Journal of Chromatography A, 1555 (2018) 30–36

Contents lists available at ScienceDirect

Journal of Chromatography A

journal homepage: www.elsevier.com/locate/chroma

Determination of transformation products of unsymmetrical dimethylhydrazine in water using vacuum-assisted headspace solid-phase microextraction☆

Dina Orazbayeva[a], Bulat Kenessov[a,*], Elefteria Psillakis[b], Dayana Nassyrova[a], Marat Bektassov[a]

[a] Al-Farabi Kazakh National University, Faculty of Chemistry and Chemical Technology, Center of Physical Chemical Methods of Research and Analysis, Almaty, 050012, Kazakhstan
[b] Technical University of Crete, School of Environmental Engineering, Chania, Greece

ARTICLE INFO

Article history:
Received 21 December 2017
Received in revised form 22 April 2018
Accepted 23 April 2018
Available online 23 April 2018

Keywords:
Headspace solid-phase microextraction
Vacuum-assisted headspace solid-phase microextraction
Multiple headspace solid-phase microextraction
Transformation products
Dimethylhydrazine
Water analysis

ABSTRACT

A new, sensitive and simple method based on vacuum-assisted headspace solid-phase microextraction (Vac-HSSPME) followed by gas chromatography-mass-spectrometry (GC–MS), is proposed for the quantification of rocket fuel unsymmetrical dimethylhydrazine (UDMH) transformation products in water samples. The target transformation products were: pyrazine, 1-methyl-*1H*-pyrazole, *N*-nitrosodimethylamine, *N*,*N*-dimethylformamide, 1-methyl-*1*H-1,2,4-triazole, 1-methyl-imidazole and *1H*-pyrazole. For these analytes and within shorter sampling times, Vac-HSSPME yielded detection limits (0.5–100 ng L^{-1}) 3–10 times lower than those reported for regular HSSPME. Vac-HSSPME sampling for 30 min at 50 °C yielded the best combination of analyte responses and their standard deviations (<15%). 1-Formyl-2,2-dimethylhydrazine and formamide were discarded because of the poor precision and accuracy when using Vac-HSSPME. The recoveries for the rest of the analytes ranged between 80 and 119%. The modified Mininert valve and Thermogreen septum could be used for automated extraction as it ensured stable analyte signals even after long waiting times (>24 h). Finally, multiple Vac-HSSME proved to be an efficient tool for controlling the matrix effect and quantifying UDMH transformation products.

1. Introduction

The use of toxic unsymmetrical dimethylhydrazine (UDMH) in heavy rockets launched from Kazakhstan, Russia, India, and China causes contamination of the environment at adjacent territories with toxic fuel residuals [1,2]. After release into the aerobic environment, UDMH undergoes oxidative decomposition with formation of numerous classes of compounds including triazoles, nitrosoamines, pyrazoles, imidazoles and pyrazines [2–4]. The major health risks associated with UDMH and its transformations products are caused by their hepatotoxic, carcinogenic, mutagenic, teratogenic and embryotoxic properties [1,5–7]. Severe liver damages including internal bleeding and cancer, as well as lung cancer and fetal death are linked to exposure to *N*-nitrosodimethylamine [8,9] and *N*,*N*-dimethylformamide [10–12]. The most stable transformation product of UDMH, 1-methyl-*1H*-1,2,4-triazole, was reported to cause adverse effects on cell membranes, blood system and hemodynamics [6].

Gas (GC) [3,13] and liquid chromatography (LC) [14] coupled to various detectors are typically used for the analysis of UDMH transformation products with GC offering greater selectivity and cost-efficiency for the more volatile UDMH transformation products. At the same time, headspace solid-phase microextraction (HSSPME) proved to be advantageous for the extraction of UDMH transformation products offering low detection limits and simplicity [13,15]. However, HSSPME extraction times as long as 60 min are needed to extract the trace amounts of these polar analytes with low Henry's law constants (K_H) from aqueous samples [15].

Vacuum-assisted HSSPME (Vac-HSSPME) was previously reported to accelerate extraction rates of low K_H analytes [16–18]. For these analytes, lowering the total pressure was found to reduce gas-phase resistance and, as such, enhance mass transfer of analytes from the aqueous or solid sample to the gas phase

☆ Selected paper from the 19th International Symposium on Advances in Extraction Technologies (ExTech 2017), 27–30 June 2017, Santiago de Compostela, Spain.

* Correspondence to: 050012 Almaty, 96a Tole bi Street, Office 403, Kazakhstan.
E-mail addresses: orazbayeva@cfhma.kz (D. Orazbayeva), bkenesov@cfhma.kz (B. Kenessov).

https://doi.org/10.1016/j.chroma.2018.04.048
0021-9673/

and then to the SPME coating [18,19]. The theory behind HSSPME sampling under low-pressure conditions has been discussed in the past [18–20], and different gas-tight devices have been proposed [19,21,22]. For aqueous samples, the most simple and effective form of Vac-HSSPME consists of introducing the liquid sample into a pre-evacuated vial sealed with a modified Mininert® valve, equilibrating the sample with the gas phase, and headspace extraction with an SPME fiber [22].

In general, the accuracy of quantification for HSSPME can be affected by the matrix effects originating from the different extraction efficiencies of analytes from different samples. Among all approaches for matrix effect control [23], multiple HSSPME (MHSSPME) has the greatest potential for the simultaneous quantification of many analytes because it allows quick determination of their total masses in each sample without using complicated calibration approaches [24,25]. MHSSPME is based on consecutive extractions from the same sample vial and obtaining the dependence of responses of an analyte after each extraction on the extraction number [25]. Based on this dependence, extraction effectiveness and total mass of an analyte in the sample can be calculated. Compared to the standard addition approach, MHSSPME does not require spiking the sample with a standard of an analyte before extraction, which is particularly important for unstable analytes. The selection of internal standard(s) suitable for the quantification of UDMH transformation products [26] and other analytes [27,28] in environmental samples when using HSSPME can be complicated.

In this work, a new method based on Vac-HSSPME was optimized and used for the quantification of UDMH transformation products in water samples. The target transformation products were pyrazine (PAn), 1-methyl-*1H*-pyrazole (MPA), *N*-nitrosodimethylamine (NDMA), *N*,*N*-dimethylformamide (DMF), 1-methyl-*1*H-1,2,4-triazole (MTA), 1-formyl-2,2-dimethylhydrazine (FDMH), 1-methyl-imidazole (MIA), formamide (FA) and *1H*-pyrazole (PAl). During the optimization step, the effects of extraction temperature and time on the intensity and precision of analytes' responses were evaluated. The proposed Vac-HSSPME method was applied to the quantification of UDMH transformation products in water samples collected at the sites of heavy rocket operation. The ability of the modified Mininert® valves to maintain stable analyte signals for extended waiting times was evaluated, and the potential for automation was discussed. The possibility of using multiple Vac-HSSPME (MVac-HSSPME) for a matrix effect control and quantifying the transformation products of UDMH has been demonstrated.

2. Experimental

2.1. Reagents, materials and samples

The list of reagents (transformation products of UDMH) and their properties are given in Table A.1 (in Supplementary material). SPME was conducted using a 85-μm Carboxen/polydimethylsiloxane (Car/PDMS, Supelco, USA) fiber.

In-house modified Mininert® valves (Restek, USA) were prepared as described in the past [22]. A cylindrical Thermogreen® LB-1 septum with half-hole (6 mm diameter × 9 mm length, Supelco, USA) was placed into a 5-mm i.d. hole drilled in Mininert® valve to ensure leak-tight sealing of the valve. The optimized valve position in commercially available headspace vials was achieved by fitting O-rings having thickness 1–2 mm.

Real water sample (melted snow with a pH 6.6) collected in Almaty, Kazakhstan, and distilled water (pH 6.4) were used for the preparation of the spiked samples and standard solutions. The effect of pH on Vac-HSSPME was not studied in this work because any change of pH can result in a degradation of UDMH and some of its transformation products [29,30] with the loss of accuracy and precision of the method. In any case, the effect of varying pH was previously found to be non-significant for the HSSPME sampling of nitrosamines [31].

2.2. Parameters of gas chromatography-mass spectrometry (GC–MS) analysis

All GC–MS analyses were performed on 6890N/5973N and 7890A/5975C systems (Agilent, USA) equipped with split/splitless and PTV (CIS 4, Gerstel, Germany) inlets, Combi-PAL (CTC Analytics, Switzerland) and MPS2 (Gerstel, Germany) autosamplers, respectively. Analytes were desorbed from the SPME fibers at 240 °C in a GC inlet working in a splitless mode. Separation was conducted using a polar 60 m × 0.25 mm DB-WAXetr (Agilent, USA) column with a 0.50 μm film thickness at the constant helium (>99.995%, Orenburg-Tehgas, Russia) flow 1.0 mL min^{-1}. The oven temperature was programmed from 40 °C (held for 10 min) to 240 °C (held for 0 min), with the heating rate 5 °C min^{-1}. The temperatures of the MS ion source, quadrupole and interface were 230, 150 and 240 °C, respectively. Detection was conducted using the electron impact ionization at 70 eV in the selected ion monitoring (SIM) mode. The MS program used for the detection of the UDMH transformation products in the SIM mode is provided in Table A.2 (in Supplementary material).

2.3. Vac-HSSPME procedure

20-mL crimp-top headspace vials containing 1.75 g of NaCl and a magnetic stir bar coated with polytetrafluoroethylene (PTFE) (10 × 6 mm) were sealed with modified Mininert® valves and air-evacuated for 120 s using a low-cost single-stage rotary vane pump (Russia). A 5-mL sample was introduced into a 20-mL crimp-top headspace vial using a 5-mL gas-tight syringe (Bioject, China). Then the sample vial was placed on the top of the magnetic stirrer PE-6100 (Ecros, Russia) connected to the in-house made thermostated heating device with the temperature controller REX-C100 (Japan) and type K thermocouple 5TC-GG-K-20-36 (Omega, USA) (Fig. A.1. in Supplementary material). The samples were then incubated for 10 min at a preset temperature and a maximum (1500 rpm according to the specifications of the magnetic stirrer) stirring speed. Upon equilibration, the SPME fiber was exposed to the headspace of the sample, and manual HSSPME extraction was performed for a preset time. After extraction, the SPME fiber was transferred to the GC inlet for desorption of analytes.

2.4. Comparing the efficiencies of Vac-HSSPME and regular HSSPME

This set of experiments was conducted using aqueous samples spiked with PAn and MPA at 100 μg L^{-1}, NDMA and DMF at 200 μg L^{-1}, and MTA, FDMH, MIA, FA, PAl at 600 μg L^{-1}. For HSSPME [15], 5.00 mL of the spiked sample were introduced into a 20-mL crimp-top headspace vial, which was then sealed with PTFE/silicone septum and aluminum caps (Zhejiang Aijiren Technology Co., China). The sample was incubated for 10 min in the agitator of the autosampler at 50 °C and 250 rpm followed by a 30-min extraction at the same temperature and agitation speed. Vac-HSSPME of the spiked sample was conducted as described in the Section 2.3 with the extraction temperature and time set at 50 °C and 30 min, respectively.

2.5. Study of the effect of extraction temperature and time on the signal intensity and precision

The experiments were conducted using 5-mL real water samples (melted snow) spiked with PAn and MPA at 100 μg L^{-1}, NDMA and DMF at 200 μg L^{-1}, and MTA, FDMH, MIA, FA, PAl at 600 μg L^{-1}. The extraction was studied at all combinations of extraction temperatures (30, 40, 50, 70 °C) and times (10, 20, 30, 40 min) in three replicates.

2.6. Validation of the method

This set of experiments was conducted on samples of real (melted snow) and distilled water spiked with the target analytes. In this and all further sets of experiments, a 10-min pre-incubation was used, and Vac-HSSPME sampling was conducted at 50 °C for 30 min at the maximum stirring speed.

For response calibration, five standard solutions of analytes in distilled water were prepared with concentration ranges of PAn 0.10–110 μg L^{-1}, MPA 0.10–104 μg L^{-1}, NDMA 0.20–205 μg L^{-1}, DMF 0.31–304 μg L^{-1}, MTA 0.71–755 μg L^{-1}, FDMH 0.66–856 μg L^{-1}, MIA 0.59–589 μg L^{-1}, PAl 0.61–686 μg L^{-1}. Calibration slopes and their standard deviations were determined by the least squares method using LINEST function of MS Excel. Recoveries were determined by analyzing two model samples with known concentrations of analytes prepared from snow water. For recovery calculations, each sample was analyzed in two replicates.

2.7. Analysis of real lake water samples collected at the heavy rocket operation sites

Five water samples collected from the different lakes located at the territory of Baikonur cosmodrome, Kazakhstan, were used for testing of the proposed method. The lake water samples were prepared as described in the Section 2.3. The external standard calibration was prepared using melted snow water. All analyses of real samples using Vac-HSSPME were conducted in triplicates.

2.8. Automation potential of Vac-HSSPME based on the stability of analytes' signals during storage

Water samples spiked with low (PAn and MPA 2 μg L^{-1}, NDMA and DMF 5 μg L^{-1}, MTA, FDMH, MIA, and PAl 15 μg L^{-1}) and medium (PAn and MPA 40 μg L^{-1}, NDMA and DMF 100 μg L^{-1}, MTA, FDMH,MIA, and PAl 300 μg L^{-1}) concentrations of analytes were analyzed in two replicates 0, 3, 6, 12, 24, 48 and 72 h after air evacuation. Air-evacuated samples were stored at room temperature, and incubated at 50 °C and 1500 rpm for 10 min before an analysis.

2.9. Multiple Vac-HSSPME (MVac-HSSPME) extraction

For evaluation of MVac-HSSPME performance, model samples and calibration standards were prepared using distilled water. The quantification using MVac-HSSPME included the following steps:

- determination of analytes' extraction efficiencies and total peak areas for a sample;
- determination of analytes' masses corresponding to their total peak areas;
- calculation of analytes' concentrations in the sample.

For the determination of analytes' extraction efficiencies by Vac-HSSPME, four consecutive extractions from two replicate sample vials were conducted. For each analyte, a dependence of the logarithm of the peak area after each extraction ($\log A_i$) on the number of extraction ($i-1$) was obtained [24]. Using this plot, a slope ($\log \beta$) was determined, and a single-stage analyte extraction effectiveness was calculated:

$$E = 1 - \beta \quad (1)$$

An analyte peak area (A) is a product of a mass of an analyte in the fiber after extraction (m_f) and linear calibration slope k [25]:

$$A = k\, m_f \quad (2)$$

An "A = f(m_f)" calibration plot was obtained for each analyte by analyzing calibration standards with accurate volume (V_s) and concentrations of analytes (C_a) using Vac-HSSPME. Mass of an analyte in the fiber was calculated using extraction effectiveness (E) determined by multiple Vac-HSSPME:

$$m_f = C_a\, V_s \mathrm{E} \quad (3)$$

From "A = f(m_f)" calibration plots, slopes (k) were determined for each analyte. This method of calibration is more accurate compared to a direct injection of standard solutions into the GC–MS system because it does not require replacement of a GC liner and re-configuration of an instrument, and injection parameters during calibration and analyses are the same.

For the samples analyzed by MVac-HSSPME, "$\log A$ = f($i-1$)" plot was obtained, and E was determined using Eq. (1). A total peak area of an analyte was calculated using the formula:

$$A_{total} = \frac{A_1}{E} \quad (4)$$

where: A_1 –peak area of an analyte after 1st extraction of the sample.

The analyte concentration in a sample was determined using the formula:

$$C_a = \frac{A_{total}}{kV_s} \quad (5)$$

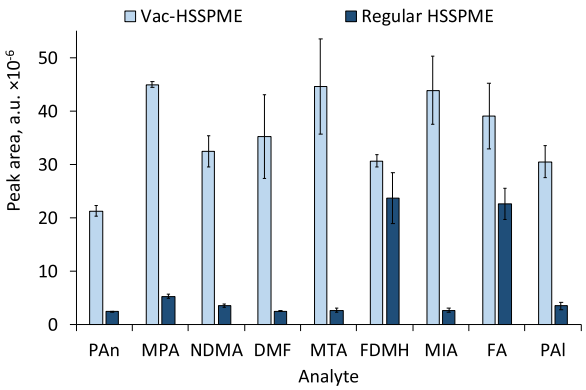

Fig. 1. Comparison of vacuum-assisted and regular HSSPME for the extraction of UDMH transformation products from water samples (extraction temperature 50 °C, sampling time 30 min).

3. Results and discussion

3.1. The effect of vacuum on the analyte responses

With Vac-HSSPME, the responses of the low K_H analytes studied here were improved compared to HSSPME (Fig. 1). In particular, compared to HSSPME, Vac-HSSPME yielded responses that were nine times higher for PAn, MPA, NDMA, and PAl, at least 14 times higher for DMF, MTA, and MIA (Fig. 1), and 1.3 and 1.8 times higher for FDMH and FA, respectively. For the latter, the lower impact of vacuum on extraction could be explained by their lower affinities to the SPME coating. Based on these initial results, Vac-HSSPME had a great potential for decreasing detection limits and/or extraction time of transformation products of UDMH. The larger extraction

Table 1
Analytical performance of Vac-HSSPME.

Compound	Linear range ($\mu g\,L^{-1}$)	R^2	Slope	RSD of slope (%)	Difference between slopes (%)	LOD ($\mu g\,L^{-1}$)	LOQ ($\mu g\,L^{-1}$)
Pyrazine (PAn)	0.1–100	0.990–0.997	601,567	2.9–5.0	18.5	$1{\cdot}10^{-3}$	$3{\cdot}10^{-3}$
1-Methyl-*1H*-pyrazole (MPA)	0.1–100	0.991–0.999	1,268,697	1.4–4.8	18.8	$5{\cdot}10^{-4}$	$2{\cdot}10^{-3}$
N-Nitrosodimethylamine (NDMA)	0.2–200	0.990–0.999	70,397	1.5–5.1	8.4	$1{\cdot}10^{-2}$	$4{\cdot}10^{-2}$
N,N-Dimethylformamide (DMF)	0.3–300	0.974–0.984	17,813	8.2–6.6	7.5	0.04	0.1
1-Methyl-*1*H-1,2,4-triazole (MTA)	0.7–700	0.992–0.997	9204	2.7–4.5	7.6	0.06	0.2
1-Formyl-2,2-dimethylhydrazine (FDMH)	7–700	0.922–0.970	202	10.3–14.5	28.5	1	4
1-Methyl-imidazole (MIA)	0.6–600	0.968–0.996	2300	7.0–18.3	19.2	0.1	0.4
Formamide (FA)	24–600	0.593–0.931	1285	45–58	106	6	21
1H-Pyrazole (PAl)	0.6–600	0.978–0.991	9850	4.9–7.5	10.0	0.01	0.04

Note: The LODs and LOQs were calculated as concentrations that provide 3:1 and 10:1 signal-to-noise (S/N) ratios, respectively. S/N were measured in calibration standards prepared in snow water with lowest concentration of each analyte.

Table 2
Spike recoveries using the developed method based on Vac-HSSPME (95% confidence intervals for two replicate measurements).

Analyte	Concentration level 1			Concentration level 2		
	Spiked ($\mu g\,L^{-1}$)	Measured ($\mu g\,L^{-1}$)	Recovery (%)	Spiked ($\mu g\,L^{-1}$)	Measured ($\mu g\,L^{-1}$)	Recovery (%)
PAn	2.2	2.5 ± 0.4	112 ± 16	13.2	13.9 ± 4.0	105 ± 30
MPA	2.1	2.4 ± 0.2	116 ± 9	12.5	10.0 ± 2.3	80 ± 19
NDMA	4.1	4.9 ± 0.3	119 ± 9	24.6	23.3 ± 8.4	95 ± 34
DMF	6.1	7.1 ± 1.2	117 ± 17	36.5	37.6 ± 2.7	103 ± 7
MTA	15.1	16.6 ± 1.3	110 ± 8	90.6	81.2 ± 28	90 ± 32
MIA	11.8	14.0 ± 1.4	119 ± 10	70.6	58.1 ± 4.9	82 ± 7
PAl	13.7	11.3 ± 2.8	83 ± 24	82.4	66.4 ± 12.8	81 ± 16

efficiencies obtained with Vac-HSSPME should also result in a lower matrix effect and greater accuracy [23].

3.2. The effects of extraction temperature and time on signal intensity and precision

For almost all target analytes, responses increased when increasing the extraction temperature and sampling time (Figs. 2 and A.2 in Supplementary material). For formamide, the responses obtained with Vac- and regular HSSPME were similar at all studied extraction times and temperatures. At 40, 50 and 70 °C, the maximum responses of most of the target analytes were observed after 30 min of Vac-HSSPME sampling, while for regular HSSPME, responses continued increasing even after 60 min of extraction at 70 °C [15]. After 30 min of Vac-HSSPME at 30 °C, maximum responses were achieved only for MTA, FDMH, and MIA.

The relative standard deviations (RSDs) of analytes' responses increased when increasing the extraction temperature, and their highest values were recorded after a 40-min extraction at 70 °C. Increasing the sampling time at extraction temperatures lower than 50 °C improved the precision. The best combination of analytes' responses and their RSDs could be achieved after 30-min extraction at 50 °C. These parameters were chosen as optimal and used in further experiments.

3.3. Validation of the method

The RSDs of the slopes of the calibration plots obtained with Vac-HSSPME were below 7.5% for most analytes (Table 1). Moreover, the difference between the slopes of the calibration plots obtained when using distilled water and melted snow water were below 19.2% for all analytes except FDMH and FA, which confirms the low matrix effect. The signals of FDMH and FA were unstable and imprecise in all experiments, and these analytes were withdrawn from further studies.

Although the optimum extraction time with regular HSSPME was doubled (60 min) [15], the LODs were 2–5 times higher for NDMA, DMF, MTA, MIA, and PAl, and 10 times greater for PAn and MPA. Moreover, Vac-HSSPME provided recoveries in the range of 80–119% (Table 2), and thus, had a great potential for certification and application in official environmental laboratories.

Table 3
Concentrations of analytes in real water samples (95% confidence intervals) determined using the developed method based on Vac-HSSPME.

Analyte	Concentration, $\mu g\,L^{-1}$				
	S1	S2	S3	S4	S5
PAn	0.94 ± 0.18	1.84 ± 0.04	3.3 ± 0.2	0.95 ± 0.02	0.53 ± 0.09
MPA	0.15 ± 0.01	1.15 ± 0.07	1.94 ± 0.19	0.51 ± 0.12	0.42 ± 0.04
NDMA	n/d	0.74 ± 0.03	1.2 ± 0.3	0.33 ± 0.07	0.32 ± 0.05
DMF	5.9 ± 1.1	26 ± 4	2.4 ± 0.5	2.9 ± 0.5	1.6 ± 0.4
MTA	n/d	2.9 ± 0.7	2.4 ± 0.3	2.4 ± 0.8	3.4 ± 0.9

Note: n/d – not detected (below LOD)

3.4. Concentrations of UDMH transformation products in real water samples

Analysis of real samples collected from lakes located in Baikonur cosmodrome region using the developed method showed the presence of five UDMH transformation products (Table 3). The highest concentrations were found for DMF and MTA, while FDMH, MIA, FA, and PAl were not detected. In the past, DMF and MTA were also the major components found in the water sample collected at the epicenter of the impact of a spent first stage of a carrier rocket [32], and MTA was the main UDMH transformation product found in soil samples [2].

3.5. Automation potential of Vac-HSSPME based on the vacuum stability of the extraction device

Automation of the Vac-HSSPME is highly important for its applicability for routine analyses because it allows improved sample throughput and lower cost of analysis. Vac-HSSPME has not yet been automated, and this limits its application. Automation of Vac-

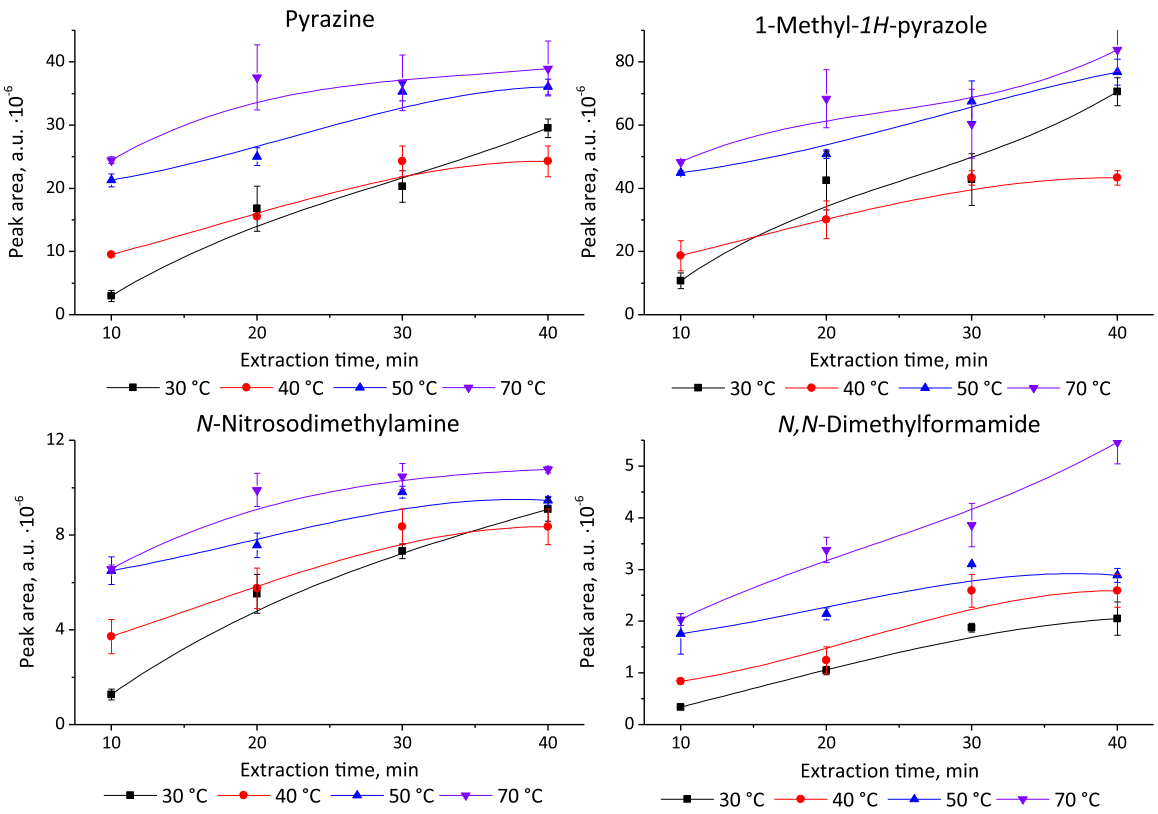

Fig. 2. Effect of extraction temperature and time on Vac-HSSPME sampling of UDMH transformation products from aqueous samples. Results for selected analytes: PAn, MPA, NDMA, DMF.

Table 4
Results of the analysis of the water sample using MVac-HSSPME.

Compound	log β	β	R^2	RSD of slopes (%)[a]	Difference between two slopes (%)	Extraction effectiveness (%)
PAn	−0.045	0.900	0.934	16.4–18.8	0.8	10 ± 2
MPA	−0.136	0.730	0.971	5.4–19.3	5.4	27 ± 4
NDMA	−0.013	0.970	0.962	13.3–16.2	3.0	3.0 ± 0.5
DMF	−0.017	0.960	0.989	5.8–18.4	8.3	3.9 ± 0.4
MTA	−0.035	0.923	0.947	13.1–21.5	9.9	17 ± 3
MIA	−0.086	0.819	0.936	16.4–18.5	16.8	18 ± 2
PAI	−0.017	0.962	0.950	5.8–19.1	2.1	3.8 ± 0.8

Note: log β – slope of a calibration plot obtained using MVac-HSSPME.
[a] Calculated using LINEST function of MS Excel.

HSSPME is possible by evacuating vials before placing them on an autosampler (e.g., CTC Combi-PAL) tray. Before being transported to a heated magnetic stirrer of an autosampler, vials have to stand on a tray for several hours, which can result in a loss of pressure and a decrease of analytical responses. The goal of this experiment was to study the stability of the responses for transformation products after evacuation of vials.

Recoveries were calculated as the ratios of the responses obtained after each studied storage time to responses obtained immediately after spiking. At a medium concentration level, responses of all analytes were in the range 78–120% during first 24 h. In the next 24 and 48 h, the responses decreased to 66–102% and 72–113%, respectively (Fig. 3A). At the low concentration level, responses of analytes during first 24 h were in the range between 72 and 115% followed by their drop to 70–113% and 61–107% in the next 24 and 48 h, respectively (Fig. 3B). Thus, the modified Mininert® valves provided good seal, and all evacuated samples could be stored on the autosampler tray for 24 h without a significant loss in accuracy.

3.6. Analysis using MVac-HSSPME

The major limitation of the MHSSPME is the loss of analytes via a hole in a septum after its puncture [23]. The leak-tight seal of Vac-HSSPME device makes it an ideal tool for conducting MHSSPME analysis because it eliminates losses of analytes caused by multiple puncturing of the septum material of the vial. Moreover, increased extraction efficiencies of analytes with low Henry's low constants achieved at low-pressure conditions can widen the range of MHSSPME-amenable analytes and decrease their sample preparation time.

The applicability of Vac-HSSPME device for MHSSPME of UDMH transformation products was evaluated for 5-mL water samples in two replicates (Table 4, Figs. A.3 and A.4 in Supplementary material). The highest values of extraction effectiveness were obtained for MPA and MIA (27 and 18%, respectively), which have same molecular masses and very close values of Henry's law constants. The RSDs of the slopes were below 22% for all analytes, and differences between slopes were less than 16.8% demonstrating the good precision of MVac-HSSPME method.

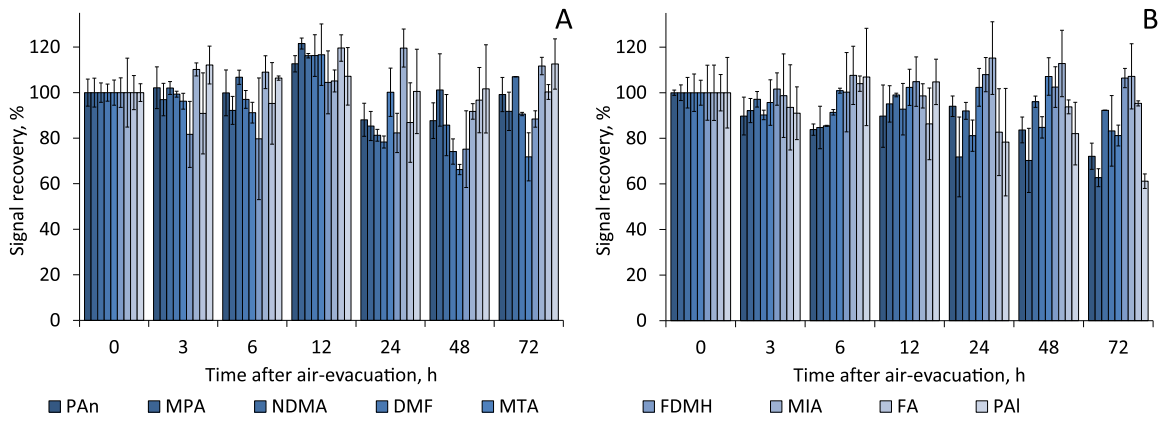

Fig. 3. Stability of the responses of analytes in low (A) and medium (B) concentrations measured 0, 3, 6 and 12, 48, and 72 h after air-evacuation of the Vac-HSSPME device.

Table 5
Spike recoveries of analytes using the developed method based on MVac-HSSPME (95% confidence intervals for two replicate measurements).

Compound	Spiked concentration ($\mu g\,L^{-1}$)	Measured concentration ($\mu g\,L^{-1}$)	Recovery (%)
PAn	44	39 ± 8	88 ± 20
MPA	42	36 ± 6	86 ± 16
NDMA	82	80 ± 13	98 ± 16
DMF	122	132 ± 15	109 ± 11
MTA	302	293 ± 50	97 ± 17
MIA	235	181 ± 23	77 ± 13
PAl	275	203 ± 42	74 ± 21

The recoveries of analytes using MVac-HSSPME were 74–109% (Table 5) indicating that MVac-HSSPME can be used for the quantification of UDMH transformation products in water samples. Moreover, even if the extraction effectiveness of NDMA, DMF and PAl (3.0, 3.9 and 3.8%, respectively) were lower than the recommended value for MHS-SPME (>5%) [24], proper recoveries were achieved (98, 109 and 74%, respectively). These results proved that the Vac-HSSPME device based on modified Mininert® valves provides great inertness and seal, and can also be used for achieving a better precision and accuracy in MHSSPME-based methods for a wider range of extraction efficiencies and analytes.

4. Conclusion

Within a short extraction time (30 min in Vac-HSSPME *vs* 60 min in regular HSSPME), Vac-HSSPME yielded extraction efficiencies that were 2–17 times greater compared to regular HSSPME, lower detection limits, less pronounced matrix effect and a better accuracy and precision. The optimum analyte responses and their RSDs were achieved when applying a 30-min extraction time at a 50 °C extraction temperature. The difference between the external standard calibration slopes obtained on real and distilled water at the optimized conditions were below 20% for all analytes except FDMH and FA, which were discarded from the method. For other analytes, recoveries when using external standard calibration were 80–119%. Thus, the developed method can be recommended for application in laboratories conducting routine analyses of water samples potentially contaminated by rocket fuel residuals. Moreover, the lower detection limits of the method (0.5–100 $ng\,L^{-1}$) will allow more efficient study of migration routes of these contaminants and stricter quality control of drinking water in the regions affected by rocket launches.

Such values were achieved due to a great seal provided by the modified Mininert® valves as developed in the reference [22]. After evacuation, these vials could maintain low-pressure conditions for up to 24 h on the autosampler tray without a significant loss in precision and accuracy. It is therefore possible to automate the method if an autosampler is capable of transporting vials with modified Mininert® valves.

The leak-tight seal provided by the valves along with the improved extraction effectiveness allowed quantification of all target analytes using MVac-HSSPME. The extraction effectiveness of these analytes were 3.8–27% with RSDs below 22%, thus potentially allowing application of this approach for controlling matrix effects when analyzing aqueous extracts from soils. Based on the current results, MVac-HSSME can also be recommended for the quantification of analytes having a low Henry's law constant. The used Vac-HSSPME device can also be used for improving the performance of analytical methods based on the MHSSPME approach.

Acknowledgements

This work was conducted under the projects "Development and implementation of "green" methods for determination of organic pollutants in soils" (No. 3661/GF4), "Development of analytical methods, materials and equipment for cost-efficient "green" environmental monitoring" (No. AP05133158), and Ph.D. project of Dina Orazbayeva all funded by the Ministry of Education and Science of Kazakhstan. The authors would like to thank the Scientific Research Center "Garysh-Ecologiya" of the Aerospace Committee of the Ministry of Investments and Development of Kazakhstan for providing real water samples.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.chroma.2018.04.048.

References

[1] L. Carlsen, O.A. Kenesova, S.E. Batyrbekova, A preliminary assessment of the potential environmental and human health impact of unsymmetrical dimethylhydrazine as a result of space activities, Chemosphere 67 (2007) 1108–1116, http://dx.doi.org/10.1016/j.chemosphere.2006.11.046.
[2] B. Kenessov, M. Alimzhanova, Y. Sailaukhanuly, N. Baimatova, M. Abilev, S. Batyrbekova, L. Carlsen, A. Tulegenov, M. Nauryzbayev, Transformation products of 1,1-dimethylhydrazine and their distribution in soils of fall places of rocket carriers in Central Kazakhstan, Sci. Total Environ. 427–428 (2012) 78–85, http://dx.doi.org/10.1016/j.scitotenv.2012.04.017.
[3] B.N. Kenessov, J.A. Koziel, T. Grotenhuis, L. Carlsen, Screening of transformation products in soils contaminated with unsymmetrical dimethylhydrazine using headspace SPME and GC–MS, Anal. Chim. Acta 674 (2010) 32–39, http://dx.doi.org/10.1016/j.aca.2010.05.040.
[4] N.V. Ul'yanovskii, D.S. Kosyakov, I.I. Pikovskoi, Y.G. Khabarov, Characterisation of oxidation products of 1,1-dimethylhydrazine by high-resolution orbitrap

mass spectrometry, Chemosphere 174 (2017) 66–75, http://dx.doi.org/10.1016/j.chemosphere.2017.01.118.
[5] L. Carlsen, B.N. Kenessov, S.Y. Batyrbekova, S.Z. Kolumbaeva, T.M. Shalakhmetova, Assessment of the mutagenic effect of 1,1-dimethyl hydrazine, Environ. Toxicol. Pharmacol. 28 (2009) 448–452, http://dx.doi.org/10.1016/j.etap.2009.08.004.
[6] L. Carlsen, B.N. Kenessov, S.Y. Batyrbekova, A QSAR/QSTR study on the human health impact of the rocket fuel 1,1-dimethyl hydrazine and its transformation products, Environ. Toxicol. Pharmacol. 27 (2009) 415–423, http://dx.doi.org/10.1016/j.etap.2009.01.005.
[7] ATSDR, Toxicological Profile for Hydrazines, Agency for Toxic Substances and Disease Registry (ATSDR), Atlanta, GA, USA, 1997, 224 p.
[8] ATSDR, Toxicological Profile for *N*-nitrosodimethylamine, Agency for Toxic Substances and Disease Registry (ATSDR), Atlanta, GA, USA, 1989, 119 p.
[9] M. Schriks, M.B. Heringa, M.M.E. van der Kooi, P. de Voogt, A.P. van Wezel, Toxicological relevance of emerging contaminants for drinking water quality, Water Res. 44 (2010) 461–476, http://dx.doi.org/10.1016/j.watres.2009.08.023.
[10] J.-C. Luo, T.-J. Cheng, H.-W. Kuo, M.J.W. Chang, Abnormal liver function associated with occupational exposure to dimethylformamide and glutathione S-transferase polymorphisms, Biomarkers 10 (2005) 464–474, http://dx.doi.org/10.1080/13547500500333648.
[11] P. Hantson, A. Villa, A. Galloy, S. Negri, G. Esabon, F. Lambiotte, V. Haufroid, R. Garnier, Dimethylformamide metabolism following self-harm using a veterinary euthanasia product, Clin. Toxicol. 48 (2010) 725–729, http://dx.doi.org/10.3109/15563650.2010.498790.
[12] G.L. Kennedy, Toxicology of dimethyl and monomethyl derivatives of acetamide and formamide: a second update, Crit. Rev. Toxicol. 42 (2012) 793–826, http://dx.doi.org/10.3109/10408444.2012.725028.
[13] S. Yegemova, N.V. Bakaikina, B. Kenessov, J.A. Koziel, M. Nauryzbayev, Determination of 1-methyl-*1H*-1,2,4-triazole in soils contaminated by rocket fuel using solid-phase microextraction, isotope dilution and gas chromatography–mass spectrometry, Talanta 143 (2015) 226–233, http://dx.doi.org/10.1016/j.talanta.2015.05.045.
[14] D.S. Kosyakov, N.V. Ul'yanovskii, K.G. Bogolitsyn, O.A. Shpigun, Simultaneous determination of 1,1-dimethylhydrazine and products of its oxidative transformations by liquid chromatography–tandem mass spectrometry, Int. J. Environ. Anal. Chem. 94 (2014) 1254–1263, http://dx.doi.org/10.1080/03067319.2014.940342.
[15] N.V. Bakaikina, B. Kenessov, N.V. Ul'yanovskii, D.S. Kosyakov, S.A. Pokryshkin, M. Derbissalin, Z.K. Zhubatov, Quantification of transformation products of unsymmetrical dimethylhydrazine in water using SPME and GC–MS, Chromatographia 80 (2017) 931–940, http://dx.doi.org/10.1007/s10337-017-3286-2.
[16] N.P. Brunton, D.A. Cronin, F.J. Monahan, The effects of temperature and pressure on the performance of Carboxen/PDMS fibres during solid phase microextraction (SPME) of headspace volatiles from cooked and raw turkey breast, Flavour Fragr. J. 16 (2001) 294–302, http://dx.doi.org/10.1002/ffj.1000.
[17] N. Reyes-Garcés, E. Gionfriddo, G.A. Gómez-Ríos, M.N. Alam, E. Boyacı, B. Bojko, V. Singh, J. Grandy, J. Pawliszyn, Advances in solid phase microextraction and perspective on future directions, Anal. Chem. 90 (2018) 302–360, http://dx.doi.org/10.1021/acs.analchem.7b04502.
[18] E. Psillakis, A. Mousouraki, E. Yiantzi, N. Kalogerakis, Effect of Henry's law constant and operating parameters on vacuum-assisted headspace solid phase microextraction, J. Chromatogr. A 1244 (2012) 55–60, http://dx.doi.org/10.1016/j.chroma.2012.05.006.
[19] E. Psillakis, Vacuum-assisted headspace solid-phase microextraction: a tutorial review, Anal. Chim. Acta 986 (2017) 12–24, http://dx.doi.org/10.1016/j.aca.2017.06.033.
[20] E. Psillakis, E. Yiantzi, L. Sanchez-Prado, N. Kalogerakis, Vacuum-assisted headspace solid phase microextraction: improved extraction of semivolatiles by non-equilibrium headspace sampling under reduced pressure conditions, Anal. Chim. Acta 742 (2012) 30–36, http://dx.doi.org/10.1016/j.aca.2012.01.019.
[21] E. Psillakis, E. Yiantzi, N. Kalogerakis, Downsizing vacuum-assisted headspace solid phase microextraction, J. Chromatogr. A 1300 (2013) 119–126, http://dx.doi.org/10.1016/j.chroma.2013.02.009.
[22] M.J. Trujillo-Rodríguez, V. Pino, E. Psillakis, J.L. Anderson, J.H. Ayala, E. Yiantzi, A.M. Afonso, Vacuum-assisted headspace-solid phase microextraction for determining volatile free fatty acids and phenols. Investigations on the effect of pressure on competitive adsorption phenomena in a multicomponent system, Anal. Chim. Acta 962 (2017) 41–51, http://dx.doi.org/10.1016/j.aca.2017.01.056.
[23] B. Kenessov, J.A. Koziel, N.V. Bakaikina, D. Orazbayeva, Perspectives and challenges of on-site quantification of organic pollutants in soils using solid-phase microextraction, Trends Anal. Chem. 85 (2016) 111–122, http://dx.doi.org/10.1016/j.trac.2016.04.007.
[24] M.T. Tena, J.D. Carrillo, Multiple solid-phase microextraction: theory and applications, Trends Anal. Chem. 26 (2007) 206–214, http://dx.doi.org/10.1016/j.trac.2007.01.008.
[25] O. Ezquerro, B. Pons, M.T. Tena, Multiple headspace solid-phase microextraction for the quantitative determination of volatile organic compounds in multilayer packagings, J. Chromatogr. A 999 (2003) 155–164, http://dx.doi.org/10.1016/S0021-9673(02)01524-8.
[26] N.V. Bakaikina, B. Kenessov, N.V. Ul'yanovskii, D.S. Kosyakov, Quantification of transformation products of rocket fuel unsymmetrical dimethylhydrazine in soils using SPME and GC–MS, Talanta 184 (2018) 332–337, http://dx.doi.org/10.1016/j.talanta.2018.02.047.
[27] D. Orazbayeva, B. Kenessov, J.A. Koziel, D. Nassyrova, N.V. Lyabukhova, Quantification of BTEX in soil by headspace SPME–GC–MS using combined standard addition and internal standard calibration, Chromatographia 80 (2017) 1249–1256, http://dx.doi.org/10.1007/s10337-017-3340-0.
[28] S. Bondarenko, J. Gan, Simultaneous measurement of free and total concentrations of hydrophobic compounds, Environ. Sci. Technol. 43 (2009) 3772–3777, http://dx.doi.org/10.1021/es8037033.
[29] M. Liang, W. Li, Q. Qi, P. Zeng, Y. Zhou, Y. Zheng, M. Wu, H. Ni, Catalyst for the degradation of 1, 1-dimethylhydrazine and its by-product *N*-nitrosodimethylamine in propellant wastewater, RSC Adv. 6 (2016) 5677–5687, http://dx.doi.org/10.1039/C5RA20481J.
[30] W.A. Mitch, D.L. Sedlak, Formation of N-nitrosodimethylamine (NDMA) from dimethylamine during chlorination, Environ. Sci. Technol. 36 (2002) 588–595, http://dx.doi.org/10.1021/es010684q.
[31] A. Llop, F. Borrull, E. Pocurull, Fully automated determination of *N*-nitrosamines in environmental waters by headspace solid-phase microextraction followed by GC–MS-MS, J. Sep. Sci. 33 (2010) 3692–3700, http://dx.doi.org/10.1002/jssc.201000527.
[32] N.V. Ul'yanovskii, D.S. Kosyakov, S.A. Pokryshkin, K.G. Bogolitsyn, Determination of transformation products of 1,1-dimethylhydrazine by gas chromatography–tandem mass spectrometry, J. Anal. Chem. 70 (2015) 1553–1560, http://dx.doi.org/10.1134/S1061934815130080.