ABSTRACT
of the thesis for the degree of Doctor of Philosophy (PhD)
on educational program «8D05301 – Chemistry»
Nadezhda V. Bakaikina
"Determination of transformation products of unsymmetrical dimethylhydrazine in soil and water using solid-phase microextraction"

Relevance of the research topic. Environmental pollution by highly toxic rocket fuel based on UDMH and its transformation products presents a danger to the population and the ecological system of the territories located near the launch and fall of separation parts of heavy launch vehicles such as "Proton", "Dnepr", and "Cyclone". Interacting with oxidizing agents, UDMH is transformed to a more than 200 transformation products, some of which are toxic and/or carcinogenic compounds. To minimize risks from the negative impact of rocket and aerospace activities, it is necessary to monitor the ecological state of environmental objects.

The available methods for simultaneous determination of the main UDMH transformation products in soil are based on solvent extraction with subsequent analysis of extracts by gas (GC) or liquid chromatography with mass spectrometric (MS), tandem mass spectrometric (MS/MS) or electrochemical detection. These techniques provide low detection limits and sufficient accuracy, but require complex, expensive and time-consuming sample preparation techniques.

Headspace solid-phase microextraction (HSSPME) is a simple and efficient method for the extraction of analytes from water and soil samples avoiding the use of toxic organic solvents. However, the determination of UDMH transformation products and other similar analytes in complex samples is limited by the matrix effect caused by the different extraction efficiency of analytes from samples of different compositions. The matrix effect can be minimized by improving the extraction efficiency and/or control using multiple SPME, internal standard and method of additions.

The aim of the thesis is to develop simple, easily automated and "green" analytical methods for quantitative and semi-quantitative determination of the main UDMH transformation products in soil and water using headspace solid-phase microextraction.

The following **research objectives** were formulated to accomplish the stated goal:

1) Study of the matrix effect on the trueness of UDMH transformation products determination in soil samples using HSSPME.

2) Study of the HSSPME parameters' effect on the accuracy of simultaneous determination of three major UDMH transformation products in soil samples, *N*-nitrosodimethylamine (NDMA), *N,N*-dimethylformamide (DMF) and 1-methyl-*1H*-1,2,4-triazole (MTA), using an internal standard (MTA-*d*3).

3) Building a correlation between the response ratios of UDMH transformation products to the internal standard obtained by HSSPME, and their concentrations in soil samples from sites of burned-out launch vehicle stages fall.

4) Development and validation of the methodology for the determination of UDMH transformation products in water samples and aqueous extracts from soil using GC-MS and GC-MS/MS.

5) Development and validation of a methodology for the determination of UDMH transformation products in soil samples using HSSPME-GC-MS/MS.

The object of the study was the determination of the UDMH transformation products in soil and water samples using headspace solid-phase microextraction.

The subject of the study was the optimization of extraction and calibration parameters to achieve acceptable trueness (apparent recovery – 70-130% for quantitative, and 30-300% for semi-quantitative analysis) and repeatability of analysis.

The research methods. The research was conducted using the scientific method: hypotheses were formulated and were subjected to experimental testing. Selective and sensitive chromatography-mass spectrometry methods of analysis were chosen for the methods development: gas chromatography with mass spectrometric detection (GC-MS) and gas chromatography with tandem mass spectrometric detection (GC-MS/MS). Headspace solid-phase microextraction (HSSPME), which combines the steps of extraction, preconcentration and cleanup, and can provide low-cost analysis of environmental samples, was selected as a sample preparation technique.

To ensure **validity and reliability** of results obtained during experiments, one or two independent variables were used, while other parameters were maintained constant. Experiments were conducted in two or three parallels with a subsequent calculation of mean values and standard deviations.

The key propositions submitted for defense:

1) Apparent recoveries of MTA, DMF, and NDMA by the method based on HSSPME-GC-MS with a 85 μm Carboxen/polydimethylsiloxane (Car/PDMS) coating at 60°C for 15 min using an internal standard MTA-*d3* for sandy and loamy soils with <1% of humus content using are 91-117, 85-123 и 64-132%, respectively.

2) The use of contaminated soil samples collected on landing sites of burned-out carrier rockets and analyzed by GC-MS after solvent extraction as calibration samples with known concentration for semi-quantitative determination of dimethylaminoacetonitrile, NDMA, DMF, MTA and 1,3-dimethyl-*1H*-1,2,4-triazole (DMTA) in soil by HSSPME-GC-MS using MTA-*d3* as an internal standard provides apparent recoveries 52-267% at lower limits of quantification 1-10 mg/kg.

3) Combining the standard addition and internal standard (using MTA-*d3*) quantification approaches improves the trueness of the quantification of NDMA, DMF, methylformamide, formamide, 3-methylpyridine, 1-methyl-*1H*-imidazole and 3-methyl-*1H*-pyrazole in sandy and loamy soils using the HS-SPME, while the standard addition approach provides better trueness for the other transformation products.

4) Optimal temperature and time of HSSPME of 9 main UDMH transformation products (NDMA, DMF, MTA, pyrazine, pyridine, 1-formyl-2,2-dimethylhydrazine, 1-methyl-*1H*-imidazole, 1-methyl-*1H*-pyrazole, *1H*-pyrazole) by 85 μm Car/PDMS coating from water samples, which provide the best combination of high peak intensities and low relative standard deviations, are 50°C and 60 min, respectively.

The main findings of the study:

1) A method for the simultaneous determination of MTA, DMF and NDMA in sandy and loamy soils with humus content < 1% by HSSPME-GC-MS was developed. It has been shown that the use of MTA-*d*3 as an internal standard allows the determination of DMF and NDMA in addition to MTA. HSSPME at 60 °C for 15 min using 85 μm Car/PDMS coating for sandy and loamy soil samples provided apparent recoveries of MTA, DMF and NDMA 91-117, 85-123 and 64-132%, respectively. The achieved detection limits of MTA, DMF and NDMA in soils under the optimized parameters were 14, 12, and 1 μg/kg, respectively. The developed analytical method will make it possible to carry out rapid and cost-effective analyses.

2) The response ratios of dimethylaminoacetonitrile, NDMA, DMF, MTA, 1,3-dimethyl-*1H*-1,2,4-triazole (DMTA), and 1-formyl-2,2-dimethylhydrazine (FDMH) to MTA-*d*3 determined using HSSPME-GC-MS correlated with the concentrations of the analytes determined in soil samples of different nature and moisture content using GC-MS after organic solvent extraction. HSSPME time and temperature do not affect the correlation quality of lines for NDMA, DMF, MTA, DMTA, and FDMH. Addition of excess water increases the data scatter but allows to decrease the matrix effect in the extraction of 1-methyl-*1H*-pyrazole and 1,5-dimethyl-*1H*-pyrazole. The developed approach can be recommended for quantification of approximate concentrations of unstable transformation products and compounds, for which standards are not available; however, HSSPME and solvent extraction should be optimized for the quantification of all analytes.

3) The optimized parameters of chemical ionization for the subsequent tandem mass spectrometric detection of UDMH main transformation products (reagent gas methane, reagent gas pressure 250 kPa, ion source temperature 150°C, ion source voltage 30 eV) allow to achieve the instrumental detection limits within 1.1-48.6 pg range (limits of detection via electron ionization at standard energy of 70 eV were 0.1-268 pg). The addition of $Ba(OH)_2 \cdot 8H_2O$ to the soil had no significant effect on the increment of extraction intensities of the of UDMH main transformation products. Addition of excess water into the samples generally had a negative effect on the responses of analytes. The optimal minimum recommended equilibration time of soil samples after standards application was 5 h at 40°C. Combining the standard addition and the internal standard (using MTA-*d*3) quantification approaches resulted in greater precision and accuracy of determination for NDMA, DMF, *N*-methylformamide, formamide, 3-methyl-*1H*-pyrazole, and *1H*-pyrazole. For the determination of FDMH, 3,5-dimethylpyrazole, 2-ethyl-*1H*-imidazole, *1H*-imidazole, *1H*-1,2,4-triazole, pyrazines and pyridines standard addition calibration is more suitable. Nevertheless, the proposed method allows the use of both approaches simultaneously.

4) A simple and automated method for the sensitive determination of the main transformation products of rocket fuel based on UDMH in aqueous samples using HSSPME-GC-MS was developed. The highest precision of the approach was obtained at an extraction temperature of 50°C and a time of 60 min. The apparent recoveries of pyrazine, 1-methyl-*1H*-pyrazole, NDMA, DMF, MTA and 1-methyl-*1H*-imidazole from aqueous samples varied from 75 to 125%. The detection limit of these analytes is below μg/L.

Scientific novelty. For the first time, the matrix effect issue, which reduces the accuracy of methods for analyzing complex matrices using HSSPME, has been studied in detail. It has been shown for the first time that the extraction effectiveness

of polar compounds with lower affinity to the extraction coating from different samples can differ by up to two orders of magnitude. The possibility of controlling the matrix effect to ensure the accuracy of determination of the main UDMH transformation products using MTA-*d*3 as an internal standard was shown. New methods for the determination of the main UDMH transformation products in soil and water samples based on HSSPME in combination with GC-MS and GC-MS/MS have been developed, which, in comparison with the known methods, provide a lower cost of analysis at comparable detection limits.

Theoretical and practical significance of the thesis.

The issue of the matrix effect and its influence on the trueness of HSSPME-based methods was studied in detail. It has been shown that for polar compounds with lower affinity to the extraction coating, the variability of extraction efficiency can theoretically reach two orders of magnitude. The selection of a suitable internal standard for quantification using HSSPME is a very challenging task due to the multitude of factors and physicochemical properties affecting the extraction effectiveness.

The novel developed methods can be recommended for application in monitoring of rocket and space activities in Kazakhstan, Russia, USA, China and other countries utilizing UDMH. The developed methods were successfully applied for the analysis of soil samples from the crash site of "Proton-M" launch vehicle and snow collected near the railway station located on the route of rocket fuel transportation to the Baikonur Cosmodrome (Kazakhstan).

Connection of the theme with the plan of research works and with various State Programs. The work was carried out within the framework of the projects funded by the Science Committee of the Ministry of Education and Science of the Republic of Kazakhstan "Development and implementation of 'green' techniques for determination of organic toxicants in soils" (3661/GF4, 2015-2017), "Development of analysis methods, materials and equipment for cost-effective 'green' environmental monitoring" (AP05133158, 2018-2020).

Approbation of the work. The results of the work were presented in the form of reports at two international conferences "Pacifichem-2015" (USA, 2015) and "Analytical chromatography and capillary electrophoresis", (Krasnodar, Russia, 2017).

Publications. Results of the work have been published as:

– two articles and one review in international journals indexed in Web of Science (Science Citation Index Expanded) with impact factors of 1.4, 4.9, and 8.4, and in Scopus with CiteScore percentiles 47, 89 и 96.

Description of the doctoral student's contribution to each of the publications:

1) Bakaikina N.V., Kenessov B., Ul'yanovskii N.V., Kosyakov D.S. Quantification of transformation products of rocket fuel unsymmetrical dimethylhydrazine in soils using SPME and GC-MS // Talanta. – 2018. – Vol.184, P.332-337. https://doi.org/10.1016/j.talanta.2018.02.047: research, methodology, validation (verification), visualization, writing the first version, editing.

2) Bakaikina N.V., Kenessov B., Ul'yanovskii N.V., Kosyakov D.S.,

Pokryshkin S.A., Derbissalin M., Zhubatov Zh.K. Quantification of transformation products of unsymmetrical dimethylhydrazine in water using SPME and GC-MS // Chromatographia. – 2017. – Vol. 80, Is. 6. – P. 931-940. http://doi.org/10.1007/s10337-017-3286-2: research, methodology, validation (verification), visualization, writing the first version, editing.

3) Kenessov B., Koziel J., Bakaikina N.V., Orazbayeva D. Perspectives and challenges of on-site quantification of organic pollutants in soils using solid-phase microextraction // Trends in Analytical Chemistry. – 2016. – Vol. 85B. – P. 111-122. http://doi.org/10.1016/j.trac.2016.04.007: research, visualization, writing individual subsections.