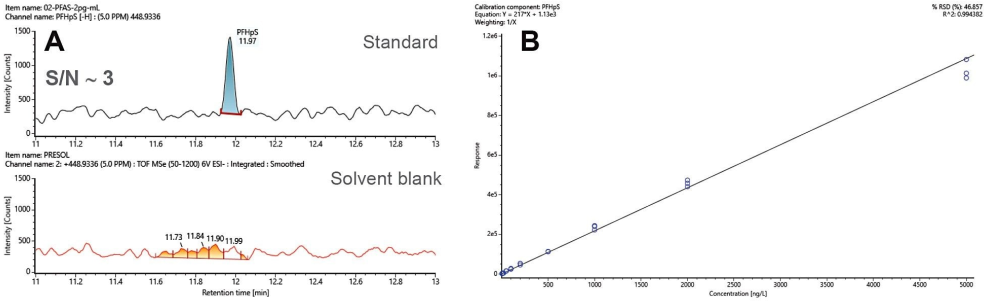

Figure 2A. Extracted ion chromatogram of PFHpS in the standard mix at 2 ng/L, with signal-to-noise ~ 3 (top panel) and the solvent blank (bottom panel). PFHpS is identified at m/z 448.9336 with mass measurement accuracy 0.4 ppm and a signal-to-noise (S/N) ~ 3. Figure 2B. Calibration curve of PFHpS from the ion response at low collision energy. The linear regression is fitted with 1/X weighting with a coefficient of determination R^2=0.99438. PFHpS is linear from 2 ng/L to 5,000 ng/L.

Figure 2A shows an extracted ion chromatogram (XIC) of PFHpS in the standard mix at 2 ng/L, and the XIC in a solvent blank sample. PFHpS is identified at *m/z* 448.9336 with mass measurement accuracy 0.4 ppm and a signal-to-noise (S/N) ~ 3 using peak-to-peak method. PFHps was not detected in the solvent blank sample. The response to PFHpS is linear over the range of concentrations from 2 to 5,000 ng/L with a coefficient of determination (R^2) 0.99438 (Figure 2B).

The dynamic range of the system covers 3 to 4 orders of magnitude, allowing quantification of PFAS analytes with standards if they are available. For this analysis, 10 µL of sample was injected onto the column, with the detection limit of PFHpS at 2 ng/L or 0.02 pg on column (2 ppt), at a (S/N) ratio of >3.

The linearity and sensitivity of all 30 studied compounds were investigated, with 26 of the compounds achieving a LLOD of $\leq$ 5 ng/L. The low limits of detection (LLOD), high limits of quantification (HLOQ), signal-to-noise (S/N), and the R^2 for each of the studied compounds are summarized in Table 1

Acronym	CAS ID	LLOD (ng/L)	HLOQ (ng/L)	S/N	R^2
11Cl-PF3OUdS	763051-92-9	1	5000	3.28	0.98915
4:2 FTSA	757124-72-4	10	10000	3.42	0.99868
6:2 FTSA	27619-97-2	10	10000	3.55	0.99886
8:2 FTSA	39108-34-4	20	10000	3.56	0.99288
9Cl-PF3ONS	756426-58-1	1	5000	5.93	0.99173
ADONA	919005-14-4	2	5000	3.97	0.99348
FOSA	754-91-6	5	10000	8.64	0.99601
GEN-X	122499-17-6	5	10000	4.05	0.99006
N-EtFOSAA	2991-50-6	50	10000	3.00	0.99847
N-MeFOSAA	2355-31-9	50	10000	2.70	0.99887
PFBA	375-22-4	5	10000	4.17	0.99757
PFBS	375-73-5	5	10000	3.88	0.99205
PFDA	335-76-2	5	5000	7.30	0.99697
PFDoA	307-55-1	5	10000	4.40	0.99362
PFDS	335-77-3	2	10000	3.38	0.98409
PFEESA	113507-82-7	1	10000	3.32	0.98899
PFHpA	375-85-9	5	10000	7.46	0.99332
PFHpS	375-92-8	2	5000	4.30	0.99438
PFHxA	307-24-4	5	10000	4.61	0.99748
PFHxS	355-46-4	1	5000	5.59	0.99233
PFMBA	863090-89-5	5	10000	5.26	0.99559
PFNA	375-95-1	5	10000	8.27	0.98491
PFNS	68259-12-1	2	5000	4.42	0.99031
PFOA	335-67-1	5	10000	6.20	0.99320
PFOS L	1763-23-1	2	5000	4.09	0.99425
PFPeA	2706-90-3	10	10000	3.46	0.99839
PFPeS	2706-91-4	1	10000	4.32	0.98883
PFTeDA	376-06-7	5	10000	4.82	0.99936
PFTrDA	72629-94-8	5	10000	6.21	0.99299
PFUnDA	2058-94-8	5	10000	5.13	0.99150

Table 1. Summary of the results of the 30 PFAS standards studied, the LLOD, the HLOQ, the signal-to-noise ratio calculated using peak-to-peak method, and the R^2.

These results highlight the outstanding sensitivity of the Xevo MRT Mass Spectrometer with 24 compounds achieving a detection limit lower than or equal to 5 ng/L (0.05 pg on column), including 11Cl-PF3OUdS, 9ClPF3ONS and PFHxS with a LOD at 1 ng/L (0.01 pg on column), and PFOS, PFDS, and PFNS at 2 ng/L (0.02 pg on column). Several of these values are lower than the method detection limits (MDL) requested by regulatory bodies where sample preparation and consequently sample concentration are required. The linearity of the PFAS compounds was demonstrated over 4 orders of magnitude with a minimum of 6 points on the calibration curve and a % RSD for the triplicate injections of < 10%. All 30 compounds were shown to have a linear response and produced quantification curves with an R^2 value of >0.98. In addition, the LLOD can be further improved by increasing the injection volume from 10 µL to 50 µL.

Quantification of PFAS in Wastewater

Groundwater samples from the Channel Islands were analyzed by direct injection. Both screening and quantitative approaches were applied for data assessment. Five PFAS compounds were identified and quantified, including linear and branched PFOS and PFHxS (Figure 3). Based on the confidence scale proposed by Charbonnet ***et al.***[7], linear PFHxS and PFOS were identified with a ***level 1a*** confidence. In contrast, PFBS, PFPeS, PFHpS, and the branched isomers of PFOS and PFHxS lacked specific fragment ions and were therefore assigned a ***level 3d*** confidence.[7]

The detected concentrations exceeded recommended thresholds defined by EU Directives 2006/118/EC and 2008/105/EC, which set limits at 0.65 ng/L of PFOS for inland waters and 0.13 ng/L for coastal waters.[8,9]

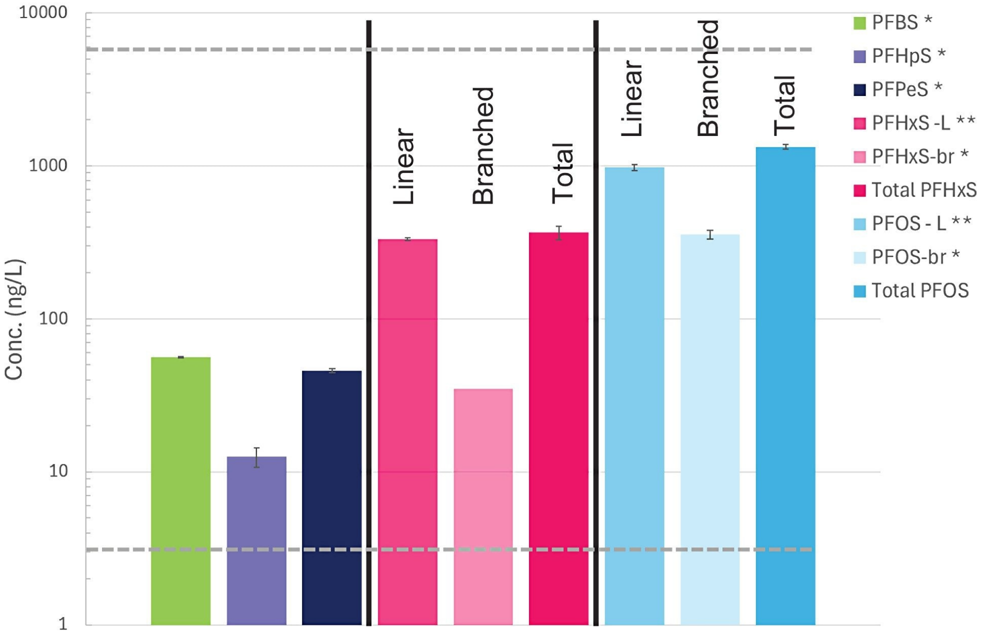

Figure 3. Summary of the quantified PFAS in Channel Islands groundwater. Linear and branched PFOS (Blue) and PFHxS (pink) were identified and quantified. Greyed dotted lines correspond to the LLOQ and the HLOQ of the method (confidence levels of identification[7]: Level 1 (**) Level 3d (*)).

The screening workflow within the UNIFI Application enabled extended screening beyond the 30-compound standard mix. No additional PFAS were identified.

Conclusion

This study demonstrates the robust analytical performance of the Xevo MRT Mass Spectrometer for the direct quantification of PFAS in groundwater. The platform consistently delivered high mass accuracy and exceptional sensitivity, with LOD below 5 ng/L for the majority of the 30 PFAS compounds evaluated. Precision was maintained across a dynamic range spanning 4 orders of magnitude, enabling confident quantification from trace to elevated concentrations. To enhance the sensitivity of the method, the injection volume can be increased from 10 µL to 50 µL.

This approach proved effective in detecting and quantifying PFAS in real-world groundwater samples from the Channel Islands, where concentrations of PFOS and PFHxS exceeded regulatory thresholds set by EU Directives.[8,9] The integration of the waters_connect Software Platform and UNIFI Application facilitated both targeted quantification and non-targeted screening within a unified data environment, enhancing throughput, traceability, and confidence in compound identification. The Xevo MRT System is well-suited for regulatory compliance workflows and exploratory screening, offering a scalable solution for laboratories addressing the growing demand for PFAS analysis in complex environmental matrices

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