Talanta 105 (2013) 347–353

Contents lists available at SciVerse ScienceDirect

Talanta

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

Determination of *N*-nitrosodiethanolamine in cosmetic products by headspace solid phase microextraction using a novel aluminum hydroxide grafted fused silica fiber followed by gas chromatography–mass spectrometry analysis

Saied Saeed Hosseiny Davarani [a,*], Leila Masoomi [a], Mohammad Hossein Banitaba [a], Hamid Reza Lotfi Zadeh Zhad [b], Omid Sadeghi [b], Azam Samiei [c]

[a] Department of Chemistry, Faculty of Sciences, Shahid Beheshti University G. C., Tehran 1983963113, Islamic Republic of Iran
[b] Department of Chemistry, Shahr-e-Rey Branch, Islamic Azad University, P. O. Box 18735-334, Tehran, Islamic Republic of Iran
[c] Mahd-e-Taban Investment Company, Vali-e-asr Ave., Tehran 1433895611, Islamic Republic of Iran

ARTICLE INFO

Article history:
Received 23 July 2012
Received in revised form
14 October 2012
Accepted 16 October 2012
Available online 26 October 2012

Keywords:
N-nitrosodiethanolamine (NDELA)
Headspace solid phase microextraction
Cosmetic
Aluminum hydroxide grafting
Gas chromatography–mass spectrometry

ABSTRACT

A method based on headspace solid phase microextraction with a new fiber, coupled with gas chromatography–mass spectrometry was developed for the determination of NDELA in cosmetic samples. The fiber provides Lewis acid–base interaction between its surface and analyte functional groups. The fiber was prepared by grafting aluminum tri-tert-butoxide on the surface of a fused silica. The optimization of SPME conditions showed that NDELA can be most effectively extracted at 70 °C, in 15 min, with a sample volume of 0.5 (V_s/V_t), stirring rate of 150 rpm, desorption time of 5 min, desorption temperature of 260 °C and at 12.5% (w/w) concentration of NaCl. Under the optimized conditions, LOD of 1 μg Kg^{-1} and a calibration curve with correlation coefficients greater than 0.9897 and a linearity range from 6 to 10000 μg Kg^{-1} were obtained. The intra-day and inter-day precision and accuracy were evaluated at four concentration levels. All of the values for accuracy and precision were lower than the acceptable limit of 15%. The fiber to fiber repeatability was 8.7%. The method was applied for the analysis of real samples including hair shampoo, body shampoo, dishwashing liquid and hand washing liquid. Relative recoveries were achieved in the range of 95–99%.

1. Introduction

N-nitrosamines are hazardous chemical compounds that may be present as contaminants in a number of products including food, drink, tobacco, rubber products and cosmetics [1]. Most nitrosamines, such as *N*-nitrosodiethanolamine (NDELA), are rated among carcinogenic or potentially carcinogenic compounds [2,3]. NDELA is a common contaminant in many commercial cosmetic products such as hand creams, face creams, shampoos, moisturizing lotions and other hand and body products [4]. The most commonly used amines in cosmetic products are di- and tri-ethanolamine and both of them can lead to the production the most frequently detected nitrosamine, NDELA [5]. NDELA is readily absorbed through the skin and is accumulated in organs such as the liver, bladder, kidneys, etc., and it induces chronic toxic effects [6,7]. Cosmetic products with 52–56,750 μg Kg^{-1} of NDELA have been notified as posing serious risks [8]. In a study of cosmetic products in 1991–1992, by the US Food and Drug Administration (FDA), NDELA was determined in 65% of the samples at levels of up to 3 μg mL^{-1} [9].

Several analytical methods have been used for the identification and determination of NDELA at the μg mL^{-1} level. Among them, there are HPLC methods combined with UV [10,11], thermal energy analyzer [12], fluorescence [13] and tandem MS [1] detection systems as well as gas chromatography coupled with flame ionization, thermal energy analyzer, electron capture and mass spectrometry detectors [14–17]. Additionally, open-tubular electrochromatography [18], ion-exchange chromatography [11],

Abbreviations: NDELA, *N*-nitrosodiethanolamine; LLE, Liquid–liquid extraction; SPE, Solid phase extraction; HS-SPME, Headspace solid phase microextraction; PDMS-DVB, Polydimethylsiloxane-divinylbenzene; NCD, Nitrogen chemiluminescence detector; PA, Polyacrylate; NDMA, *N*-nitrosodimethylamine; NDEA, *N*-nitrosodiethylamine; NPIP, *N*-nitrosopiperidine; NPYR, *N*-nitrosopyrrolidine; TGA, Thermal gravimetric analysis; PTFE, polytetrafluoroethylene; NDPA, *N*-nitrosodi-n-propylamine; NMOR, *N*-nitrosomorpholine; NDBA, *N*-nitrosodi-n-butylamine; NDBzA, *N*-nitrosodibenzylamine; NDPheA, *N*-nitrosodiphenylamine; NDCHA, *N*-nitrosodicyclohexylamine; NMEA, *N*-nitrosomethylethylamine; DLLME, Dispersive liquid–liquid microextraction

* Corresponding author. Tel.: +98 21 22431667; fax: +98 21 22431663.
E-mail addresses: ss-hosseiny@sbu.ac.ir, h.davarani@gmail.com (S.S.H. Davarani).

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http://dx.doi.org/10.1016/j.talanta.2012.10.053

differential pulse polarography [19] and thin layer chromatography [20] have been used for the analysis of NDELA. Furthermore, an ion-pair liquid chromatography method with C16-cetyltrimethylammonium chloride, as the ion-pair agent, for the determination of four non-volatile *N*-nitrosoamino acids [21] and the reverse phase HPLC method with anion complex agent and UV detection [22] have been reported.

A number of conventional extraction and clean-up procedures for determining nitrosamines have been described, including low-temperature vacuum distillation, liquid–liquid extraction (LLE), and solid phase extraction (SPE) [23–25]. The US EPA method for the determination of nitrosamines in water samples is based on a SPE–GC–MS/MS analysis [26]. An ISO standard method for the determination of *N*-nitrosodiethanolamine in cosmetics is also available [1]. In this method, sample clean-up is performed using either SPE with a C18 cartridge or LLE using dichloromethane when the samples are not dispersible in water. The extracts are then analyzed by HPLC–MS/MS.

All the methods described above suffer from some disadvantages, such as application of complex and time-cosuming procedures for sample preparations (i.e., solvent extraction, filtration, etc.), hazardous waste production and rather expensive instrumention (e.g., GC–MS/MS or HPLC–MS/MS).

Solid phase microextraction (SPME) developed by Arthur and Pawliszyn in 1989 [27], is a solvent free extraction method which has many advantages compared to conventional preparation methods. It can be easily automated [28] and does not require environmentally hazardous solvents [29]. SPME has found a wide range of applications in environmental science, industrial hygiene, process monitoring, forensic sciences, toxicology, biology, drugs and foods [28–32]. Commercially available SPME fibers have been used for the analysis of various *N*-nitrosamines in wastewater [33], beer [34] and food [35]. Grebel et al. [33] studied the determination of *N*-nitrosamines in wastewater using a commercially available polydimethylsiloxane-divinylbenzene (PDMS-DVB) fiber and three gas chromatography (GC) detection systems [nitrogen chemiluminescence detector (NCD), nitrogen–phosphorus detector and chemical ionization mass spectrometry]. They showed that the application of HS-SPME in conjunction with a GC–NCD instrument is an excellent choice for the analysis of *N*-nitrosamines, reducing the total analysis time to only 1.25 h (versus 3–20 h for other isolation techniques) and providing good selectivity and low detection limits. Andrade et al. [35] compared PDMS-DVB and polyacrylate (PA) SPME fibers for HS-SPME–GC-thermal energy analyzer detection of *N*-nitrosamines. This investigation showed that the PDMS-DVB fiber with intermediate polarity is more sensitive to *N*-nitrosodimethylamine (NDMA) and *N*-nitrosodiethylamine (NDEA). On the other hand, the polar PA-coated fiber, was more efficient for the extraction of the more polar compounds of *N*-nitrosopiperidine (NPIP) and *N*-nitrosopyrrolidine (NPYR).

Commercial SPME fibers are commonly prepared by simple physical deposition of the coatings on the surface of the fused silica fiber [29]. Commercial SPME sorbent coatings have generally good extraction properties; however some aspects of their performance can be improved such as chemical, thermal and mechanical stability. They are also expensive and cover a limited range of the sample polarity. Most commercially available fibers (such as PDMS) are nonpolar and the others (e.g., Carboxen/PDMS), which are relatively polar, are characterized by a reduced thermal stability [36]. To improve the performance of SPME for NDELA, which is a small polar molecule, a new fiber coating has to be developed. In this work, we introduce a new surface modification route for the preparation of a new SPME coating based on the covalent grafting process. This work is also the first report on the application of SPME for the extraction of *N*-nitrosamines from cosmetic products and the application of SPME for the extraction of NDELA from any media. For the preparation of the fiber, a straightforward grafting process was used for the modification of a fused silica surface using aluminum tri-tert-butoxide. A fiber based on aluminum compounds that functions as a Lewis acid [37] as well as an oxophile [38] would be advantageous for the extraction of NDELA. This expectation is in accordance with the results of some previous studies on modified adsorbents for the capturing of *N*-nitrosamines, in which the aluminum incorporation into the framework of MCM-41 and other silica based adsorbents, enhances their adsorptive capacity owing to the generation of acidic sites in the adsorbent [39–41]. The affecting parameters, including salting out effect, stirring rate, sample volume, extraction temperature and extraction time were optimized. The effects of desorption temperature and desorption time on the obtained response from GC–MS analysis were studied and optimized. Finally, the developed method was applied to real sample analysis.

2. Material and methods

2.1. Reagents and materials

The *N*-nitrosodiethanolamine and sodium chloride were acquired from Sigma-Aldrich (Milwaukee, WI, USA). Aluminum tri-tert-butoxide was obtained from Merck (Darmstadt, Germany). All other chemicals including toluene and NaOH were reagent-grade products and purchased from Merck.

2.2. Apparatus

The GC–MS analyses were performed on a Shimadzu Qp-2010 plus (Kyoto, Japan). Helium was used as the carrier gas with a flow rate of 1 mL min^{-1}. The separation of extracted compounds was performed on an RTX-5 MS column (30 m length, 0.025 mm I.D., 0.25 μm df, crossbond, 5% diphenyl-95% dimethyl polysiloxane). The column was obtained from Chromspec company (Brockville, Canada). The initial column temperature was set at 80 °C. Then, the temperature was increased to 100 °C at a rate of 4 °C min^{-1} and maintained for 6 min. Finally, the column temperature was raised up to 250 °C at a rate of 40 °C min^{-1} and held for 2 min. The transfer line temperature was 260 °C. Electron ionization mass spectra were recorded at 70 eV ionization energy. Full scan spectra were recorded and NDELA was quantified using the ion of m/z=87 $(M\text{-}1\text{-}CH_2CH_2OH_2)^+$ as the target ion. The identification was also confirmed by the retention time of the target ion and the qualifier-to-target ion ratio. A mass to charge ratio of 72 was used as the qualifier ion. Thermal gravimetric analysis (TGA) was carried out on a Bahr STA-503 instrument under air atmosphere. The SPME syringe was purchased from Azar Electrode Co. (Uromieh, Iran). A Heidolph heater/stirrer was used for heating and stirring the samples.

2.3. Preparation of SPME fiber

The aluminum hydroxide grafted fused silica fiber was prepared according to a grafting route [42,43]. The grafting process of aluminum hydroxide on fused silica is shown schematically in Fig. 1. The polymeric coating of a damaged fused silica column (O.D.=0.32 mm and length of 7 cm) was removed by burning in a flame. Both ends were then sealed by flame. Then, its surface was cleaned with acetone and water. Afterwards, the fiber surface was activated by NaOH solution (2 M) for 4 h. After washing the fiber with water and drying under vacuum at 70 °C, 1 cm of fused silica was placed in a 0.1 mol L^{-1} aluminum tri-tert-butoxide solution

in toluene, under N_2 atmosphere for 24 h to allow the covalent attachment of aluminum hydroxide to the substrate. Then, the fiber was heated at 200 °C for 20 min. Finally, it was washed by toluene followed by washing with chloroform, drying at room temperature and conditioning at 260 °C in a flow of N_2 gas. As cited in previous works the grafting process can proceed with high efficiency [44].

2.4. The SPME GC–MS analysis

For the headspace solid phase microextraction (HS-SPME) procedure, a 10 mL of water diluted sample (with sample:water ratio of 3 g:5 g) and 1 g of NaCl with a magnetic stirring bar were placed in a 20 mL sample vial. After sealing the vial by polytetrafluoroethylene (PTFE) septum, the vial was placed on a stirrer and was stirred at a rate of 250 rpm for 1 min to homogenize the mixture. The fiber was then placed in the inner needle of a syringe and withdrawn into the outer needle of the syringe. The outer needle of the syringe was passed through the PTFE septum and the fiber was exposed in the headspace above the aqueous phase and the solution was stirred at a rate of 150 rpm, at 70 °C for 15 min. Then the fiber was introduced into the GC injection port at a temperature of 260 °C for 5 min for the desorption of the analyte.

Initially, selected experiments were performed to optimize the main parameters affecting the GC–MS response of the extracted NDELA from water-diluted sample (containing 2000 μg Kg^{-1} NDELA and 1 g of NaCl). These parameters were the percentage of added sodium chloride (%NaCl), stirring rate, sample volume (V_s/V_t), extraction temperature (T_{ext}), extraction time (t_{ext}), desorption temperature (T_{des}) and desorption time (t_{des}). The parameters were optimized by varying one of them at a time, keeping the other parameters constant. The extractions were repeated three times for each condition. A fiber blank was run between each sample to avoid carry over effects.

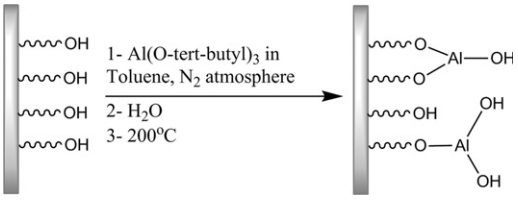

Fig. 1. Proposed scheme of possible covalent attachment of aluminum to the substrate.

2.5. Method validation

The analytical performance of the proposed method was validated through the determination of linearity range, correlation coefficient, limit of detection (LOD), limit of quantification (LOQ), accuracy and precision under the optimized SPME conditions. The linear range was obtained by standard addition method with seven concentration levels. The linearity of the calibration curve was verified by Mandel fitting test at the confidence level of 95%. A diluted mixture (with water:mixture ratio of 3 g:5 g) of a homemade shampoo containing the major components of shampoo, except coconut diethanol amide which is the main source of NDELA was used to evaluate LOD and LOQ. Standard solutions with concentrations near LOD and LOQ values were prepared by using this diluted mixture. Two standard curves were prepared in the concentration ranges of the LOD (1–5 μg Kg^{-1}) and LOQ (4–12 μg Kg^{-1}). Then, the following equations were used to calculate the LOD and LOQ, respectively [45]:

$$\mathrm{LOD} = 3\ s/m_1$$
$$\mathrm{LOQ} = 10\ s/m_2$$

where s is the standard deviation of the response sample blank (estimated from the 10 independent sample blanks measured once each), m_1 is the slope of the standard curve in the concentration range of LOD and m_2 is the slope of the standard curve in the concentration range of LOQ.

The accuracy and precision of the method were determined by performing five consecutive analysis of water-diluted samples spiked with NDELA at LOQ concentration level (3.4 μg Kg^{-1}) and three concentrations representing the low, medium and high

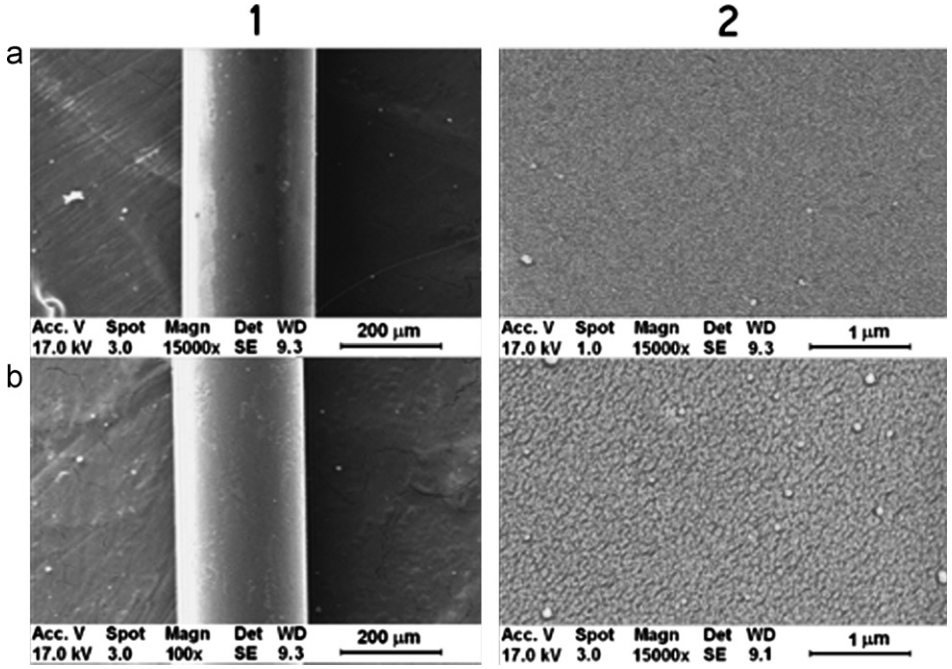

Fig. 2. Scanning electron micrograph of fused silica fiber (a) before starting the grafting process (b) after modification of surface via the grafting process. (1) magnification of 100 × and (2) magnification of 15,000 × .

portions of the standard curves (8, 1000 and 8000 μg Kg^{-1}). Intra-day accuracy and precision were calculated on a single day using five replicates at each concentration level. Inter-day accuracy and precision were calculated using five replicates at each concentration level over five consecutive days. The fiber to fiber repeatability was estimated using three fibers, which were constructed under the same conditions. Three replicates were carried out on each fiber and the extractions were accomplished from a 200 μg Kg^{-1} standard solution.

2.6. Real Samples

The proposed method was applied for the determination of NDELA in different cosmetic samples. Commercial cosmetic products from various manufactures were purchased from local stores in Tehran (Iran) from 2008 to 2010 and kept at 4 °C until analysis. The real samples were analyzed according to the procedure described in Section 2.4 under optimum conditions. Standard addition method was used for the quantification of NDELA in cosmetics.

3. Result and discussion

3.1. Aluminum hydroxide fused silica fiber properties

The proposed fiber is simply composed of a layer of grafted aluminum hydroxide on a fused silica substrate and has low porosity and thickness. Fig. 2 shows the SEM images from the surface of the fused silica fiber before and after surface modification. Although some changes occur in the morphology of the fused silica surface, it is obvious from these figures that no appreciable changes in the thickness of the fiber occurs during the modification of the surface.

In order to show that the presence of aluminum hydroxide on the surface of the fiber is important for the extraction of NDELA, an aluminum hydroxide grafted fused silica fiber was compared to an activated-surface fused silica fiber which was prepared by using NaOH solution. While the aluminum hydroxide grafted fused silica fiber extracted NDELA, no significant extraction was obtained with the activated-surface fused silica.

As expected, thermal gravimetric analysis (TGA) of the fiber shows no mass loss, even up to 500 °C. The fiber can be conditioned at 300 °C for an hour without any significant loss in the extraction efficiency. This temperature is higher than the recommended conditioning temperature for commercial fibers (200–280 °C), e.g. Carboxen/divinylbenzene fiber. The thermal stability of this fiber is better than that of commercial fibers, because its surface is simply covered by the grafted aluminuim which is covalently attached to the substrate. The fiber proved to be stable and reusable for more than 85 extractions and desorptions at 260 °C.

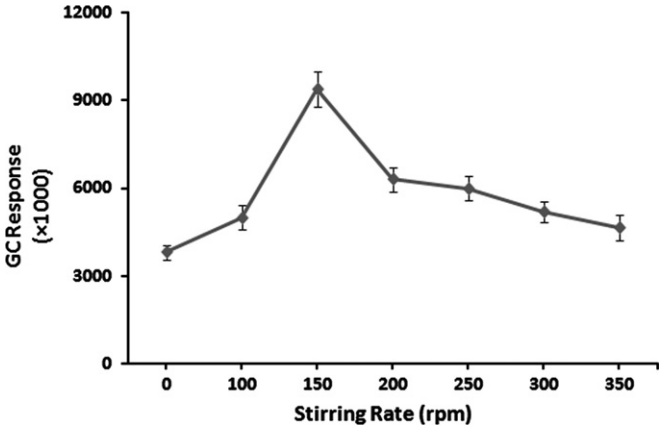

Fig. 3. Effect of stirring rate on the extraction of NDELA using aluminum hydroxide grafted fused silica SPME fiber. Extraction conditions: extraction temperature (T_{ext}) of 60 °C, extraction time (t_{ext}) of 30 min, desorption temperature (T_{des}) of 260 °C, desorption time (t_{des}) of 5 min and 12.5% salt addition. All results are presented as a mean of triplicate experiment with one standard deviation.

3.2. Optimization of extraction conditions

To obtain a reproducible and sensitive method based on headspace SPME, the influence of several parameters including salt concentration, stirring rate, sample volume, extraction temperature, extraction time, desorption temperature and desorption time were considered. HS-SPME is favorable for the extraction of NDELA since it is known to extend the fiber lifetime.

3.2.1. Salting out effect

To study the effect of ionic strength in the extraction process, different amounts of NaCl were added into the samples. When the amount of salt increased up to 12.5%, the GC response for the analyte increased. However, further addition of salt to the solution decreased the GC response. An initial increase and then a decrease in GC response with increase in the concentration of

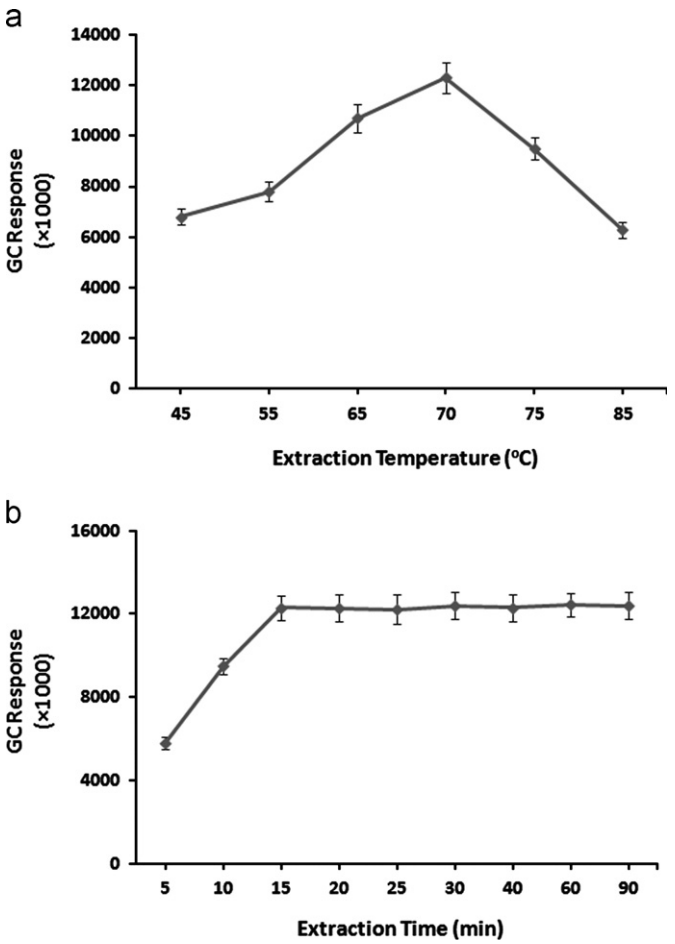

Fig. 4. Effects of (a) extraction temperature; and (b) extraction time; on the extraction of NDELA using aluminum hydroxide grafted fused silica SPME fiber. Extraction conditions: stirring rate at 150 rpm, desorption temperature (T_{des}) of 260 °C, desorption time (t_{des}) of 5 min, 12.5% salt, sample volume of 0.5 and extraction time (t_{ext}) of 30 min for (a) and extraction temperature (T_{ext}) of 70 °C for (b). All results are presented as a mean of triplicate experiment with one standard deviation.

sodium chloride can be explained by two simultaneously occurring processes. Initially, up to 12.5% (w/w) of NaCl concentration, the GC response was increased due to the salting out effect (i.e., decreasing analyte solubility in aqueous phase) which enhances the partitioning of analyte into the headspace [46,47]; but as the salt concentration increases, an electrostatic interaction of analytes with salt ions in the solution dominates, affecting the amount of analyte driven to the headspase. Thus, 12.5% (w/w) NaCl was chosen as the optimum value for subsequent experiments.

3.2.2. Stirring rate

The effect of stirring rate for aluminum hydroxide grafted fused silica SPME fiber is shown in Fig. 3. The stirring rate ranged between 140 rpm and 350 rpm. Higher stirring rates could not be studied due to the excessive formation of foam. In the stirring rates above 150 rpm, the GC response decreased significantly. This decrease might be attributed to the some foam formation at stirring rates above 150 rpm. Thus, 150 rpm was selected as the optimum stirring rate.

3.2.3. Sample volume

Since the sensitivity of the SPME procedures is proportional to the amount of analyte in the sample, it is expected that increasing the sample volume will augment the GC response. However, from the SPME theory, if the sample volume becomes significantly larger than the fiber and headspace capacities, no enhancement of the response can be achieved by increasing the volume of sample. In order to evaluate the sample volume effect on the HS-SPME efficiency, a set of experiments were carried out. The range of sample volume tested was from 4 to 16 mL. Results show that when sample volume was fixed at 10 mL (sample volume/total volume = 0.5) a maximum response could be identified.

3.2.4. Extraction temperature

In this study, extraction temperatures were studied in a range from 45 to 85 °C at 30 min extraction time. Fig. 4a shows the effect of extraction temperature on the extraction efficiency. At the temperatures lower than 45 °C, the NDELA extraction was low but when the temperature increased up to 70 °C, the amount of extracted analyte increased. However, for temperatures higher than 70 °C, the amount of extracted analyte started to decrease. Indeed, temperature can influence the extraction efficiency due to several different effects. From one side, headspace/sample partition coefficient of the analyte increases with enhanced

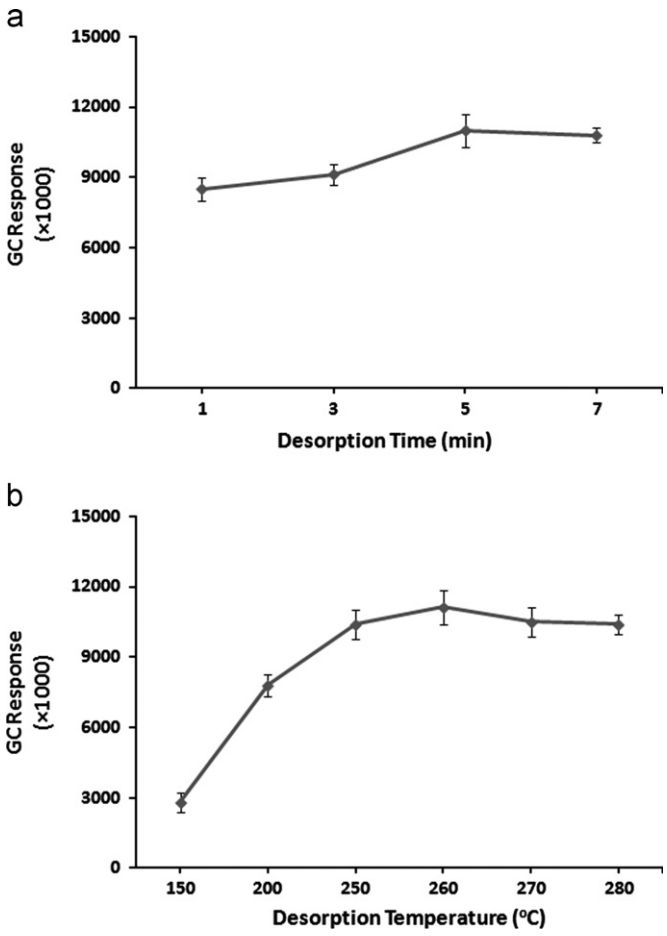

Fig. 5. Effect of (a) desorption temperature; and (b) desorption time; on the extraction of NDELA using aluminum hydroxide grafted fused silica SPME fiber. Extraction conditions: extraction temperature (T_{ext}) of 70 °C, extraction time (t_{ext}) of 15 min, stirring rate at 150 rpm, 12.5% salt addition and desorption time (t_{des}) of 5 min for (a) and desorption temperature (t_{des}) 260 °C for (b). All results are presented as a mean of triplicate experiment with one standard deviation.

Table 1
Intra- and inter-day accuracy and precision for the determination of NDELA.

Concentration (μg Kg^{-1})	Precision		Accuracy
	Mean ± SD (μg Kg^{-1})	CV (%)	Bias (%)
Intra-day (n=5)			
3.40	3.50 ± 0.24	6.9	2.9
8.00	8.21 ± 0.49	6.0	2.6
1000	962 ± 50	5.3	−3.8
8000	8270 ± 256	3.1	3.4
Inter-day (n=5)			
3.40	3.61 ± 0.25	6.9	6.2
8.00	8.30 ± 0.60	7.2	3.7
1000	953 ± 62	6.5	−4.7
8000	8321 ± 286	3.4	4.0

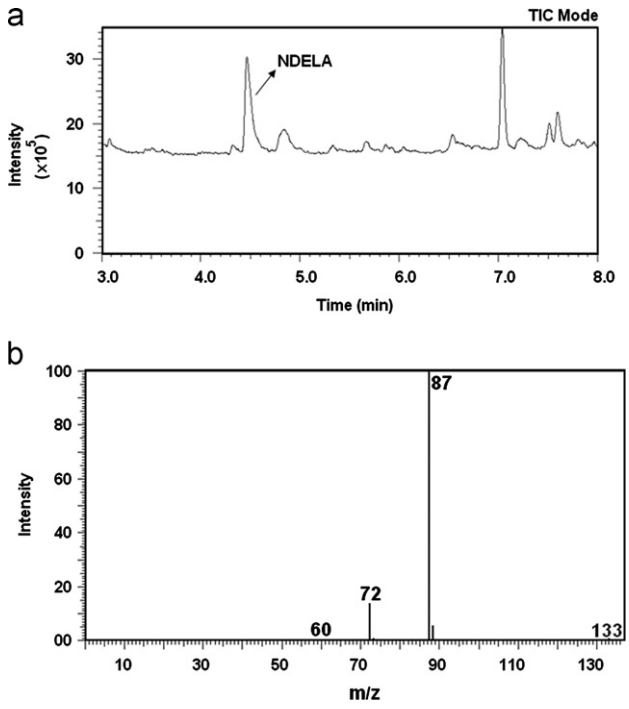

Fig. 6. (a) Typical GC–MS chromatogram of extracted NDELA from hair shampoo (160 μg Kg^{-1}) with the aluminum hydroxide-fused silica SPME fiber under optimum conditions and (b) mass spectrum of NDELA obtained under experimental conditions.

temperature which leads to a higher concentration of the analyte in the headspace and results in a higher amount of extracted analyte at equilibrium conditions. However, higher temperatures may also have the negative effect of a less favorable coating/headspace partition coefficient because the fiber equilibrium process is an exothermic process and any increase in sampling temperature will decrease recovery [48]. In this study the optimum extraction temperature was taken as 70 °C.

3.2.5. Extraction time

In the HS-SPME technique, the equilibrium of the analyte between the vapor phase and the fiber coating is crucial. Thus, the extraction time was optimized to determine the optimum time to reach the equilibrium. Fig. 4b shows the effect of the extraction time on the GC response of NDELA. The highest GC response was obtained with a time of 15 min for NDELA and at longer extraction times, no significant changes in GC response were observed. The extraction time of 15 min is shorter than all other extraction times that have been reported in other works on the extraction of NDELA [1,22].

3.2.6. Desorption temperature and desorption time

It is important to study the desorption temperature and desorption time to ensure that there is no carryover effects, The fiber coating stays intact and no substantial changes occur in the properties of the coating at the applied temperature. Various desorption temperatures from 150 to 280 °C and various desorption times from 1 to 7 min were investigated. The optimum desorption temperature and the optimum desorption time were found to be 260 °C (Fig. 5a) and 5 min (Fig. 5b), respectively. Since there was no significant change in GC response in temperatures 260–280 °C, the lowest temperature in this range was chosen as the optimum temperature for the desorption of NDELA.

3.3. Method validation

The calibration curve was prepared over a linear range from 6 to 10000 μg Kg^{-1} with correlation coefficient (R) of greater than 0.9897. In order to verify if the fitted linear model effectively provided the best fit, Mandel fitting test was used. The F value found at the 95% confidence level was lower than that reported in the *F*-table ($p > 0.05$), showing that a quadratic model is not significantly better than a linear model for fitting the experimental data. The estimated LOD and LOQ were 1 and 3.3 μg Kg^{-1}, respectively. The values of intra-day precision and accuracy and inter-day precision and accuracy are provided in Table 1. The accuracy and precision should not exceed 15%, except for LOQ

Table 2
Determination of NDELA in real samples.

Samples	NDELA content ± SD[a] (μg Kg^{-1})	Recovery ± SD[b] (%)
Shampoo 1	83 ± 5	96 ± 0.5
Shampoo 2	160 ± 10	97 ± 5
Body shampoo	50 ± 3	99 ± 2
Dishwashing liquid	4800 ± 100	95 ± 4
Hand washing liquid	6800 ± 110	98 ± 2

[a] $n=5$.
[b] $n=5$.

Table 3
A comparison between the proposed method with some other published works for *N*-nitrosamine analysis.

Sample matrix	Analytes	Sample preparation method	Detection method	Linear range	Limit of detection	Recovery%	RSD%	Ref.
Cosmetics	NDELA	HS-SPME	GC–MS	6–10000 (μg Kg^{-1})	2 (μg Kg^{-1})	95–99%	< 6.1	This work
Cosmetics	NDELA	SPE/LLE	Ion-pair HPLC–UV	30–10000 (μg L^{-1})	10 (μg L^{-1})	86.9/51.8	0.9/5.6	[22]
Cosmetics	NDELA	SPE/LLE	LC–MS/MS	0–1600 (μg Kg^{-1})	22.8 (μg g^{-1})	48.3–112.7/ 41.3–60.3	No data	[1]
Cosmetics	NDMA[a], NDEA[b], NDPA[c], NMOR[d], NDBA[e], NDBzA[f], NPYR[g], NPIP[h], NDPheA[i], NDCHA[j]	SPE	GC–MS/MS	50–10000 (μg L^{-1})	2.5–10 (mg Kg^{-1})	85.2–102.3	3.05–9.24	[50]
Wastewater	NDMA[a], NDEA[b], NDPA[c], NMOR[d], NPYR[g], NPIP[h], NDBA[e]	HS-SPME[l]	GC–NCD[o]	No data	15–110 (ng L^{-1})	94–115	9–30.7	[33]
Food	NDMA[a], NDEA[b], NPYR[g], NPIP[h]	HS-SPME[m]	GC–TEA	60–720 ng (for 2.5 g of sample)	3 (μg Kg^{-1})	105–110	5–12	[35]
Beer	NDMA[a]	HS-SPME[l]	GC–MS	8000–32000(μg L^{-1})	0.8830 (μg L^{-1})	—	4.6	[34]
Drinking water	NDMA[a], NMEA[k], NDEA[b], NDPA[c], NDBA[e], NPYR[g], NPIP[h]	SPE	GC–MS/MS	0.5–50 (ng L^{-1})	0.26–0.66 (ng L^{-1})	87.1–104	4–11	[26]
Water samples	NDMA[a], NMOR[d], NMEA[k], NPYR[g]	Not required	HPLC–CL	5–1000 (ng L^{-1})	1.5 (ng L^{-1})	90.4–111.4	0.7–4.5	[51]
Meat products	NDMA[a], NDEA[b], NDPA[c], NPYR[g], NPIP[h], NDBA[e]	SPE	GC × GC–NCD[o]	1–400 (μg L^{-1})	1.61–3.86 (μg L^{-1})	76–85	No data	[52]
Meat products	NDMA[a], NMEA[k], NDEA[b], NPYR[g], NMOR[d], NDPA[c], NPIP[h], NDBA[e], NDPheA[i]	DLLME[n]	GC–MS	0.05–200 (μg L^{-1})	0.12–0.46 (μg Kg^{-1})	94.5	5.9–10	[53]

[a] *N*-nitrosodimethylamine.
[b] *N*-nitrosodiethylamine.
[c] *N*-nitrosodi-n-propylamine.
[d] *N*-nitrosomorpholine.
[e] *N*-nitrosodi-n-butylamine.
[f] *N*-nitrosodibenzylamine.
[g] *N*-nitrosopyrrolidine.
[h] *N*-nitrosopiperidine.
[i] *N*-nitrosodiphenylamine.
[j] *N*-nitrosodicyclohexylamine.
[k] *N*-nitrosomethylethylamine.
[l] With polydimethylsiloxane/divinylbenzene fiber.
[m] With polydimethylsiloxane/divinylbenzene and polyacrylate fibers.
[n] Dispersive liquid–liquid microextraction.
[o] Nitrogen chemiluminesence detector.

concentration level in which accuracy and precision should not exceed 20% [49]. All obtained values for accuracy and precision were lower than 15%. Hence, the developed method is found to be accurate over the studied concentration ranges. The estimated fiber to fiber repeatability was 8.7%.

3.4. Real samples analysis

After setting the optimized conditions, the determination of NDELA in the real samples was carried out in five replicates by the standard addition method. Fig. 6 shows a typical chromatogram of the extraction of NDELA from hair shampoo and the mass spectrum of NDELA obtained in this experiments. Samples of cosmetics were examined for NDELA as shown in Table 2. Every real sample was analyzed five times and the average concentration values and corresponding standard deviations are reported. The high level of NDELA in some real samples is probabely due to problems in raw materials and/or the production process and it is obvious that these products should be notified as posing serious risks [8]. To obtain recoveries, NDELA was spiked at a concentration level of 20 $\mu g\,Kg^{-1}$ and the analyses were carried out five times for each real sample. Good relative recoveries were achieved for NDELA from 95 to 99%.

Table 3 provides a comparison of linear range, limit of detection, recovery% and RSD% between the present work and previous methods for the analysis of *N*-nitrosamines (including NDELA). It is obvious that the present work provides better linear range and recovery than other methods. It also provides a good detection limit, considering the usage of GC–MS as the detection method instead of GC–MS/MS and LC–MS/MS.

4. Conclusions

A new aluminum hydroxide grafted fused silica SPME fiber was successfully prepared by means of a grafting process for the first time. This new fiber showed superior extraction efficiency for NDELA in cosmetics compared to other proposed methods (Table 3). The synthesized fiber had good thermal stability up to 500 °C. It could also be used at high temperatures up to 300 °C without any significant changes in its properties. The effect of various parameters on the HS-SPME–GC–MS analysis of NDELA were studied by using this fiber and the optimized conditions were applied to the analysis of real samples. Good recoveries for NDELA determination in real samples were obtained with good precision. Being rapid, inexpensive and solvent free, this method is suitable for routine analysis of NDELA in cosmetic products.

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