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ORIGINAL

Determination of 1,1-Dimethylhydrazine and its Transformation Products in Soil by Zwitterionic Hydrophilic Interaction Liquid Chromatography/Tandem Mass Spectrometry

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Abstract
1,1-Dimethylhydrazine is widely used as a fuel by some classes of carrier rockets. Being an extremely toxic and reactive substance, it gives a number of hazardous transformation products and poses a serious threat to the ecological state of the launch sites and territories used for landing of spent rocket parts. On the basis of studies of the retention of analytes on the sulfobetaine zwitterionic stationary phase, the HILIC–ESI-MS/MS method for simultaneous and rapid determination of unsymmetrical dimethylhydrazine and six major products of its transformation (methylhydrazine, *N*-nitrosodimethylamine, *N,N*-dimethylformamide, 1-methyl-1,2,4-1H-triazole, 1,1,4,4-tetramethyl-2-tetrazene, 1,1-dimethylguanidine) was developed. The achieved detection limits for the analytes were 0.02–7 μg L^{-1} and, for most compounds, they are significantly lower compared to the existing IC–MS/MS method. Direct combination of HILIC–MS/MS with preliminary pressurized extraction with acetonitrile allowed analysis of peat bog soils contaminated with rocket fuel within 40 min, including all sample preparation steps. The developed method was successfully tested on a sample of real soil from the falling place of the spent carrier rocket stage.

Keywords HILIC · HPLC–MS/MS · Zwitterionic stationary phase · 1,1-Dimethylhydrazine · Transformation products · Rocket propellant · Peaty soil

Introduction

1,1-Dimethylhydrazine (unsymmetrical dimethylhydrazine, UDMH), is widely used as a main component of rocket propellants by some classes of carrier rockets in Russia, Kazakhstan, India and China [1]. UDMH is an extremely toxic substance with mutagenic and teratogenic properties [2, 3] and, if released into the environment, poses a serious threat to the ecological state of the launch sites and territories used for landing of spent rocket parts [4]. The maximum permissible concentrations (MPC) of UDMH established in Russia for water and soil are 0.5 μg L^{-1} and 0.1 mg kg^{-1}, respectively. The similar MPC levels were adopted in Kazakhstan (0.5 μg L^{-1} and 0.05 mg kg^{-1}). Taking into account carcinogenic activity, US National Institute for Occupational Safety and Health (NIOSH) recommends that the levels of UDMH in workplace air not exceed 0.15 mg m^{-3} for a 2-h period [5].

Being a highly reactive substance, UDMH is readily exposed to oxidative transformations in the environment giving a wide range of toxic products such as methylhydrazine, *N*-nitrosodimethylamine (NDMA), *N,N*-dimethylformamide (DMF), 1-methyl-1H-1,2,4-triazole (MT), 1,1,4,4-tetramethyl-2-tetrazene (TMT), and others [6–8]. Reacting with the carbonyl groups of lignohumic substances in soils, UDMH forms hydrazones [9], capable both of hydrolysis with liberation of free 1,1-dimethylhydrazine, and further oxidative transformation. This complicates the range of products formed and leads to the existence in the soils of several forms of UDMH, differing in the degree of mobility [10].

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The development and improvement of methods for the highly sensitive determination of UDMH and the most important products of its transformations in complex matrices is an important and still unsolved problem, despite significant progress and a number of publications in this field [11].

GC–MS, especially in combination with solid phase microextraction, is a preferred method for the determination of volatile non-ionic transformation products, such as NDMA or DMF [12–14]. The use of tandem (QqQ) mass spectrometric detection allowed, along with the increase in the selectivity of the analysis, to decrease significantly the detection limits of the analytes and expand the range of analytes determined in the simultaneous presence [14–16]. The determination of hydrazines is possible only after preliminary derivatization by various reagents [17, 18] to prevent undesirable interactions of analytes with the surface of the capillary columns. A similar approach is also used in HPLC with spectrophotometric or fluorometric detection to improve the hydrophobicity of the analytes and to provide sufficient sensitivity of the analysis due to the introduction of chromophores or fluorophores into their structure [19–21]. Despite the merits of this approach, the sample preparation procedure is significantly more complicated, the duration of the analysis increases with the possible decrease in the reproducibility of the results.

Probably, the most widely known method for the direct determination of hydrazines is ion chromatography (IC) with separation on a sulfocation-exchange stationary phase and amperometric detection (AD) [17, 22, 23]. The replacement of AD with mass spectrometry makes it possible to significantly expand the range of the detectable components [24] by including electrochemically inactive compounds in it. Some suppression of the ionization of the analytes due to the use of high buffer concentrations with IC separation can be successfully compensated by the use of tandem (QqQ) mass spectrometry [25], which provides detection limits 1–2 orders of magnitude lower than HPLC–MS [24] with significantly greater selectivity and sensitivity, comparable to AD [23]. For example, for detection of UDMH and MH, detection limits of 13 and 18 μg L^{-1} were obtained, respectively [25].

A promising alternative to the available HPLC methods for the separation of hydrazines and highly polar products of their transformation is hydrophilic interaction liquid chromatography (HILIC), characterized by high separation efficiency, rapid analysis and good retention of strongly polar compounds. The use of mobile phases containing a large amount of organic solvent (up to 97%) in HILIC mode favorably affects the possibility of combining chromatography and mass spectrometry [26]. For the first time, the applicability of HILIC for the separation of hydrazine and its three methylated derivatives (UDMH, MH, 1,2-dimethylhydrazine) in the analysis of pharmaceutical preparations is shown in [27]. Due to the use of the nitrogen sensitive chemiluminescent detector (CLND) in this study, the authors confined themselves to the use of aliphatic alcohols (methanol, ethanol, isopropanol) as organic components of the mobile phase, which is generally not characteristic of the HILIC mode [28]. Among the various stationary phases tested (amine, amide, diol, zwitterionic), only zwitterionic, containing sulfobetaine groups, showed good retention and separation. A similar conclusion was made in [29] using acetonitrile as the main component of the mobile phase. In combination with amperometric detection, it was possible to achieve detection limits for UDMH and MH at a level of 0.1 μg L^{-1} without additional preconcentration steps. Despite the high sensitivity, this approach is characterized by insufficient selectivity, which is extremely important in the analysis of such complex objects as soils. In addition, it does not allow to determine the most important products of transformation of UDMH, which do not undergo oxidation on the glassy carbon electrode.

Overcoming these deficiencies by combining HILIC with tandem mass spectrometric detection and development on this basis, the rapid method for simultaneous determination of unsymmetrical dimethylhydrazine and its most important transformation products is the aim of the present study.

Experimental

Analytes

Based on the literature data on toxicity and possible concentration levels of the UDMH transformation products in soils [10, 11, 16, 25], we selected as the analytes, in addition to UDMH, six compounds: MH, NDMA, DMF, MT, TMT, 1,1-dimethylguanidine (DMG) (Fig. 1). Two important components—formaldehyde dimethylhydrazone and formic acid dimethylhydrazide—were not included in this list due to the instability at the relatively low pH of the mobile phase used in HILIC that we observed in the preliminary experiments.

Chemicals and Materials

1,1-Dimethylhydrazine (≥ 98%), methylhydrazine (≥ 98%) and 1,1-dimethylguanidine sulfate (97%) were purchased from Sigma-Aldrich (Steinheim, Germany). 1-methyl-1H-1,2,4-triazole was purchased from Fluorochem (Hadfield, UK). *N*,*N*-Dimethylformamide (≥ 99.8%) was purchased from LabScan (Gliwice, Poland). Certified standard solutions of *N*-nitrosodimethylamine and 1,1,4,4-tetramethyltetrazene with the concentration 1 mg mL^{-1} were purchased from Ecoanalitika (Moscow, Russia).

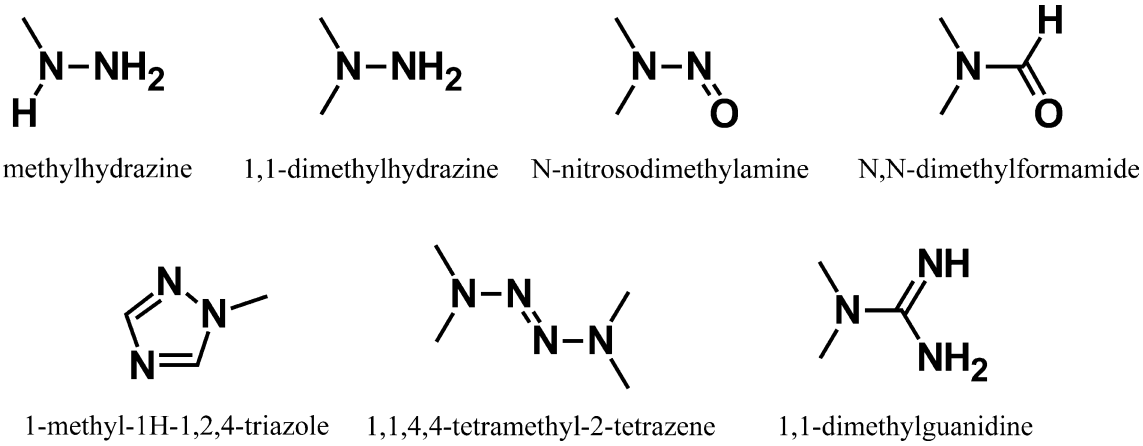

Fig. 1 Structural formulae of analytes

HPLC-hypergradient grade acetonitrile (Cryochrom, S.-Petersburg, Russia), HPLC–MS grade methanol and isopropanol (Merck, Darmstadt, Germany), ultrapure (Type I) Milli-Q water, 10 M aqueous solution of ammonium formate (HPLC grade), ammonium acetate (ACS reagent, ≥97%), formic and acetic acids (ACS reagent, ≥98%) were purchased from Sigma-Aldrich (St. Louis, USA) and used for mobile phase and working solutions preparation.

HPLC-grade acetonitrile (Cryochrom, S.-Petersburg, Russia), barium hydroxide hydrate (pure, Panreac, Barcelona, Spain), acetic and sulfuric acids (chem. pure, Component-Reaktiv, Moscow, Russia) were used for soil pressurized extraction, system flushing and further treatment of extracts obtained.

Standard Solutions Preparation

Stock aqueous solutions of UDMH, MH, DMF, MT, and DMG with the concentrations 1000 mg L^{-1} were prepared from precisely weighed portions of pure compounds and stored at 4 °C no longer than 48 h. Calibration solutions of analytes in the concentration range 0.0001–10 mg L^{-1} were prepared by consecutive dilutions of stock solutions mixture with acetonitrile and used immediately after preparation.

Chromatographic Analyses

An HPLC–MS/MS system consisting of a tandem mass spectrometer with a triple quadrupole LCMS-8030 equipped with an electrospray ionization (ESI) source and LC-30 "Nexera" liquid chromatograph (Shimadzu, Kyoto, Japan) was used. HPLC system included DGU-A5 vacuum degasser unit, two LC-30AD pumps, CTO-20A column oven, SIL-30AC autosampler, and CBM-20A system controller.

Control of the HPLC–MS/MS system, collection and processing of data were carried out using the LabSolutions software (Shimadzu, Kyoto, Japan).

HILIC separations were carried out at 40 °C on a Nucleodur HILIC column (Macherey-Nagel, Duren, Germany), 150 × 3 mm, particle size 3 µm, with sulfobetaine zwitterionic stationary phase. Mobile phase flow rate was 0.5 mL min^{-1}, injection volume—5 µL. ESI(+)—MS detection was carried out in the selected reactions monitoring (SRM) regime in accordance with the data of Ref. [25] (Table 1). The following parameters of ion source were used: temperature of the heating block and the desolvation line—250 °C, capillary voltage—4.5 kV, nebulizing and drying gas (N_2) flow rates—3 and 15 L min^{-1}, respectively.

Table 1 Parameters of mass spectrometric detection of analytes in SRM mode

Analyte	Molecular mass, Da	Precursor ion, *m/z*	Product ion, *m/z*	Collision energy, eV
MT	83.1	84	30[a]	25
			43	10
TMT	116.2	116	44[a]	12
			72	9
DMF	73.1	74	46[a]	20
			31	20
NDMA	74.1	75	58[a]	20
			43	20
DMG	87.1	88	71[a]	21
			46	17
UDMH	60.1	61	44[a]	20
			45	20
MH	46.1	47	32[a]	15
			30	17

[a]Used for quantification

To increase the signal-to-noise ratio, a time program for recording ion transitions was used.

The determination of the analytes by IC–MS/MS was performed in accordance with the previous work [25] using the same instrumentation. Chromatographic separation was carried out on a Nucleosil-100-5SA column, 125 × 4.6 mm, particle size 5 µm (Macherey-Nagel, Duren, Germany) with a sulfocation-exchange stationary phase. Aqueous 50 mM ammonium acetate buffer solution (pH 5.4) with addition of methanol (3:1) was used as a mobile phase. The flow rate was 1 mL min^{-1}, injection volume—20 µL.

GC–MS/MS analysis was performed according to Ul'yanovskii et al. [15, 16] on an Agilent 7000B GC–MS/MS system (Agilent, Santa Clara, USA) comprising an Agilent 7890A gas chromatograph and a triple quadrupole mass spectrometric detector. The separation was carried out on an HP-INNOWax (Agilent, Santa Clara, USA) capillary column, 30 m × 0.25 mm with a 0.25 µm stationary phase layer. The injection volume was 2 µL with a split 5:1, inlet temperature 170 °C. The program of the thermostat was as follows: starting temperature 100 °C, gradient 10 °C min^{-1}, final temperature 190 °C. The operation parameters of the GC–MS were as follows: helium (99.9999%) carrier gas, control of gas flow at a constant pressure (103 kPa), interface temperature 230 °C, and ion source temperature 230 °C, electron ionization (EI) with the energy 70 eV. The nitrogen and helium were used as a collision and buffer gases in collision cell, respectively.

All chromatographic analyses were performed in at least five replicates.

Soil Sample Preparation

The samples (ca. 0.5 kg) of peat bog soil were collected in 2014 from the depth 0–30 cm at the epicenter of the falling place of first stage of "Cyclone-3" carrier rocket in Arkhangelsk region of Russia. According to the results of analysis, the contents of moisture and ash (recalculated for oven-dried sample) were 89 and 2.6%, respectively. After collection, soil samples were placed into gastight plastic containers, frozen and stored at − 18 °C. Immediately before analysis, the sample was defrosted and mixed thoroughly with a spatula to achieve uniformity. The same collection and preparation procedures were applied to the blank soil sample (not contaminated with rocket fuel) which was taken simultaneously at a large distance (> 1 km) from fall place.

The pressurized extraction was performed using ASE-350 (Dionex, Sunnyvale, USA) accelerated solvent extraction system according to the earlier reported and validated procedure [16]. Barium hydroxide octahydrate (25 g) and soil sample (10 g) were mixed in glass beaker using spatula. A 5 g portion of mixture was placed into 10-mL stainless steel extraction cell and extracted with 90% aqueous acetonitrile in nitrogen (99.99%) atmosphere at a temperature 100 °C and pressure 100 bar. Two extraction cycles (10 min each) were performed. At the next stage, cell was rinsed with a fresh portion of extractant (6 mL). The final volume of obtained extract was about 30 mL. To prevent the contamination of extraction system with barium salts, all lines were flushed after extraction with 3% aqueous solution of acetic acid and then with deionized water.

To remove completely the dissolved barium hydroxide, the obtained extract was neutralized by dropwise addition of 1 M sulfuric acid to pH 3–5. After centrifugation, supernatant was filtered through 0.22 µm nylon membrane and injected into chromatography system.

Results and Discussion

Optimization of Chromatographic Separation

The use of a zwitterionic stationary phase requires maintaining certain pH and ionic strength by adding buffer salts to the mobile phase to control the degree of ionization of the betaine groups and analytes, and suppress undesirable ion-exchange interactions of the stationary phase with the analytes. The phosphate buffer solution successfully used for this purpose in [29] is incompatible with mass spectrometric detection due to its non-volatility. In preliminary experiments, we tested buffers based on ammonium salts of formic and trifluoroacetic acids. In the latter case, separation was not achieved because of the propensity of trifluoroacetate ions to ion-pair interactions with analytes. In this regard, further studies on optimizing the composition of the mobile phase were carried out using an ammonium formate buffer solution.

The most important parameter determining the eluting power of the mobile phase in HILIC is the content of the aqueous component in it. When the concentration of acetonitrile is varied in the range of 75–90%, the retention times for DMF, MT, NDMA and TMT are only slightly dependent on the mobile phase composition, while they are characterized by low retention factors ($k \leq 1$). In contrast, due to high polarity and capability for ionic interactions with stationary phase, alkylhydrazines and DMG are characterized by strong retention, as well as a sharp increase in k values with an increase in the organic solvent content in the mobile phase (Fig. 2). Elution of these compounds occurs in the reverse order in comparison with ion chromatographic separation [17, 25] and correlates with the presence of hydrophobic groups in the molecule structure. This fact reflects the decisive contribution to the retention mechanism of non-ion-exchange interactions (the distribution of analytes between the aqueous stationary and non-aqueous mobile phases).

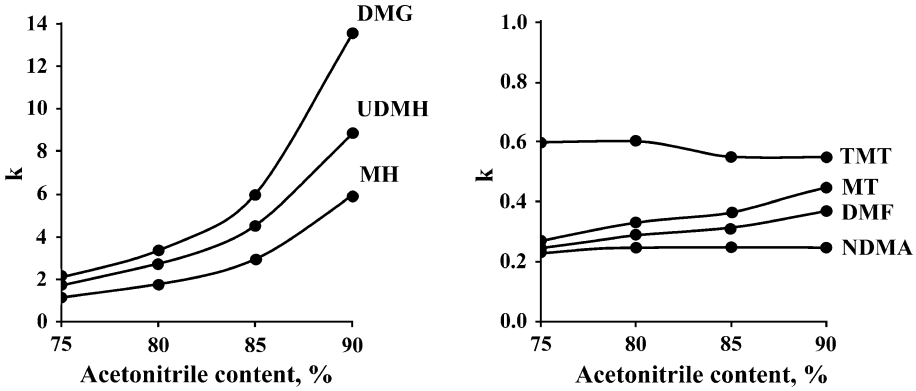

Fig. 2 Dependence of retention factors of analytes on acetonitrile content in mobile phase

The content of the organic solvent in the mobile phase has also a strong influence on the sensitivity of mass spectrometric detection. With an increase in the percentage of acetonitrile, the intensity of chromatographic peaks is reduced significantly (TMT is an exception) (Supplementary, Fig. S1). At the same time, the efficiency of precursor ions generation does not drop for the majority of compounds, which is reflected in the dependence of the peak areas on the fraction of acetonitrile in the mobile phase (Supplementary, Fig. S2). This indicates that the positive effect of the additions of acetonitrile on the electrospray process in the ion source predominates with respect to the suppression of ESI(+) ionization of analytes by an aprotic solvent. In this regard, the main factor determining a decrease in the sensitivity of the method with an increase in the content of the organic component of the mobile phase is the smearing of chromatographic zones. As an optimal composition of the mobile phase, the content of acetonitrile in the range of 75–85% can be accepted, which is a compromise between the quality of chromatographic separation and the efficiency of precursor ions generation. Further studies were carried out with an acetonitrile concentration of 80%.

The pH of the mobile phase in the zwitterionic HILIC determines the acid–base equilibria of both the analytes and the charged functional groups of the sulfobetaine stationary phase and, as a consequence, the retention of analytes and the selectivity of the analysis. The effect of pH was studied in the range 2.5–6.5, the boundaries of which are determined by the long-term stability of the zwitterionic silica-based adsorbent.

It was found that the retention of DMF, NDMA and MT does not depend on the pH value in the whole investigated range due to their low protonation ability. TMT is characterized by weak retention (Fig. 3), however, using a pH less than 3.5 allows to increase the *k* to a value of 0.65 and, thus, reduce the probability of matrix interferences. The retention factors of the remaining analytes increase almost linearly with increasing pH. This reflects the contribution of ion-exchange interactions of alkylhydrazinium and 1,1-dimethylguanidinium cations with sulfonic groups of the stationary phase, the partial protonation of which in acidic media leads to a decrease in retention times. At pH 4 and above, the chromatographic peaks of DMG, MH and UDMH are significantly broadened and distorted, which can be related either to the appearance of their molecular forms in the solution, or to interactions with the active sites of the stationary phase.

The use of the mass spectrometric detection of positively charged ions determines the positive effect of acid addition on the sensitivity of analysis (Fig. 4). For all analytes under study, the heights of the chromatographic peaks as well as their areas (Supplementary, Fig. S3) are sharply increased, as the pH is lowered from 4 to 2.5 due to the increase in

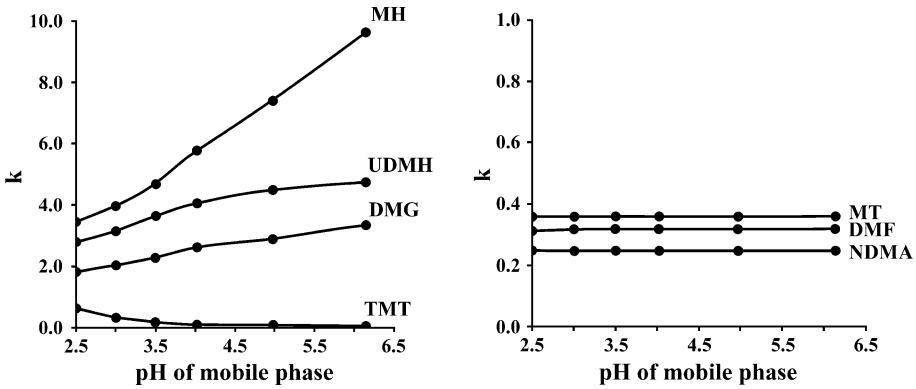

Fig. 3 Dependence of retention factors of analytes on pH of buffer solution

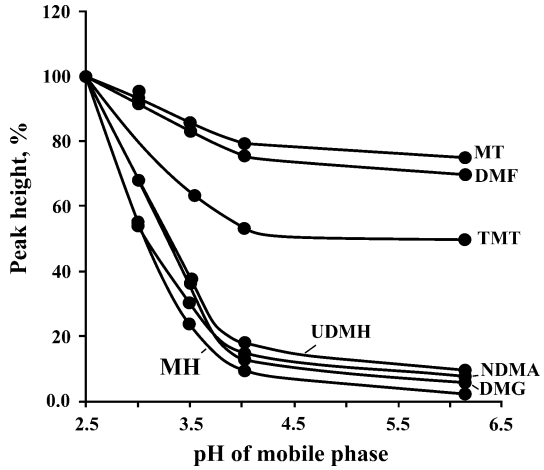

Fig. 4 Effect of buffer solution pH on heights of chromatographic peaks (the relative height of each peak at pH 2.5 is taken as 100%)

the protonation efficiency. Based on the results presented, it is preferable to use the lowest values of the mobile phase pH. In this connection, the value of 2.5 was chosen as the working one.

A study of the effect of buffer solution ionic strength showed that using an ammonium formate concentrations of less than 15 mM (on column) leads to a loss of resolution and the unacceptable broadening of chromatographic peaks. In the range of 10–100 mM, the concentration of ammonium formate practically does not affect the *k* values of the analytes, which decrease insignificantly with increasing ionic strength of the mobile phase. At the same time, a high concentration of ions (> 50 mM) suppresses the ionization of the analytes in the ion source of the mass spectrometer. Optimum results from the point of view of chromatographic resolution and sensitivity of mass spectrometric detection are achieved with a mobile phase ionic strength of 25 mM.

Of great interest is the observed drastic difference in the effect of the ionic strength of formate and phosphate buffer solutions on the retention of hydrazines. As was shown earlier [27], an increase in the concentration of ammonium dihydrogen phosphate leads to a significant increase in the retention factors of MH and UDMH at the same pH value of the solution. In our opinion, this phenomenon can be explained by the greater polarizability of phosphate ions in comparison with formate ions, as well as by the presence of certain amounts of doubly charged ions $[HPO_4]^{2-}$ in the mobile phase. Their association with internal quaternary ammonium cations of zwitterionic sulfobetaine groups leads to the shielding of positively charged centers and the acquisition of a negative charge by the surface of the stationary phase. This effect leads to an increase in the proportion of ion-exchange interactions of cationic forms of analytes with a stationary phase in retention mechanism and increasing of retention factors' values.

To achieve complete separation of the analytes and to reduce the duration of the chromatographic analysis, a gradient elution profile was optimized, allowing the analysis to be performed in less than 9 min (Fig. 5). It was found that column equilibration between consecutive runs does not require significant time and takes no more than 3 min.

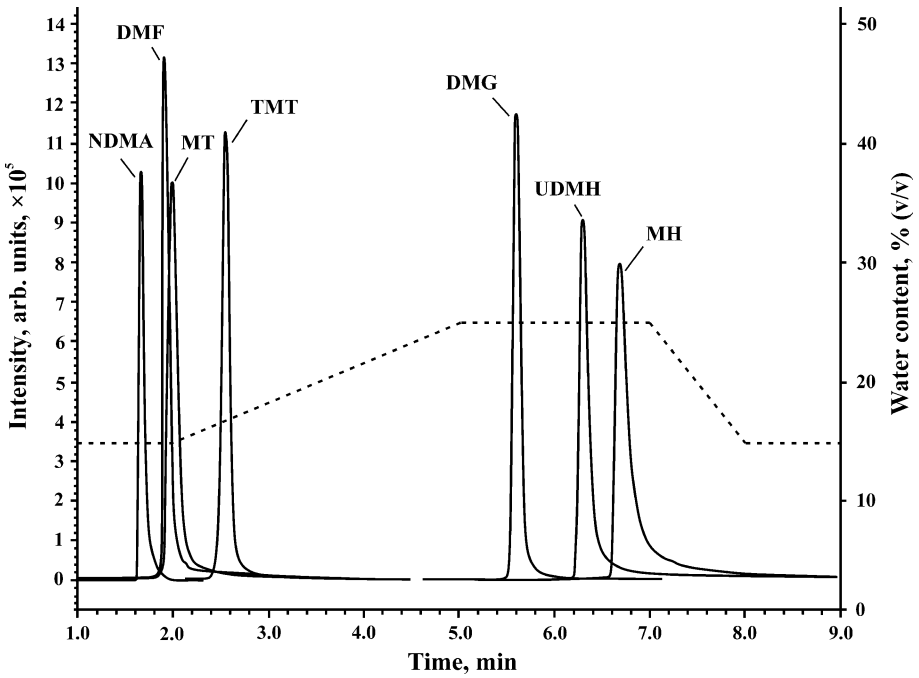

Fig. 5 The HILIC–ESI(+)-MS/MS chromatogram of analytes' model mixture and elution gradient profile. Concentrations of NDMA, DMF, MT, UDMH, and MH—10 mg L^{-1}, TMT—0.5 mg L^{-1}, DMG—0.05 mg L^{-1}

Injection Solvent

The sample solvent plays an important role in HILIC because of the significant affinity of the stationary phase to many polar solvents and, first of all, to water [30]. To test the effect of the injection solvent, in addition to acetonitrile and aqueous formate buffer solution with pH 2.5 as components of mobile phase, we used methanol, water, and 1 M hydrochloric acid, used by different authors to extract UDMH and its transformation products from soils [10, 25, 31]. As a criterion for their suitability for HILIC–MS/MS analysis, the width at half the height ($W_{1/2}$) of the chromatographic peaks of both non-ionic compounds with low retention (MT, DMF) and strongly retained hydrazines (UDMH, MH), as well as the retention time (t_R) of analytes were used.

The data obtained using the model solutions of these four compounds in different solvents (Supplementary, Table S1) show that the optimal injection solvent is acetonitrile. The greatest negative effect on the separation of analytes is produced by methanol, the use of which leads to a two- to threefold increase in the peak widths of the weakly retained analytes and the corresponding drop in the sensitivity of the analysis. Water and formate buffer solution exert a similar effect on the chromatographic peaks of MT and DMF, broadening them 1.5–2 times and making separation impossible. Acceptable results are achieved only by diluting aqueous solutions with acetonitrile in a ratio of 1:2 or more. Injection of the sample in 1 M aqueous hydrochloric acid, in contrast to water, not only leads to a loss of separation efficiency, but also to a significant change in retention times, especially for alkylhydrazines. In this case, to obtain reproducible results, in addition to dilution with acetonitrile, pre-neutralization of the acid is required.

Quantification

The obtained calibration dependences of the area of the chromatographic peak on the concentration for all the compounds being studied are linear over a wide range of concentrations (3–4 orders of magnitude) and are described by an equation of the form $y = ax$ with a correlation coefficient (r^2) greater than 0.995 (Table 2).

The detection limits (LOD) and the lower limits of quantification (LLOQ) were calculated on the basis of the signal-to-noise ratio 3 and 10, respectively, and refined by analyzing model mixtures of analytes in acetonitrile with concentrations close to corresponding LLOQ values.

The obtained detection limits (Table 2) lie in the range from 0.02 to 7 μg L^{-1}. The sensitivity of the developed approach is significantly (by 1–2 orders of magnitude) inferior to the methods of HILIC-AD [29] in the determination of hydrazines and GC–MS/MS [14–16] in the determination of volatile transformation products (MT, DMF, NDMA). At the same time, the HILIC–MS/MS method, in contrast to the above, allows simultaneous determination of hydrazines (UDMH and MH) and the most important oxidation products of rocket fuel. In addition, the LOD value obtained for TMT turned out to be comparable with the result of GC–MS/MS, and the determination of DMG by gas chromatography without preliminary derivatization is impossible at all.

Most valid comparison can be regarded by the developed approach to IC–MS/MS, allowing the simultaneous determination of a similar set of analytes [25]. In general, the sensitivity of both methods is comparable for the most of components being determined. Nevertheless, the use of hydrophilic chromatography gives a significant (by an order of magnitude) gain in the detection limits of TMT and UDMH, as well as a two to threefold decrease in the LOD values for NDMA, MH and DMG. Taking into account the use of the same instrument in both cases and the identical conditions for recording SRM transitions, the higher sensitivity of HILIC–MS/MS can be explained by better conditions for electrospray ionization of the analytes (a high content of an organic solvent in the mobile phase with lower boiling point and a surface tension), as well as a higher efficiency of separation on the HILIC stationary phase.

It should also be noted that in this study, the volume of the sample introduced into the chromatographic column was 5 μL compared to 20 μL in the IC–MS/MS method [25]. The parameters of the used column allow to increase the injection volume to 10–20 μL without significant loss

Table 2 Calibration dependences ($y = ax$) for the area of chromatographic peak versus analyte concentration, limits of detection and quantification of analytes by the HILIC–MS/MS method

Analyte	Linear concentration range, μg L^{-1}	a	r^2	LOD, μg L^{-1}	LLOQ, μg L^{-1}
MT	20–20,000	50,800	0.997	6.7	22
TMT	1–2000	519,000	0.999	0.3	1.0
DMF	20–20,000	85,600	0.999	7.1	23
NDMA	20–20,000	13,100	0.998	5.5	18
DMG	0.1–200	4,230,000	0.998	0.02	0.07
UDMH	10–20,000	718,000	0.997	1.7	5.6
MH	20–20,000	224,000	0.995	6.6	22

of separation efficiency and to reduce further the detection limits. Furthermore, the availability of HILIC zwitterionic stationary phases with a particle size of less than 2 µm opens additional possibilities to improve the sensitivity and to reduce analysis time using shorter UHPLC columns.

Soil Analysis

The need to use acetonitrile as an injection solvent requires the introduction of an additional step of sample preparation, including a change of solvent. In the simplest case, dilution of the sample with acetonitrile can be used as such a step leading to a significant increase in detection limits. In this regard, the most promising application of the developed approach is the analysis of soils in combination with preliminary pressurized extraction with acetonitrile. This method of sample preparation was validated and showed exceptionally high efficiency in GC–MS/MS determination of a wide range of UDMH transformation products in peaty soil contaminated with rocket fuel [16].

The absence of matrix interferences was demonstrated by the spike recovery test using the acetonitrile extract of blank soil sample (Supplementary, Table S2). The recovery values for all analytes lied in the range of 88–106% at the concentration level of 50 µg L^{-1}.

Analysis of the obtained acetonitrile extract of peat bog soil (Supplementary, Fig. S4), collected at the fall place of the first stage of the carrier rocket, without additional stages of sample preparation (except sulfuric acid addition to neutralize barium hydroxide), allowed to determine 6 out of 7 target compounds (with the exception of NDMA). The main product of the transformation is 1-methyl-1*H*-1,2,4-triazole, the concentration of which is 15 ± 1 mg kg^{-1} (Table 3). The lowest content is typical for TMT and DMG (0.010 ± 0.001 and 0.025 ± 0.004 mg kg^{-1}, respectively). UDMH and MH were detected in close amounts (8.6 and 10 mg kg^{-1}, respectively).

Table 3 Results of analysis of peat bog soil polluted with rocket fuel by HILIC–MS/MS and corroborative methods

Analyte	Content in soil, mg kg^{-1}			
	HILIC–MS/MS	GC–MS/MS	IC–MS/MS	HILIC-AD [29]
TMT	0.010 ± 0.001	n/d	n/d	–
NDMA	n/d	0.024 ± 0.008	n/d	–
DMF	1.7 ± 0.2	1.4 ± 0.2	1.6 ± 0.2	–
MT	15 ± 1	14 ± 2	16 ± 1	–
UDMH	8.6 ± 0.8	–	7.7 ± 0.9	108 ± 11
MH	10 ± 1	–	9.9 ± 0.9	11 ± 4
DMG	0.025 ± 0.004	–	0.018 ± 0.003	–

n/d not detected

It is worth noting the simplicity and rapidity of the approach used. It makes possible, with a minimum number of operations, to carry out analysis of the soil within 40 min including sample preparation.

The thorough validation of the method for determining such reactive compounds as asymmetric dimethylhydrazine and most of its transformation products using conventional approaches is difficult. The reason is rapid interaction of analytes with humic substances of soils and the formation of several forms of analytes with different degrees of mobility [10]. In this regard, to confirm the correctness of the developed approach, we used a comparison of the results of analysis of the soil sample studied, obtained by various independent methods. These include IC–MS/MS [25] with preliminary dilution of the acetonitrile extract with water (1:3), as well as GC–MS/MS with direct introduction of the extract into the chromatographic system [16].

The results obtained (Table 3) demonstrate that, due to higher sensitivity, only the HILIC–MS/MS method allowed the determination of TMT. When determining DMF and MT, the concentrations obtained by the three methods are almost identical. Similarly, identical results were obtained by HILIC–MS/MS and IC–MS/MS in determining UDMH, MH and DMG, for which gas chromatographic separation cannot be used without preliminary derivatization. This suggests the absence of significant matrix effects in the determination of analytes using HILIC separation and, consequently, the applicability of the developed approach to the analyses of real objects.

It is curious to compare the results of the determination of alkylhydrazines with the recently published data obtained for the same soil sample by HILIC-AD with preliminary distillation of the analytes to dryness from a mixture of soil with a 50% aqueous solution of NaOH [29]. While for methylhydrazine both methods yielded contents which differ within the error of the analysis, a tenfold decrease of UDMH content is observed when using acetonitrile extraction under pressure as compared to distillation. This is explained by the fact that during the pressurized extraction mobile forms of UDMH are extracted, while the more stringent distillation conditions ensure the release of UDMH from the corresponding hydrazones and thus the determination of the total content of the analyte [23]. Methylhydrazine, being an intermediate of UDMH degradation, preferably presents in the soil in a free state, which results in identity of the concentrations obtained with the two different methods of sample preparation.

Conclusion

Due to the mixed retention mechanism, zwitterionic hydrophilic chromatography allows the rapid and simultaneous determination of unsymmetrical dimethylhydrazine and the

most important products of its oxidative transformations, which differ greatly in their properties. The use of tandem (QqQ) mass spectrometric detection with electrospray ionization makes it possible to reach detection limits of analytes at the level of 0.02–7 μg L^{-1} with a linear concentration range of at least 3 orders of magnitude. For most analytes, the sensitivity achieved is significantly higher than the IC–MS/MS method, while for UDMH and TMT, the LOD values obtained are an order of magnitude lower despite a significantly smaller injection volume of the sample. The most important advantage of the developed method is its ability to combine it with highly efficient pressurized extraction of analytes with acetonitrile for the analysis of soils contaminated with rocket fuel without the need to change the solvent or dilute the sample. The developed method was successfully tested on a sample of peat bog soil from the fall place of the spent carrier rocket stage.

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Compliance with Ethical Standards

Conflict of interest The authors declare no conflicts of interest in relation to this research.

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