ANALYSIS OF FLUORINATED SULFONAMIDES AND SULFONAMIDE ETHANOLS (FOSA/FOSEs) BY VARIOUS TYPES OF MASS SPECTROMETRIC TECHNIQUES

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Abstract

Various types of mass spectrometric techniques for the analysis of neutral organic fluorinated compounds were tested. The various types of mass techniques used were gas chromatography coupled to low resolution single quadropole mass spectrometry (GC-LRMS), in the negative chemical ionization (NCI) mode, GC high resolution MS (GC-HRMS), in the electron impact (EI) mode, and GC tandem mass spectrometry (GC-MS/MS) working both in the NCI and positive CI mode. Compounds studied were neutral fluorinated sulfonamides and sulfonamide (FOSAs/FOSEs). GC-MS/MS was found to be the best technique to use, based on both selectivity and sensitivity with instrumental detection limits IDLs ranging from 0.3 to 0.7 pg/µl. IDLs for GC-HRMS and GC-LRMS were 0.9 to 29 pg/µl and 1.6 to 20 pg/µl respectively.

Introduction

Ever since perfluorinated chemicals (PFCs) were found in both humans and biota across the world[1, 2], their transportation pathways have been discussed. Recent findings suggest that volatile precursor compounds, such as fluorotelomer alcohols (FTOHs) and fluorinated sulfonamides and sulfonamide ethanols (FOSAs/FOSEs), undergo atmospheric transport followed by degradation to the more stable perfluorooctanesulfonate (PFOS) and perfluorooctanic acid (PFOA)[3-5]. FOSAs/FOSEs have been used in a variety of products with water- and dirt-repelling properties. N-ethylated FOSAs/FOSEs have primarily been used for paper products and performance chemicals (e.g. as aqueous fire fighting foam, AFFF, and as an insecticide, Sulfuramid), while N-methylated compounds mainly have been used in fabric coatings[6]. FOSAs/FOSEs have been analyzed in different media, including air samples and solid matrices, such as different food, fish, and Arctic marine mammal liver samples, mainly using GC-PCI/NCI-MS[7, 8]. EI has been used for the determination of standard purities, but showed low intensity of the molecular ions and no specific fragments were formed. PCI has been used for the simple and definite mass spectra produced, although NCI has been used for confirmation purposes[7].

Material and methods

The following native and deuterated fluorinated standards were used; N-Me-FOSA, d-N-Me-FOSA, N-Et-FOSA, d-N-Et-FOSA, PFOSA, N-Me-FOSE, d7-N-Me-FOSE, N-Et-FOSE, d9-N-EtFOSE, all supplied by Wellington laboratories. Three different types of GC-MS instruments were used. An Agilent 6890 GC oven was used for all analyses. For the LRMS analysis, this GC was coupled to a single quadropole mass spectrometer, working in the negative chemical ionization mode, measuring most abundant fragments using single ion recording (SIR). High resolution analysis was performed on a Waters Micromass Autospec Ultima, operated in the electron impact mode, monitoring the most abundant fragments using SIR. Tandem mass spectrometry (MS/MS) was performed using Waters Micromass Quattro Micro GC. The MS/MS acquisitions were performed in the EI, NCI and PCI mode. GC oven temperature programs used started at 80 °C (50 °C for GC-MS/MS), held for two minutes (0.5 min for GC-MS/MS) then ramped to 275 °C. For final analysis and calculation of instrumental detection limits (IDLs), two (14%-cyanopropyl-phenyl)-methylpolysiloxane based phase columns were used. A BP 10 from SGE was used for GC-LR and HRMS analysis, whereas an Agilent DB 1701 was used for the MS/MS analysis (30 m x 0.25 mm id x 0.25 µm). In addition two other columns, a 30 m DB5-MS and an RTX 50 (0.25 x 0.25), were tested, but with little success to improve the chromatography of the target compounds. Splitless injection was used for all

techniques, injecting 1 µl on GC-HRMS and GC-MSMS, and 2 µl on GC-LRMS, all using helium as the carrier gas. Methane was used as reagent gas for CI. Scanning acquisitions were performed using the different techniques after which the most abundant fragments or transitions were chosen for SIR or multiple reaction monitoring (MRM). Chosen m/z fragments and transitions are shown in Table 1.

Table 1. FOSAs/FOSEs fragments monitored in SIR mode for GC-HRMS and GC-LSMS, and transitions monitored in MRM mode for GC-MS/MS and retention times.

	GC-HRMS		**GC-LRMS**		**GC-MSMS**	
Compound	m/z	t_R (min)	m/z	t_R (min)	Transition	t_R (min)
N-Me-FOSA	430.0083	10.09	94	10.08	94 > 63.9	8.59
					94 >64.9	8.59
d-N-Me-FOSA	433.0276	10.07	97	10.06	97 > 63.9	8.57
N-Et-FOSA	447.9994	10.26	108	10.28	108 > 64.9	8.75
					108 > 63.9	8.75
d-N-Et-FOSA	450.0120	10.23	113	10.24	113 > 63.9	8.72
	430.0083	10.23				
N-Me-FOSE	525.9769	12.15	494	12.19	138 > 64.9	10.02
	462.0150	12.15			138 > 74	10.02
d7-N-Me-FOSE	531.0084	12.11	145	12.13	145 > 65.9	10.05
	467.0464	12.11				
N-Et-FOSE	447.9994	12.64	508	12.67	152 > 64.9	10.32
					152 > 88	10.32
d9-N-EtFOSE	451.0182	12.58	161	12.6	161 > 65.9	10.29

Calibration standards in methanol with native FOSAs/FOSEs at concentrations of 2, 10, 50, 100, 250, and 1250 pg/µl, and labeled compounds at 100 pg/µl were acquired using the different MS techniques described.

Results and Discussion

Instrumental detection limits were calculated from concentrations at a signal-to noise (S/N) ratio of 3. Calculated values are shown in Table 2. Tandem mass spectrometry proved to be the best choice with IDLs ranging from 0.3 to 0.7 pg/µl, when injecting 1 µl. GC-MS/MS IDLs are in the same range as Jahnke et al, 2007, when analyzing air samples[7], and somewhat better than Martin et al, 2002[9], Stock et al, 2004[4], and Shoeib et al, 2004[10]. MS/MS is also the preferable choice with multiple transitions monitored for confirmatory purposes. Choice of LR-NCI versus HR-EI/MS depends on the compound class monitored. For the analysis of FOSAs, lower IDLs are achieved using LR-NCI-MS, while HR-EI/MS gives lower IDLs for FOSEs. Injection volumes for GC-HRMS and GC-MS/MS were 1 µl while 2 µl was injected into the GC-LRMS.

Comparing GC-HRMS operating at 10 000 resolution, in the EI mode, and low resolution MS in the NCI mode, the results are surprisingly better for the methylated sulfonamides (N-Me-FOSA, d-N-Me-FOSA) when using the low resolution instrument. For the ethanols the high resolution instrument performed better. Overall when taking both the amides and the ethanols into account, the GC-MS/MS, in the NCI mode, showed the best IDLs. FOSAs/FOSEs could also be run in the PCI mode. Several of the modes tested were also applied on spiked sample matrices, including human serum and several food stuffs, showing that FOSEs showed better selectivity in the PCI mode, although the NCI mode proved to be the best for FOSAs. The PCI mode has been shown to give simpler but more specific fragments compared to the NCI mode, while the NCI mode has often been used for confirmationonly[7].

Table 2. Instrumental detection limits (IDLs) in pg/µl using GC-EI-HRMS, GC-NCI-LRMS, and GC-NCI-MSMS, calculated from concentrations at a S/N ratio of 3.

	GC-EI-HRMS[a]	GC-NCI-LRMS[b]	GC-NCI-MS/MS[b]
Compound	pg/µl	pg/µl	pg/µl
N-Me-FOSA	14	1.6	0.5
d-N-Me-FOSA	29	2.3	0.7
N-Et-FOSA	2.3	1.6	0.3
d-N-Et-FOSA	0.9	2.8	0.5
N-Me-FOSE	2.5	20	0.6
d7-N-Me-FOSE	2.0	13	0.6
N-Et-FOSE	9.7	16	0.4
d9-N-EtFOSE	1.7	20	0.6

[a] When injecting 1 µl.
[b] When injecting 2 µl.

The linearity was tested by injecting a six point calibration curve on each instrument at concentrations of 2, 10, 50, 100, 250, and 1250 pg/µl for native compounds, and 100 pg/µl for deuterated compounds. The results are given as relative response factors (RRFs) in Table 3, together with the linear ranges obtained from the RRFs.

Table 3. Linear range in pg/µl and relative standard deviation of RRFs when injecting calibration standards at a concentration of 2, 10, 50, 100, 250, and 1250 pg/µl for native compounds, and 100 pg/µl for deuterated FOSAs/FOSEs on GC-HRMS, GC-LRMS and GC-MS/MS.

Compound	GC-HRMS m/z	rsd RRFs [a]	Linear range (pg/µl)[a]
N-Me-FOSA	430.0083	5 %	100 – 1250
N-Et-FOSA	447.9994	6 %	10 – 1250
N-Me-FOSE	525.9769	10 %	2 – 1250
	462.0150	9 %	2 – 1250
N-Et-FOSE	447.9994	8 %	2 – 1250
	GC-LRMS m/z		
N-Me-FOSA	94	6 %	10 – 1250
N-Et-FOSA	108	7 %	2 -1250
N-Me-FOSE	494	18 %	50 – 1250
N-Et-FOSE	508	8 %	50 – 1250
	GC-MS/MS transition		
N-Me-FOSA	94 > 63.9	15 %	2 – 250
	94 >64.9	4 %	2 – 250
N-Et-FOSA	108 > 64.9	3 %	2 – 250
	108 > 63.9	6 %	2 – 250
N-Me-FOSE	138 > 64.9	14 %	2 – 1250
	138 > 74	15 %	2 – 1250
N-Et-FOSE	152 > 64.9	15 %	2 – 1250
	152 > 88	15 %	2 – 1250

[a] RRF values from concentrations resulting in non-detected peaks have been excluded when calculating the RRFs and obtaining the linear ranges.

N-Me-FOSA could not be detected using GC-HRMS in EI mode at concentrations of 2, 10, and 50 pg/µl, these concentrations have been excluded from the RRF calculations: resulting in a linear range over concentrations of 100 – 1250 pg/µl only. For N-Et-FOSA, using the high resolution instrument, the linear range was over a concentration range of 10 – 1250 pg/µl when excluding the first point in the calibration curve. Using the low resolution instrument, N-Me-FOSE and N-Et-FOSE could not be detected at 2 and 10 pg/µl, N-Me-FOSA could not be detected at 2 pg/µl, resulting in linearity ranges over 50 – 1250 pg/µl for N-Me-FOSE and N-Et-FOSE and 10 – 1250 pg/µl for N-Me-FOSA. For the sulfonamides (N-Me-FOSA

and N-Et-FOSA) when using the MS/MS in the NCI mode, the highest point in the calibration curve was excluded due to interferences of the natural ^{13}C isotope present in the native compounds, which accounts for 1 % of the native isotope distribution. When analyzing high concentrations of sulfonamides the selectivity using chosen fragments in the NCI mode in MS/MS is affected by natural ^{13}C isotopes.
The analysis of fluorinated sulfonamides and sulfonamide ethanol poses several chromatographic difficulties; especially PFOSA suffers from band broadening when repeated injections are performed. Chromatographic improvement could possibly be done with different column phases, with carefully cleaning the inlet and changing liner and septa often when analyzing these compounds.

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