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MICROEXTRACTION AND GAS CHROMATOGRAPHIC DETERMINATION OF PARABENS

Summary of doctoral dissertation
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VILNIAUS UNIVERSITETAS
FTMC CHEMIJOS INSTITUTAS

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PARABENŲ MIKROEKSTRAKCIJA IR DUJŲ CHROMATOGRAFINIS NUSTATYMAS

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1. INTRODUCTION

Parabens are *p*-hydroxybenzoic acid esters. Since parabens have no perceptible odour, taste, have neutral pH and due to their bactericidal and fungicidal properties they are used extensively as preservatives in cosmetics, personal care products, pharmaceutical products and even in foods and beverages.

For many years parabens were considered to have low toxicity, primarily causing allergic reactions. However, some years ago it was demonstrated that parabens are readily absorbed through the skin from body care products and their hydrolysis by skin esterases is incomplete. Parabens are oestrogenic, affect the human endocrine system and probably cause breast cancer and male reproductive disorders. A higher rate of melanoma in younger people correlates with greater use of paraben-containing skincare/sun protection products, and high concentrations of propylparaben and butylparaben show genotoxicity. Moreover, parabens may undergo different transformation reactions rendering even more toxic pollutants. For example, tap water and swimming pool water is amended with free chlorine to ensure its bacteriological quality. In the presence of chlorine, parabens can be converted into more toxic and persistent chlorinated by-products. The presence of parabens was determined in wastewater, swimming pool water, river water and even in tap water. Because of the presence of parabens in the environment and their negative effects on human health, there is an increasing interest in their trace analysis.

Gas chromatography is one of the most common methods for parabens analysis. Due to their polar nature, prior to GC analysis parabens are often derivatized to reduce their adsorption in the chromatographic system, to improve sensitivity, peak separation and peak symmetry. Since the concentration of parabens in the environment are rather low and cosmetics present rather complex matrices for the analysis, it is necessary to apply a preconcentration or isolation step prior to the chromatographic analysis.

In recent years, microextraction techniques are gaining a growing interest. Different liquid-phase microextraction (LPME) techniques such as single drop microextraction (SDME), hollow fibre liquid phase microextraction (HFLPME), dispersive liquid-liquid microextraction (DLLME) have been suggested.

The aim of this work was to develop liquid-phase microextraction methods – single drop microextraction, hollow fibre liquid phase microextraction and dispersive liquid-liquid microextraction – for parabens extraction and to apply the methods for determination of parabens in water samples and cosmetic products.

The main tasks set to achieve the aim were as follows:

1. To develop single drop microextraction methods for underivatized and derivatized parabens.
2. To develop hollow fibre liquid phase microextraction methods for underivatized and derivatized parabens.
3. To develop dispersive liquid-liquid microextraction methods for underivatized and derivatized parabens.
4. To compare prepared microextraction methods and evaluate the influence of derivatization on the paraben extraction efficiency.
5. To apply prepared microextraction methods for the determination of parabens in real samples.

Statements for defence:

1. Proposed microextraction methods of parabens are efficient, simple, rapid and cheap.
2. Derivatization of parabens prior to microextraction procedure improves sensitivity of determination of parabens.
3. Proposed microextraction methods of parabens are suitable for real samples analysis.
4. The choice of the proper microextraction method depends on the sample matrix.

2. EXPERIMENTAL

Gas chromatography was carried out on a Varian 3400 (Palo Alto, CA, USA) gas chromatograph equipped with a flame ionisation detector coupled with integrator SP4290 (Spectra-Physics San Jose, CA, USA) and a Equity^{TM}-5 fused silica capillary column (30 m × 0.53 mm, 1.5 μm film thickness) supplied by Supelco (Bellefonte, PA, USA). The splittless injection mode was used. The following gas flow rates were used: carrier (nitrogen) 10, make-up gas (nitrogen) 20, hydrogen 30 and air 300 mL/min. For sample injection 10 μL microsyringe by Hamilton (Reno, NV, JAV) was used.

Single drop microextraction procedure

Single-drop microextraction was performed in a 12 mL volume vial closed with a PTFE coated septum placed in the cap. The vial was placed on a magnetic stirrer (MLW RH3, Germany). For the extraction, 10 mL of aqueous solution was used. Single-drop microextraction was performed with a commercially available 10 μL microsyringe (Hamilton, Reno, NV, USA). During the extraction, the syringe was fixed above the extraction vial so that the needle could pass the septum and the needle tip appeared about about 1 cm under the surface of the solution for direct SDME or about 0.5 cm above the surface of the solution for the headspace SDME. Then a drop of the extracting solvent was suspended from the needle tip. After the extraction, the drop was retracted back into the needle and injected directly into the gas chromatograph.

Hollow-fibre liquid phase microextraction procedure

HFLPME was carried out using an Accurel Q 3/2 polypropylene hollow fibre membrane (Membrana, Wuppertal, Germany) with a 200 μm wall thickness, 0.2 μm pore size and 600 μm internal diameter. The hollow fibre was cut into 1.8 cm length pieces. One end of each piece was heat-sealed using soldering iron. The effective internal volume of a piece of the hollow fibre was approximately 5 μL. Before use, the hollow fibres were sonicated in acetone for 10 min, then removed and allowed to dry at room temperature. Each piece was used only once. The unsealed end of the fibre was connected to a 0.7 cm diameter syringe needle inserted through the silicone rubber septum in an extraction vial cap. For several minutes the hollow fibre was immersed into the receiving phase. The receiving phase impregnated its walls and penetrated inside the hollow fibre, filling it completely. Then the fibre was withdrawn from the receiving

phase, washed with distilled water in order to eliminate the excess of the receiving phase, and immersed into into the sample solution. The sample vial was placed on a magnetic stirrer. After the extraction, the vial cap together with the needle and hollow fibre was removed from the vial and 1 μL of the extract was withdrawn with a 10 μL microsyringe and injected into the gas chromatograph.

Dispersive liquid-liquid microextraction procedure

DLLME method is based on ternary component solvent system. Eight mL of aqueous solution of methylparaben, ethylparaben, propylparaben and butylparaben were placed in a 12 mL centrifuge tube with a conic bottom. To the aqueous solution the mixture of the solution containing a water-miscible disperser solvent and a water-immiscible extraction solvent containing an internal standard was rapidly injected using a 1 mL syringe. The cloudy solution formed was centrifuged for 2 min at 5000 rpm. Organic phase with the analytes was sedimented on the bottom of the tube. One μL of the sedimented phase was taken using a 10 μL microsyringe (Hamilton, Reno, NV, USA) and injected into the gas chromatograph.

Derivatization before microextraction procedure

For paraben derivatization, to 10 mL (SDME, HFLPME) or 8 mL (DLLME) of paraben solution 0.02 g/mL $K_2HPO_4 \times 3H_2O$ and 10 mL (SDME, HFLPME) or 8 mL (DLLME) of acetic anhydride were added.

3. RESULTS AND DISCUSSION

3.1. Single drop microextraction of parabens

The SDME method is very uncostly and simple, carry-over free, uses especially small quantities of organic solvents (up to few μL), the choice of organic solvents is broad and it gives many possibilities to optimize the extraction conditions. We applied the method for the extraction of underivatized and derivatized parabens.

3.1.1. Single drop microextraction of underivatized parabens

The volatility of underivatized parabens is too low for headspace SDME, and for this reason, parabens were extracted using direct SDME. In the direct SDME method, a drop is suspended directly from a tip of a microsyringe needle immersed into the aqueous phase.

Method optimization

Selection of a proper extraction reagent is one of the main conditions that ensure a high extraction efficiency. Five different solvents, carbon tetrachloride, amyl acetate, octanol-1, *n*-octane, toluene, were tested for the extraction of parabens.

Octanol-1 and *n*-octane were impracticable for the extraction, because they fall down from the microsyringe needle tip. Amyl acetate showed the best extracting efficiency and was chosen as an extracting solvent for the further work.

1–5 μL amyl acetate drop volumes were examined. 2–5 μL drops were difficult to handle, they tended to fall down from the microsyringe needle tip. In order to obtain a good extraction efficiency and repeatability, 1 μL of amyl acetate was selected for our work.

The total amount of the analytes transferred in the drop reaches its maximum when the equilibrium between the two immiscible phases is established. Extraction time between 5 and 30 min was evaluated.

Despite ethylparaben and propylparaben did not reach the equilibrium after 20 min, in order to have an acceptable analysis time, for the further work we chose non-equilibrium conditions and established a 20 min extraction time.

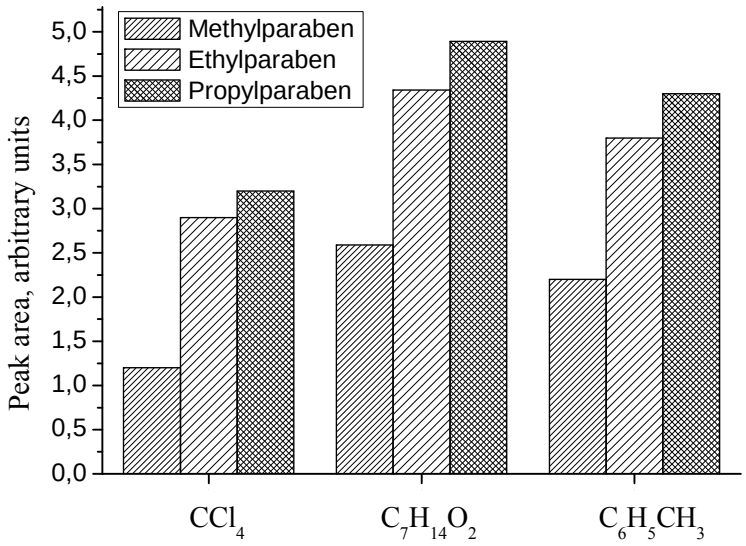

Fig. 1. Effect of extraction solvent on extraction efficiency. Direct SDME conditions: sample volume 10 mL, concentration of parabens 10 μg/mL, extracting solvent volume 1 μL, extraction time 10 min, solution stirring rate 200 rpm.

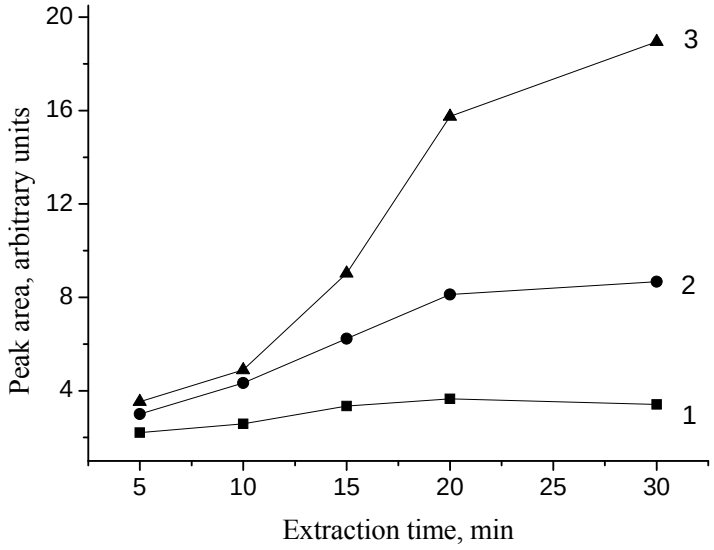

Fig. 2. Effect of extraction time on extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben. Direct SDME conditions: sample volume 10 mL, concentration of parabens 10 μg/mL, extracting solvent (amyl acetate) volume 1 μL, solution stirring rate 200 rpm.

To investigate the effect of salt on direct SDME of parabens, extraction was performed in the presence of different concentrations of NaCl (0.1–0.4 g/mL).

The results are presented in Fig. 3. demonstrate that the addition of NaCl (up to 0.2 g/mL) increases the extraction efficiency. However, with the further increase of NaCl concentration the decrease of extraction efficiency was observed. In further experiments, 0.2 g/mL of NaCl was added to the samples.

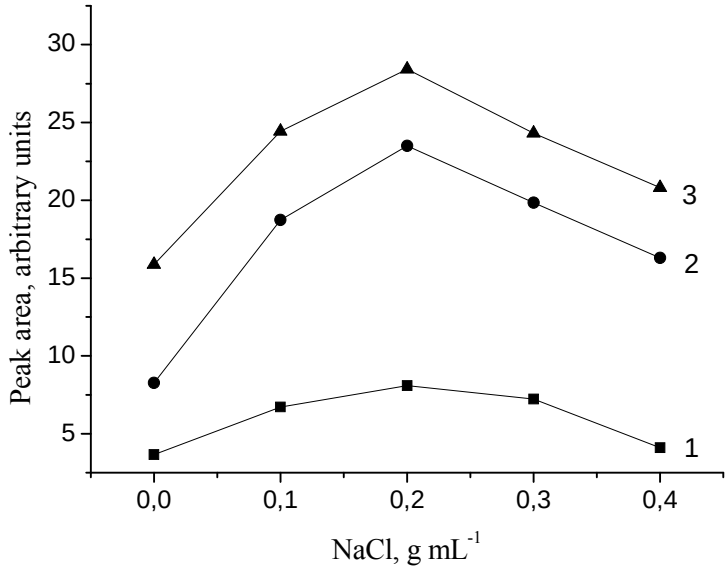

Fig. 3. Effect of NaCl content on the extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben. Direct SDME conditions: sample volume 10 mL, concentration of parabens 10 μg/mL, extracting solvent (amyl acetate) volume 1 μL, extraction time 20 min, solution stirring rate 200 rpm.

Analytical perfomance of the method

The quality parameters of the suggested method, such as linearity, detection limits and repeatability, were calculated under the optimized extraction conditions. In order to alleviate injected extract volume error and to improve repeatability, *n*-nonadecane (5 μg/mL) was added to the extraction solvent as an internal standard.

The calibration curves were drawn with three replicate injections of the extracts obtained after applying direct SDME procedure with 10 calibration points. The linear ranges for all the analytes were up to 10 μg/mL. The correlation coefficients were 0.995–0.997. To calculate the detection limits, three replicate extractions were performed. The detection limits, defined as a triple base-line noise, are presented in Table 1.

The repeatabilities was determined by five repetition analysis for two concentrations of parabens. Relative standard deviations (RSDs) were calculated and summarized (Table 1).

Table 1. Detection limits and repeatabilities

Analyte	Detection limits, µg/L	RSD, % (n = 5)	
		c = 1 µg/mL	c = 10 µg/mL
Methylparaben	102	12.4	11.9
Ethylparaben	80	11.8	11.2
Propylparaben	60	12.6	12.1

3.1.2. Single drop microextraction of derivatized parabens

3.1.2.1. Optimization of derivatization conditions

The purpose of the derivatization prior to GC analysis is to convert the native form to less polar and more volatile species. In addition, in-sample derivatization accomplished before the extraction step can increase the extractability of the analytes. According to the literature *in-situ* acetylation with acetic anhydride is especially simple and fast, it was chosen in this work as a paraben derivatization procedure.

The influence of derivatization on the paraben peaks shape has been examined. For this purpose, chromatograms of underivatizes and derivatized parabens were obtained under the same chromatographic conditions. For parabens derivatization, to 10 mL of 10 mg/mL paraben solution 0.5 g of $K_2HPO_4 \times 3H_2O$ and 100 µL of acetic anhydride were added. A chromatographic benefit of derivatization can be evidently seen in Fig. 4. Underivatized parbens produced asymmetric, broad peaks with significant tailing due to the interaction of hydroxyl groups with the chromatographic system. Derivatized paraben peaks improved in the shapes, were higher and narrower than underivatized paraben peaks.

Acetylation with acetic anhydride is normally performed in the presence of hydrogencarbonate or pyridine, however, according to the literature the use of hydrogenphosphate leads to higher extraction efficiencies than the hydrogencarbonate. Thus, in our work, di-potassium hydrogenphosphate was used as a basic catalyser.

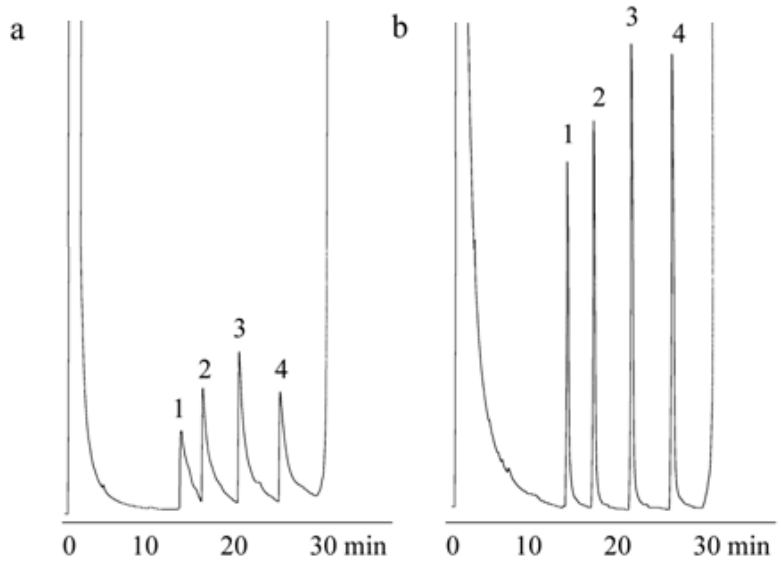

Fig. 4. Chromatograms of underivatized (a) and derivatized (b) paraben solution: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben.

The influence of pH on derivatization efficiency was examined, and it was determined that the increase in the paraben peak area took place at pH up to 7.5–8.0. At pH < 7.5, peaks of derivatized and underivatized parabens were observed in the chromatogram. At pH values higher than 8, derivatization efficiency did not change anymore, and only derivatized paraben peaks were present. Thus, for the further work, pH of the sample solution was adjusted to 9 by the addition of 0.02 g/mL $K_2HPO_4 \times 3H_2O$.

3.1.2.2 Direct single drop microextraction of derivatized parabens

Method optimization

In order to select a proper extraction solvent, carbon tetrachloride, amyl acetate, octanol-1, *n*-octane, toluene and *o*-xylene were tested for the extraction of derivatized parabens.

Octanol-1 was impracticable for the extraction, because it falls down from the microsyringe needle tip. Amyl acetate showed the best extracting efficiency and was chosen as an extracting solvent for the further work.

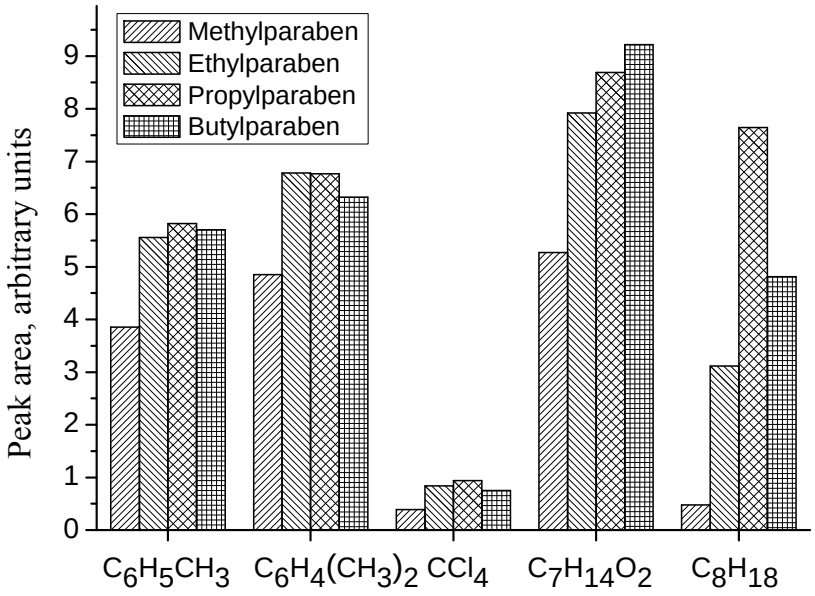

Fig. 5. Effect of extraction solvent on extraction efficiency. Direct SDME conditions: sample volume 10 mL, concentration of parabens 10 μg/mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 10 μL, extracting solvent volume 1 μL, extraction time 20 min, solution stirring rate 200 rpm.

In order to obtain a good extraction efficiency and repeatability, a 1 μL of amyl acetate drop volume was selected for our work.

Extraction times between 5 and 30 min were evaluated. As it is seen in Fig. 6, the peak areas of extracted parabens increases up to 20 min. However, with the further increase of extraction time the decrease of extraction efficiency is presented. Probably because of a long extraction time, organic drop volume was decreasing and amount of extracted analytes was also decreasing. For the further work, an extraction time of 20 min was chosen.

To investigate the effect of salt on the direct SDME of derivatized parabens NaCl (0.1–0.3 g/mL) was added. As it is seen in Fig. 7., with the increase of NaCl concentration the extraction efficiency is decreasing. In order to avoid this, in further experiments NaCl was not added into the samples.

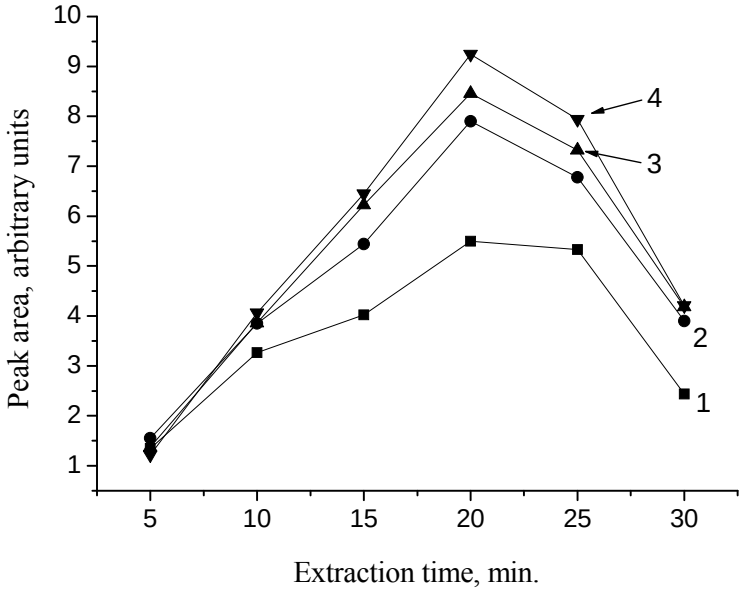

Fig. 6. Effect of extraction time on extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben. Direct SDME conditions: sample volume 10 mL, concentration of parabens 10 μg/mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 10 μL, extracting solvent (amyl acetate) volume 1 μL, solution stirring rate 200 rpm.

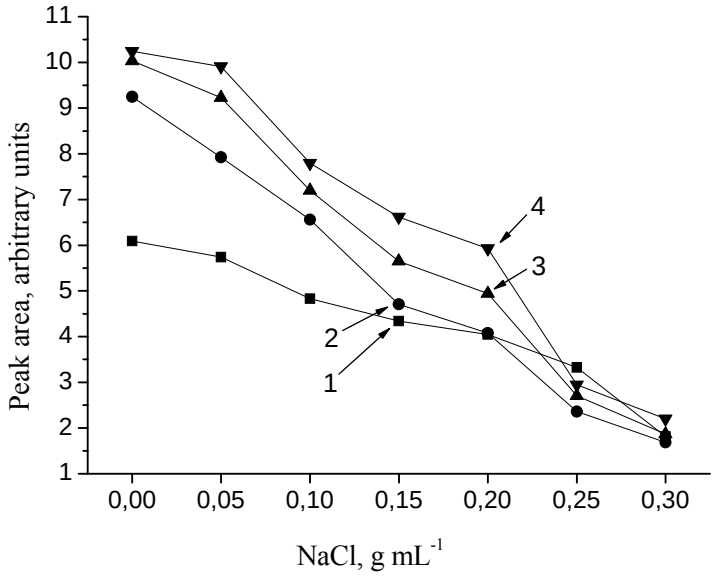

Fig. 7. Effect of NaCl content on the extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben. Direct SDME conditions: sample volume 10 mL, concentration of parabens 10 μg/mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 10 μL, extracting solvent (amyl acetate) volume 1 μL, extraction time 20 min, solution stirring rate 200 rpm.

Analytical perfomance of the method

The quality parameters of the suggested method, such as linearity, detection limits and repeatability, were calculated under the optimized extraction conditions. *n*-Hexadecane (0.5 μg/mL) was added to the extraction solvent as an internal standard.

The calibration curves were drawn with three replicate injections of the extracts obtained after applying direct SDME procedure with 7 calibration points. The linear ranges for all the analytes were up to 10 μg/mL. The correlation coefficients were 0.997–0.998. The detection limits relative standard deviations are presented in Table 2.

Table 2. Detection limits and repeatabilities

Analyte	Detection limits, μg/L	RSD, % (n = 5)	
		c = 1 μg/mL	c = 10 μg/mL
Methylparaben	30	10.0	6.9
Ethylparaben	14	8.8	5.2
Propylparaben	18	8.3	5.6
Butylparaben	27	10.7	5.1

3.1.2.3. Headspace single drop microextraction of derivatized parabens

Derivatized parabens are volatile and can be analyzed using headspace SDME. Analytes readily pass from the aqueous phase into the headspace, meanwhile less volatile compounds remain in the water and do not interfere with the analysis.

Method optimization

First of all, for headspace SDME the same solvents as for direct SDME were tested. When the extraction was carried out at a room temperature, no paraben peaks were observed in the chromatogram. Probably at a room temperature parabens volatility is too low. Further, in order to increase analytes volatility, headspace SDME was carried out at 50 °C temperature. Unfortunately, after 7–10 min organic drops evaporated. Thus we tested extracting solvents with a higher boiling point (dibutyl phthalate (boiling point 340 °C) and dioctyl phthalate (boiling point 384 °C)). As dioctyl phthalate showed higher extraction efficiency, it was chosen as the parabens extractant.

In order to select a proper extraction temperature, teperatures between 20 and 90 °C were investigated. As it can be seen in Fig. 8, 70 °C temperature is the optimum.

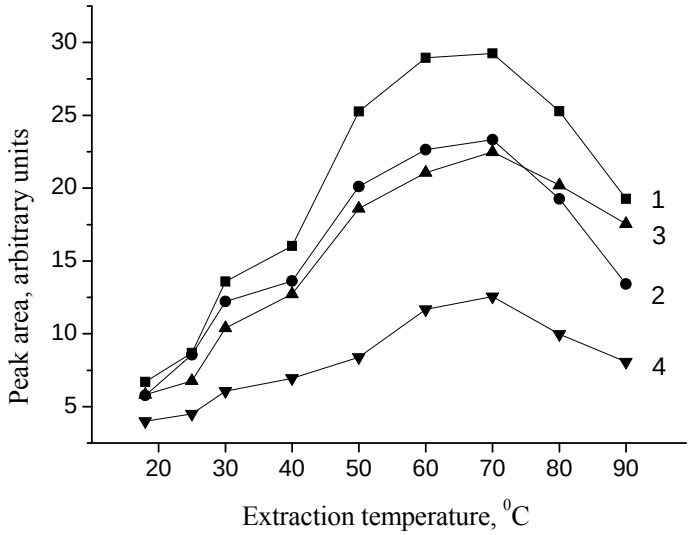

Fig. 8. Effect of extraction temperature on extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben. Headspace SDME conditions: sample volume 10 mL, concentration of parabens 10 μg/mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 10 μL, extracting solvent (dioctyl phthalate) volume 1 μL, solution stirring rate 800 rpm.

In order to obtain a good extraction efficiency and repeatability, 1 μL of amyl acetate drop volume was selected for our work.

The extraction time was examined by exposing the solvent drop to the headspace for 5–30 min. As it can be seen in Fig. 9, 20 min is the optimum.

In order to increase the extractability of the analytes, before extraction paraben solution was stirred at 70 °C temperature without extracting solvent. This will help analytes to pass to the gaseous phase. Paraben solution was incubated at 70 °C temperature up to 40 min and then extracted 20 min at the same temperature.

With increase of incubation time up to 20 min extraction efficiency also increased. In further experiments 20 min incubation time was selected.

The ionic strength of the solution was modified by adding NaCl up to 0.3 g/mL. The results demonstrated that the addition of NaCl up to 0.2 g/mL increases the extraction efficiency. Thus, in further experiments, 0.2 g/mL of NaCl was added to the samples.

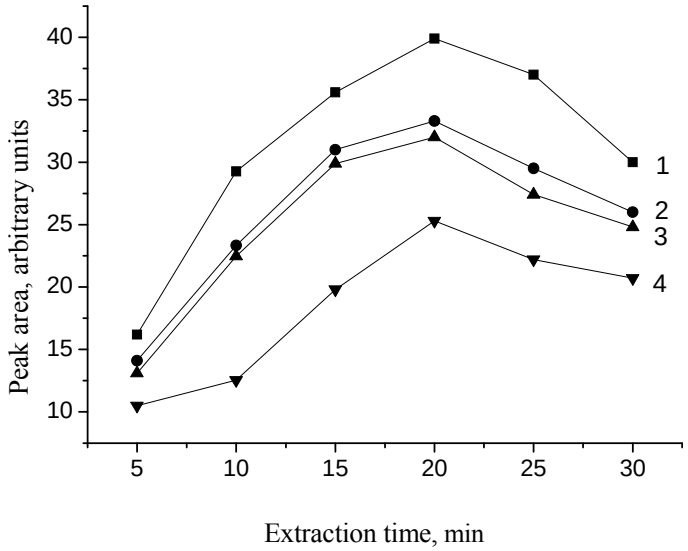

Fig. 9. Effect of extraction time on extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben. Headspace SDME conditions: sample volume 10 mL, concentration of parabens 10 μg/mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 10 μL, extracting solvent (dioctyl phthalate) volume 1 μL, solution stirring rate 800 rpm.

Analytical perfomance of the method

The quality parameters of the suggested method, such as linearity, detection limits and repeatability, were calculated under the optimized extraction conditions. *n*-Hexadecane (0.5 μg/mL) was added to the extraction solvent as an internal standard.

The linear ranges of the calibration curves for all the analytes were up to 10 μg/mL. The correlation coefficients were 0.996–0.997. The detection limits and relative standard deviations are presented in Table 3.

RSDs are up to 32.2 % and it shows that repeatabilities are not good.

Table 3. Detection limits and repeatabilities

Analyte	Detection limits, μg/L	RSD, % (n = 5)	
		c = 1 μg/mL	c = 10 μg/mL
Methylparaben	260	32.2	23.8
Ethylparaben	380	24.8	15.3
Propylparaben	450	23.8	18.6
Butylparaben	580	25.1	18.6

Application of the method

Comparison of different SDME modes of parabens (Tables 1–3) shows that lower detection limits are obtained using SDME of derivatized parabens. Thus, the methods were applied for real samples analysis.

The facial tonic "Matt Touch" (Lumene) was analysed using direct SDME. Because of a large amount of ethanol in tonic it was impossible to analyse it without preliminary dilution. Thus, a 100-fold dilution of the tonic was needed. A chromatogram of the diluted tonic is presented in Fig. 10. The concentrations of the analytes were calculated using the standard addition method and were determined to be 180, 70, 38 and 60 mg/L for methylparaben, ethylparaben, propylparaben and butylparaben, respectively.

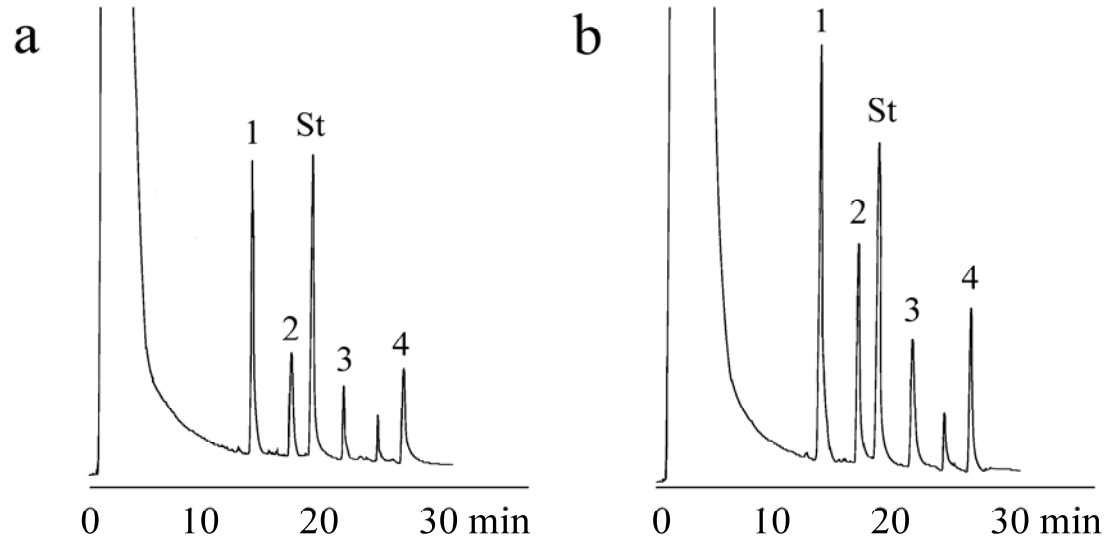

Fig. 10. Chromatograms of 100-fold diluted facial tonic: a – unspiked, b – spiked with a standard solution of parabens (10 μg/mL): 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben, St – *n*-hexadecane. Direct SDME conditions: sample volume 10 mL, concentration of parabens 1 mg/mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 10 μL, extracting solvent (amyl acetate) volume 1 μL, extraction time 20 min, solution stirring rate 200 rpm.

Hand cream "Margarita" (Biok) was analysed using headspace SDME. A chromatogram of the cream is presented in Fig. 11. The concentrations of the analytes were calculated using the standard addition method and were determined to be 284, 320, 213 and 185 μg/g for methylparaben, ethylparaben, propylparaben and butylparaben, respectively.

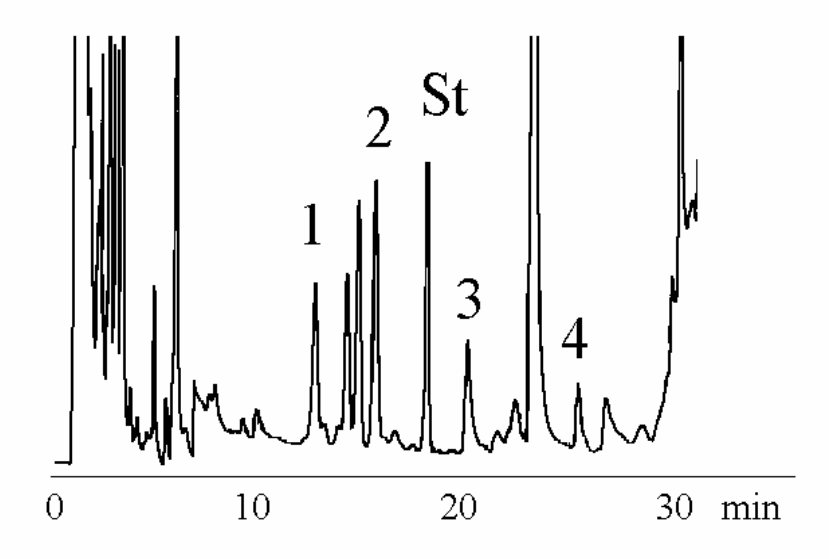

Fig. 11. Chromatograms of a cream: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben, St – *n*-hexadecane. Headspace SDME conditions: sample amount 1 g, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 10 μL, extracting solvent (amyl acetate) volume 1 μL, extraction time 20 min, incubation time 20 min, extraction temperature 70 °C, solution stirring rate 800 rpm.

3.2. Hollow fibre liquid phase microextraction of parabens

The technique utilizes porous hydrophobic polypropylene hollow fibre as a membrane. The fibre is impregnated with an organic phase and inside the hollow fibre is a receiving phase (the same or different from that used for impregnation). HFLPME is simple and fast, also enables clean extract formation. The low cost of the hollow fibre enables to dispose each extraction unit after a single extraction and thus to exclude cross-contamination problems from sample to sample and to avoid the need of regeneration of the extraction unit.

We examined HFLPME of underivatized and of derivatized parabens.

3.2.1. Hollow fibre liquid phase microextraction of underivatized parabens

Method optimization

The extracting solvent used in HFLPME has to meet some requirements: to extract the analytes quite well, to be practically insoluble in water and to be separated from the analyte peaks in the chromatogram. In addition, it must penetrate the polypropylene fibre pores. Moreover, for convenience, the optical properties of the solvent should allow to

see the solvent in the hollow fibre in order to control whether the hollow fibre is well-filled.

In order to select a proper extraction solvent, five different solvents were tested: carbon tetrachloride, *n*-octane, toluene, chlorobenzene and amyl acetate. Carbon tetrachloride was too volatile (boiling point 76.7 °C). After 15 min extraction less than 1 μL solvent remained in the capillary. The extraction efficiencies of the other four solvents are shown in Fig. 12.

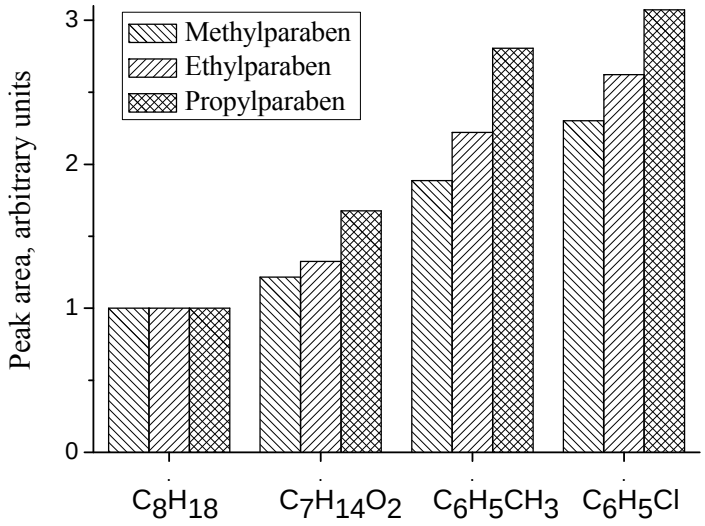

Fig. 12. Effect of extraction solvent on extraction efficiency. HFLPME conditions: sample volume 8 mL, concentration of parabens 5 μg/mL, extraction time 15 min, solution stirring rate 1500 rpm.

Octane and amyl acetate showed lower extraction efficiencies. In addition, those two solvents were practically invisible in the hollow fibre so it was difficult to observe the receiving phase. In contrast, immediately after immersion into toluene or chlorobenzene, the fibre walls became transparent and the solvent level in the capillary could be easily seen. Within a few minutes the solvent filled the fibre. Thus, impregnation of the fibre walls and fibre filling were accomplished in a single step and the delicate procedure of filling the hollow fibre with a microsyringe was eliminated. As chlorobenzene showed higher extraction efficiency (Fig. 12), it was chosen as the parabens extractant.

Since the receiving phase is protected by the hollow fibre, there is a possibility to apply high stirring rates and thus to reduce the time required to reach the equilibrium of

the analytes between the aqueous and the receiving phases. In this work we used the magnetic stirrer's maximum rate (1500 rpm).

HFLPME is an equilibrium extraction technique, thus the amount of the parabens extracted depends on the equilibration time, which is reached when the further increase in the extraction time does not result in a significant increase in the amount of extracted parabens. Maximum extraction efficiency would be achieved when equilibrium is established. Extraction time between 10 and 70 min was evaluated. The equilibrium was not reached even after a 70 min extraction. However, it is possible to work at a non-equilibrium state if constant extraction conditions are maintained. For further work a 40 min extraction was chosen as it was sufficiently long to reach high extraction efficiency yet dissolution or evaporation of the receiving phase was not observed.

The ionic strength of the solution was modified by adding different concentrations of NaCl.

Extraction efficiency gradually increases with increasing NaCl concentration and the maximum signal was achieved when the solution was saturated with NaCl. In further experiments, 0.4 g/mL of NaCl was added to the samples.

Analytical perfomance of the method

The quality parameters of the suggested method, such as linearity, detection limits and repeatability, were calculated under the optimized extraction conditions. Tetradecane (50 μg/mL) was added to the extraction solvent as an internal standard.

The calibration curves were drawn with three replicate injections of the extracts obtained after applying HFLPME procedure with 7 calibration points. The linear ranges for all the analytes were up to 30 mg/L. The correlation coefficients were 0.996–0.998. The detection limits and relative standard deviations are presented in Table 4.

Table 4. Detection limits and repeatabilities

Analyte	Detection limits, μg/L	RSD, % (n = 5)	
		c = 1 μg/mL	c = 10 μg/mL
Methylparaben	200	11.7	8.1
Ethylparaben	30	9.0	6.5
Propylparaben	10	7.6	9.4

Application of the method

Tap water from the laboratory was analysed. The tap water sample was analysed immediately without pretreatment. The water was free of parabens, or their concentrations were below the detection limits (Fig. 13. (b)). To assess the matrix effect, 8 mL of tap water was spiked with 0.1, 1 and 2 μg/mL of parabens and analyzed. Parabens concentrations were determined from calibration curves obtained in distilled water. The data demonstrate little natural water matrix effect on HFLPME.

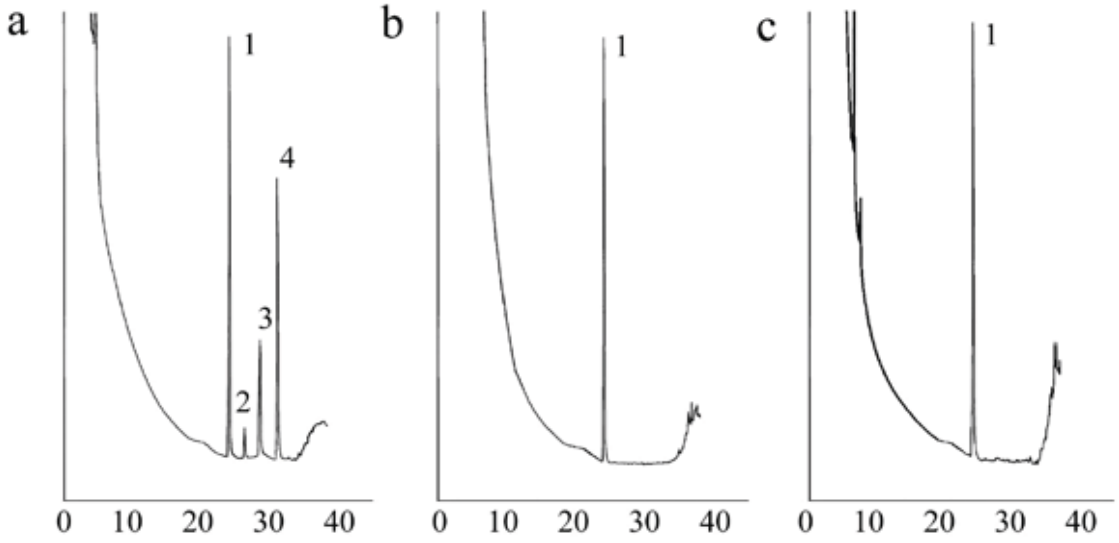

Fig. 13. Chromatograms of (a) standard solution of parabens, (b) tap water, and (c) urine obtained after HFLPME: 1 – internal standard tetradecane, 2 – methylparaben, 3 – ethylparaben, 4 – propylparaben. HFLPME conditions: concentration of each analyte in the standard solution is 1 μg/mL, extracting solvent (chlorobenzene), extraction time 40 min, concentration of NaCl 0,4 g/mL, solution stirring rate 1500 rpm.

Parabens tend to absorb from body care products into the body and are found in human urine. Urine is a more complex matrix than tap water. However, as HFLPME enables clean extraction, we expected HFLPME to extract parabens from urine without pretreatment. Urine HFLPME extracts were colourless and transparent and no paraben peaks were observed (Fig. 13. (c)). Matrix effects on extraction efficiency were studied by analysis of urine spiked with 0.1, 1 and 2 μg/mL of each analyte. Concentrations were determined from calibration curves obtained in distilled water. Relative recoveries were 55.9–67.7 % indicating a significant matrix effect. To eliminate this, parabens concentrations were determined by the method of standard additions, after adding 0.1, 1 and 2 μg/mL of each analyte to the sample. Relative recoveries were 96.6–104.1 %.

3.2.2. Hollow fibre liquid phase microextraction of derivatized parabens

Method optimization

In order to increase the extractability of the parabens we use paraben derivatization. Optimisation of derivatization conditions and the influence of pH on derivatization efficiency presented in a chapter 3.1.2.1.

Octanol-1, chlorobenzene, bromobenzene and *o*-xylene were tested as extracting solvents. For preliminary studies, extraction was carried out for 20 min. As one can see in Fig. 14, the highest extraction efficiency was obtained using octanol-1. However, octanol-1 was practically invisible in the hollow fibre, so it was rather inconvenient for the work. Contrarily, the walls of the hollow fibre immersed into *o*-xylene, chlorobenzene or bromobenzene became transparent; thus, it was possible to observe how the solvent filled the space inside a hollow fibre. The extraction efficiencies of *o*-xylene, chlorobenzene and bromobenzene were quite similar. As chlorobenzene had the lowest boiling point, its retention time in the chromatogram was less than that of *o*-xylene and bromobenzene; chlorobenzene was better separated from the analytes and thus was chosen as an extracting solvent for parabens.

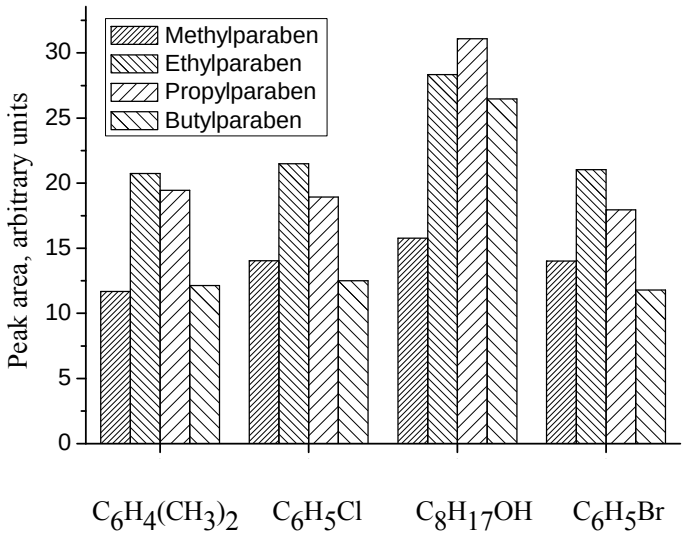

Fig. 14. Effect of extraction solvent on extraction efficiency. HFLPME conditions: sample volume 10 mL, concentration of parabens 10 mg/L, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 10 μL, extraction time 20 min, solution stirring rate 800 rpm.

Extraction times between 5 and 40 min were evaluated. The peak areas of extracted parabens leveled off after about 30 min. The optimum sample extraction time of 30 min was therefore chosen to achieve maximum sensitivity without extending the time of analysis.

To investigate the effect of salt on the HFLPME of derivatized parabens, extraction was performed in the presence of different concentrations of NaCl (from saltless up to saturation). The results demonstrate that the extraction efficiency gradually decreased with increasing the concentration of NaCl. On the basis of the obtained results, NaCl was not added in the further experiments.

Analytical perfomance of the method

The quality parameters of the suggested method were calculated under the optimized extraction conditions. *n*-Hexadecane (10 μg/mL) was added to the extraction solvent as an internal standard.

The calibration curves were drawn with three replicate injections of the extracts obtained after applying HFLPME procedure with 7 calibration points. The linear ranges for all the analytes were up to 10 mg/L. The correlation coefficients were 0.997–0.999. The detection limits and relative standard deviations are presented in Table 5. Detection limits of the developed method were lower than those obtained for underivatized parabens (Table 4).

Table 5. Detection limits and repeatabilities

Analyte	Detection limits, μg/L	RSD, % (n = 5)	
		c = 0.1 μg/mL	c = 1 μg/mL
Methylparaben	18	8.9	5.2
Ethylparaben	9.1	4.5	5.3
Propylparaben	6.4	7.7	5.6
Butylparaben	5.1	9.2	5.5

Application of the method

The facial tonic “Matt Touch” (Lumene) was analysed. First of all, the tonic was analysed without preliminary dilution. In 10 mL of the tonic, 0.2 g of $K_2HPO_4 \times 3H_2O$ was dissolved, 10 μL of acetic anhydride was added, and HFLPME was carried out for 30 min. The GC analysis of the extract showed that the concentrations of parabens

did not fall into the linear ranges of calibration curves. Thus, a 100-fold dilution of the tonic was needed. The chromatogram of the diluted tonic is presented in Fig. 15. The concentrations of the analytes were calculated using the standard addition method and were determined to be 168, 59, 33 and 53 mg/L for methylparaben, ethylparaben, propylparaben and butylparaben, respectively.

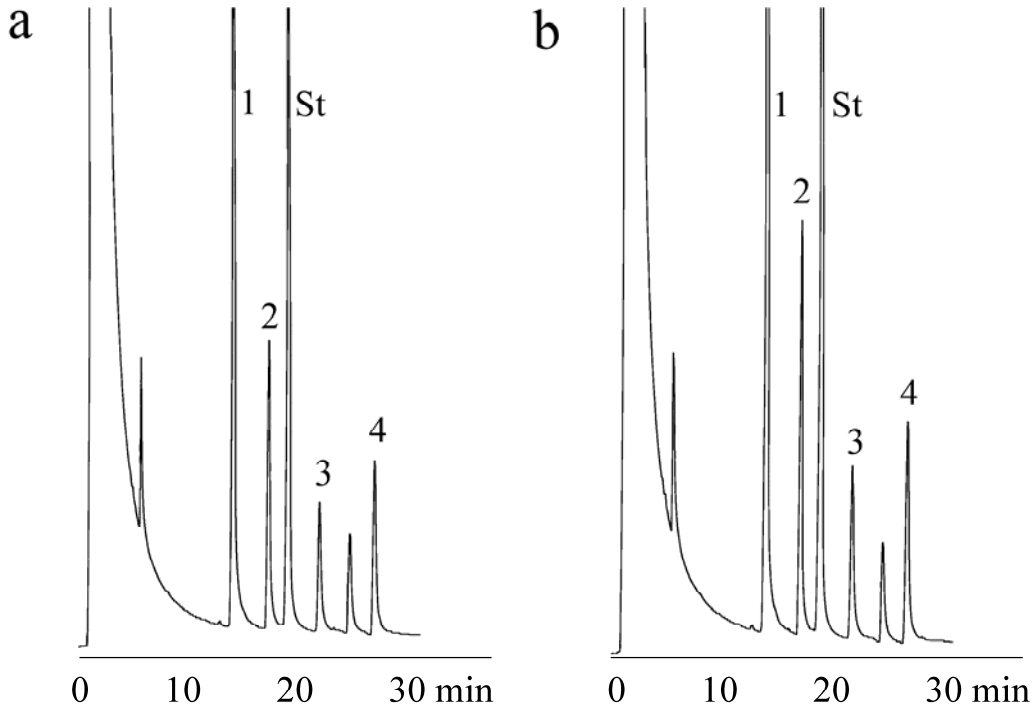

Fig. 15. Chromatograms of 100-fold diluted facial tonic: a – unspiked, b – spiked with a standard solution of parabens (0.5 mg/L): 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben, St – *n*-hexadecane. HFLPME conditions: sample volume 10 mL, concentration of parabens 10 mg/L, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 10 μL, extracting solvent chlorobenzene, extraction time 30 min, solution stirring rate 800 rpm.

3.3. Dispersive liquid-liquid microextraction of parabens

DLLME is simple to operate, rapid and inexpensive extraction method with high preconcentration factors and low sample volume requirements.

We examined DLLME of underivatized and of derivatized parabens.

3.3.1. Dispersive liquid-liquid microextraction of underivatized parabens

Method optimization

An extraction solvent for DLLME should fulfil some requirements: generally, it should have higher density than water, should demonstrate a good extraction capability of the compounds of interest, and its solubility in water should be low. Most of halogenated solvents answer those requirements, thus chloroform, carbon tetrachloride, chlorobenzene, bromobenzene and 1,2-dichlorobenzene were compared in the extraction of parabens.

In order to select a proper extraction solvent, a solution containing acetone and extraction solvent was rapidly injected into aqueous paraben solution. The cloudy solution formed was centrifuged, and organic phase was taken for analysis. Chloroform was not suitable for paraben extraction as it was too soluble in the aqueous phase (8 g/L), so a cloudy solution and consequently a separate organic phase did not form. CCl_4 presented a significantly lower extraction efficiency than halogenated aromatic solvents (Fig. 16). This fact corresponds rather well to the principle "like dissolves like", as parabens also contain a benzene ring. As the extraction efficiency of C_6H_5Cl, C_6H_5Br and $C_6H_4Cl_2$ was similar, in order to achieve an easier chromatographic separation of the analytes from the solvent peak, a solvent with the lowest boiling point (C_6H_5Cl) was chosen for the extraction.

To investigate the effect of the extraction solvent volume, a solution containing 0.5 mL of acetone and different volumes of extraction solvent was rapidly injected into aqueous paraben solution, and centrifugation was carried out. With increasing the extraction solvent volume, the peak areas initially increased and reached the maximum at 20 μL. Probably because of a partial sedimentation of chlorobenzene on the centrifuge tube walls, in the case of 15 μL chlorobenzene, its volume in the bottom of the centrifuge tube was too small, and together with the extraction phase some water phase was withdrawn into a microsyringe.

Thus, the real amount of the injected extraction phase was less than 1 μL, resulting in decreased peak areas of the analytes. On the other hand, when the extraction solvent volume exceeded 20 μL, because of the more intensive dilution of the analytes, the peak

areas of the analytes decreased (Fig. 17). To achieve low detection limits, 20 μL of extracting solvent was selected.

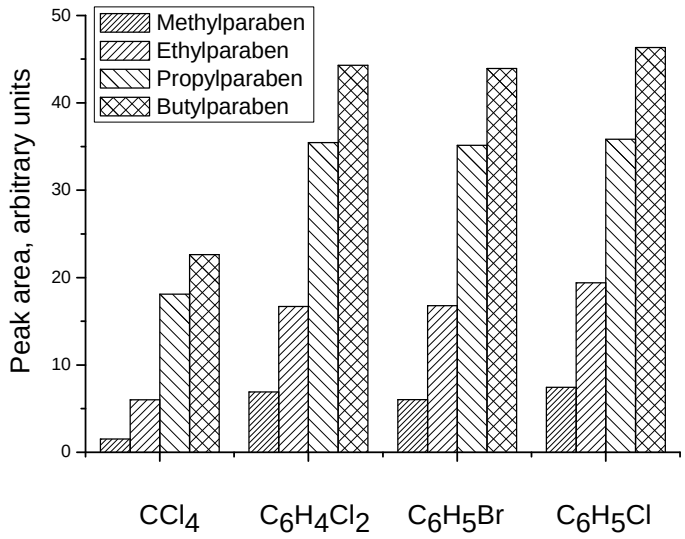

Fig. 16. Effect of extraction solvent on extraction efficiency. DLLME conditions: sample volume 8 mL, concentration of parabens 10 mg/L, acetone volume 0.5 mL, extraction solvent volume 40 μL, solution centrifugation time 2 min and stirring rate 5000 rpm.

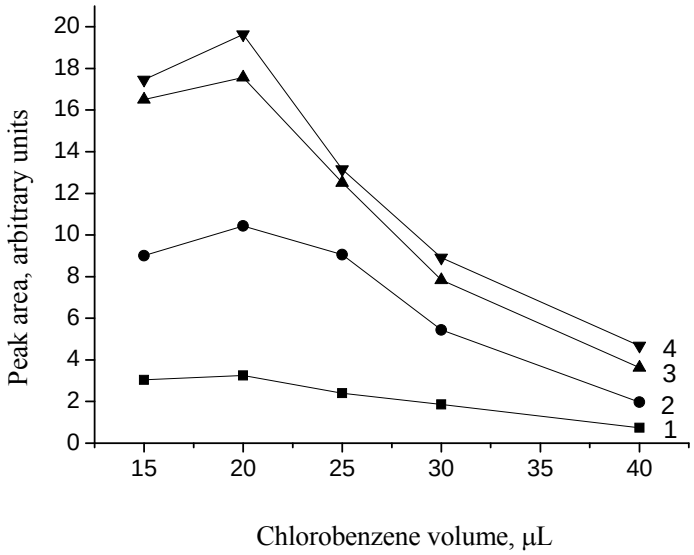

Fig. 17. Effect of extraction solvent (chlorobenzene) volume on extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben and 4 – butylparaben. DLLME conditions: sample volume 8 mL, concentration of parabens 10 mg/L, acetone volume 0.5 mL, extraction solvent volume 40 μL, solution centrifugation time 2 min and stirring rate 5000 rpm.

The main requirement for disperser solvent is its miscibility with extraction solvent and aqueous phase. Only a few solvents fulfil this requirement. In most of the publications concerning DLLME, acetone, acetonitrile and methanol were examined as disperser solvents. According to the results presented in the publications, the recovery variations using different disperser solvents were not remarkable. Referring to the data and considering its low toxicity and cost, acetone was selected as a disperser solvent in our work.

To investigate the effect of the disperser solvent volume, different acetone volumes (0.2–1.5 mL) and 20 μL of extracting solvent were used. At a low acetone volume the cloudy state was not stable and probably this caused lower extraction efficiency. On the other hand, with the increase of acetone volume the solubility of the parabens in water-acetone mixture increased and their concentration in the sedimented phase decreased. As it can be seen in Fig. 18, 0.4–1.0 mL acetone volume is the optimum. In order to have a convenient 0.5 mL acetone-chlorobenzene mixture volume for the injection and considering that the optimum chlorobenzene volume is 20 μL, 0.48 mL of acetone volume was selected for the further work.

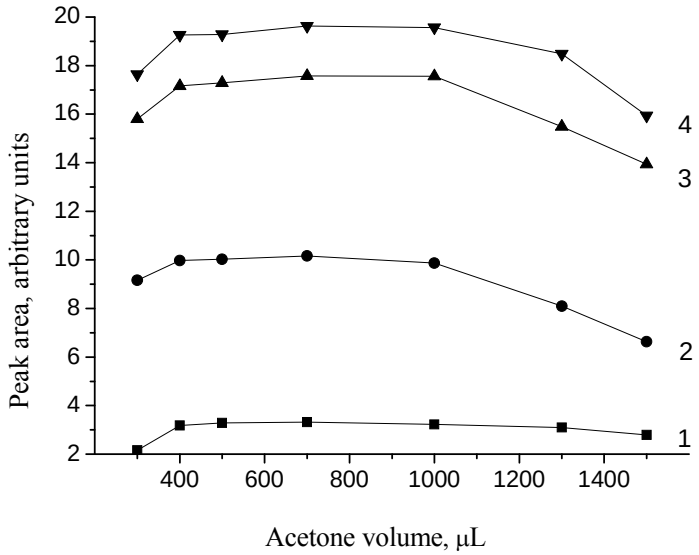

Fig. 18. Effect of disperser solvent (acetone) volume on extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben and 4 – butylparaben. DLLME conditions: sample volume 8 mL, concentration of parabens 10 mg/L, extraction solvent volume 20 μL, solution centrifugation time 2 min and stirring rate 5000 rpm.

DLLME extraction time was defined as the time interval between the injection of the mixture of disperser and extraction solvents and the centrifugation. Extraction time up to 20 min was investigated. Peak area variations at different extraction times were not significant. Evidently, due to a large surface area between the aqueous and organic phase, 20–30 seconds (time between the injection and the beginning of the centrifugation) are sufficient for extraction.

The ionic strength of the solution was modified by adding NaCl. When chlorobenzene was used as an extracting solvent, small quantities of NaCl (up to 0.075 g/mL of NaCl) promoted the transport of the analytes to the extracting drop. However, with the further increase of NaCl concentration, the sedimented phase did not form anymore, possibly because of the water phase density which increased with NaCl addition. Thus, the density of the organic phase was lower than that of the aqueous phase. Therefore, the organic phase formed the upper phase in the two-phase system. In order to avoid this, in further experiments NaCl was not added to the samples.

Analytical perfomance of the method

The quality parameters of the suggested method, such as linearity, detection limits and repeatability, were calculated under the optimized extraction conditions. *n*-Nonadecane (5 μg/mL) was added to the extraction solvent as an internal standard.

The calibration curves were drawn with three replicate injections of the extracts obtained after applying DLLME procedure with 7 calibration points. The linear ranges for all the analytes were up to 10 μg/mL. The correlation coefficients were 0.997–0.999. The detection limits and relative standard deviations are presented in Table 6.

Table 6. Detection limits and repeatabilities

Analyte	Detection limits, μg/L	RSD, % (n = 5)	
		c = 1 μg/mL	c = 10 μg/mL
Methylparaben	210	11.2	10.6
Ethylparaben	23	10.3	9.8
Propylparaben	15	9.7	6.8
Butylparaben	8	7.8	6.5

Application of the method

The proposed method is particularly useful when small concentrations of parabens in simple and clean matrices have to be determined. Tap water from the laboratory and swimming pool water were analysed. The tap water sample was analysed immediately, and swimming pool water was analysed in 4 hours after sampling without any pretreatment. The results showed, that the tap water was free of parabens or their concentrations were below detection limits. Butylparaben (28 μg/L; RSD = 9.8, n = 3) was determined in the swimming pool water (Fig. 19). Its main source might be body care cosmetics used by the swimming pool visitors.

To assess the matrix effect, 8 mL of tap water and of swimming pool water were spiked with 1 and 10 μg/mL of parabens. Chromatograms of nonspiked and spiked swimming pool water extracts are presented in Fig. 19. Data of the analysis demonstrated a low matrix effect on DLLME with the recoveries close to 100 %.

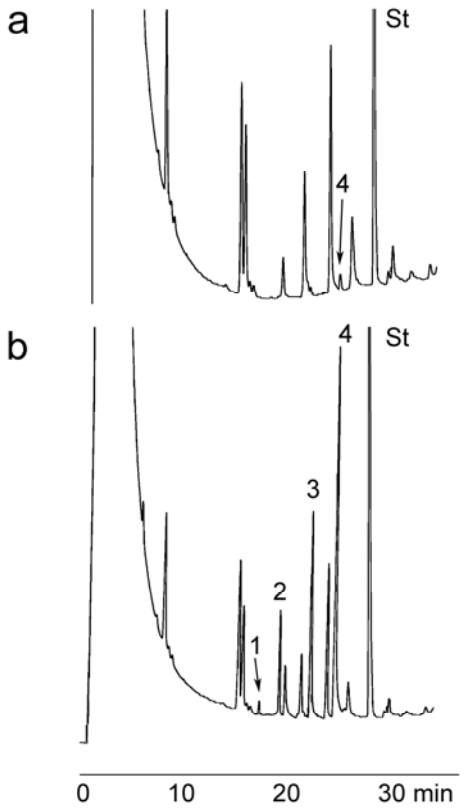

Fig. 19. Chromatograms of swimming pool water: a – non spiked, b – spiked with a standard solution of parabens (1 mg/L). 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben, St – *n*-nonadecane. DLLME conditions: sample volume 8 mL, extraction solvent volume 20 μL, acetone volume 0.48 mL, solution centrifugation time 2 min and stirring rate 5000 rpm.

3.3.2. Dispersive liquid-liquid microextraction of derivatized parabens

Method optimization

In order to increase the extractability of the parabens we use paraben derivatization. Optimisation of derivatization conditions and the influence of pH on derivatization efficiency presented in a chapter 3.1.2.1.

Carbon tetrachloride, chlorobenzene, bromobenzene and ethyl benzoate were compared in the extraction of derivatized parabens.

CCl_4 presented lower extraction efficiency than the solvents containing aromatic ring (Fig. 20). Extraction efficiencies of C_6H_5Cl and C_6H_5Br were similar and higher than that of ethyl benzoate. In order to achieve easier chromatographic separation of the analytes from the solvent peak, chlorobenzene, the solvent with the lower boiling point (boiling point of C_6H_5Cl is 132 °C and of C_6H_5Br is 153 °C) was chosen for the extraction.

To investigate the effect of the extraction solvent volume, a solution containing 0.5 mL of acetone and different volumes of chlorobenzene was used for DLLME. With the increase in extraction solvent volume peak areas initially increased and reached the maximum at 20 μL. Probably, because of a partial sedimentation of chlorobenzene on the centrifuge tube walls, in the case of 15 μL chlorobenzene, its volume in the bottom of the centrifuge tube was too small and some water phase instead of extraction phase was withdrawn into a microsyringe. On the other hand, when the extraction solvent volume exceeded 20 μL, because of the bigger dilution of the analytes, peak areas of the analytes decreased (Fig. 21). Thus, 20 μL of extracting solvent was selected.

Considering its low toxicity and cost, acetone was selected as a disperser solvent in our work.

To investigate the effect of the disperser solvent volume, different acetone volumes (0.1–1.0 mL) and 20 μL of extracting solvent were used. As it can be seen in Fig. 22, 0.2–0.4 mL acetone volume is the optimum. In order to have a convenient 0.3 mL acetone-chlorobenzene mixture volume for the injection and considering that the optimum chlorobenzene volume is 20 μL, 0.28 mL of acetone volume was selected for the further work.

As in the case of DLLME of underivatized parabens, 20–30 seconds (the time between the injection and the beginning of the centrifugation) are sufficient for extraction.

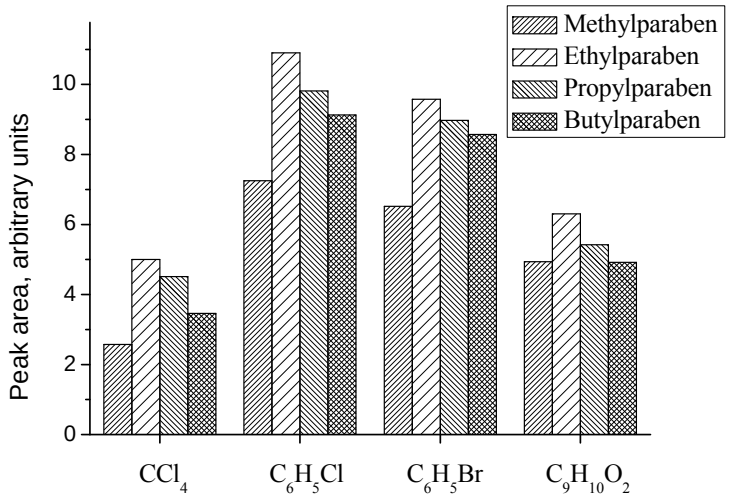

Fig. 20. Effect of extraction solvent on extraction efficiency. DLLME conditions: sample volume 8 mL, concentration of parabens 10 μg/mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 8 μL, acetone volume 0.5 mL, extraction solvent volume 40 μL, solution centrifugation time 2 min and stirring rate 5000 rpm.

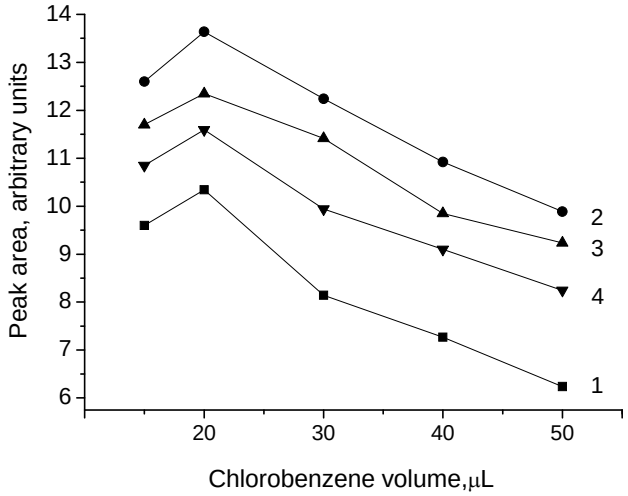

Fig. 21. Effect of extraction solvent volume on the extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben and 4 – butylparaben. DLLME conditions: sample volume 8 mL, concentration of parabens 10 μg/mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 8 μL, acetone volume 0.5 mL, solution centrifugation time 2 min and stirring rate 5000 rpm.

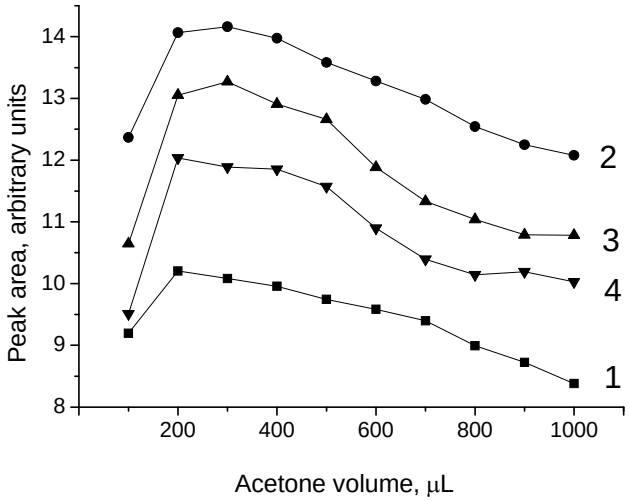

Fig. 22. Effect of disperser solvent volume on the extraction efficiency: 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben and 4 – butylparaben. DLLME conditions: sample volume 8 mL, concentration of parabens 10 μg/mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 8 μL, extraction solvent volume 20 μL, solution centrifugation time 2 min and stirring rate 5000 rpm.

The ionic strength of the solution was modified by adding NaCl. When chlorobenzene was used as an extracting solvent, up to 0.1 g/mL of NaCl promoted the transport of the analytes to the extracting drop. With the further increase of NaCl, the water phase density increased and the density of the organic phase resulted lower than that of the aqueous phase. Because of that the organic phase formed the upper phase in two-phase system and did not sediment any more. In order to avoid this, in further experiments NaCl was not added to the samples.

Analytical perfomance of the method

The quality parameters of the suggested method were calculated under the optimized extraction conditions. *n*-Hexadecane (10 μg/mL) was added to the extraction solvent as an internal standard.

The calibration curves were drawn with three replicate injections of the extracts obtained after applying DLLME procedure with 7 calibration points. The linear ranges for all the analytes were up to 10 μg/mL. The correlation coefficients were 0.997–0.999. The detection limits and relative standard deviations are presented in Table 7.

Detection limits of the developed method were lower than those obtained for underivatized parabens (Table 6).

Table 7. Detection limits and repeatabilities

Analyte	Detection limits, μg/L	RSD, % (n = 5)	
		c = 0,1 μg/mL	c = 1 μg/mL
Methylparaben	22	11.0	5.9
Ethylparaben	4.2	9.3	6.4
Propylparaben	3.3	8.3	6.8
Butylparaben	2.5	9.3	7.4

Application of the method

Tap water from the laboratory and river Neris water were analysed. The tap water sample was analysed immediately, and river water was analysed in 4 hours after the sampling. Prior to the extraction, water samples were filtered through a 0.45 μm membrane filter. The results showed, that the both water samples analysed were free of parabens or their concentrations were below detection limits.

To assess the matrix effect, 8 mL of tap water and river water were spiked with 0.1 μg/mL of parabens. Chromatograms of nonspiked and spiked river water extracts are presented in Fig. 23. The data of the analysis demonstrate little matrix effect on DLLME with the recoveries close to 100 %.

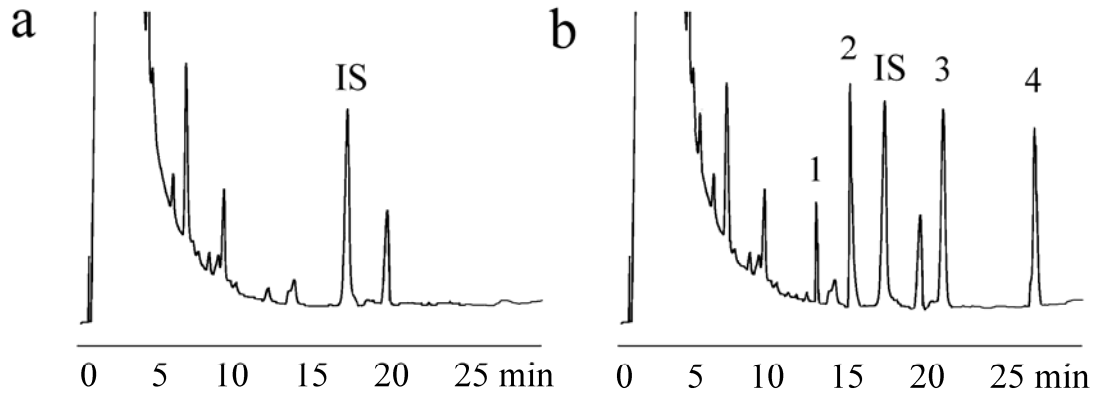

Fig. 23. Chromatogram of Neris river water: a – unspiked, b – spiked with a standard solution of parabens (0.1 mg/L). 1 – methylparaben, 2 – ethylparaben, 3 – propylparaben, 4 – butylparaben, IS – *n*-hexadecane. DLLME conditions: sample volume 8 mL, concentration of $K_2HPO_4 \times 3H_2O$ 0.02 g/mL, acetic anhydride volume 8 μL, extraction solvent volume 20 μL, acetone volume 280 μL, solution centrifugation time 2 min and stirring rate 5000 rpm.

3.4. Comparison of microextraction methods of parabens

In this chapter all the examined microextraction methods are compared and their advantages and shortcomings are revealed.

One of the most important advantages of all the mothods studied is that the methods use very small quantities (1–20 μL) of toxic organic solvents.

The fastest microextraction technique was dispersive liquid-liquid microextraction, the microextraction itself occured in few seconds and additional 2 minutes served for centrifugation of the sample. Other methods are longer (SDME and HFLPME).

Detection limits for underivatized parabens were higher than for derivatized parabens. Also much higher detection limits were obtained using headspace single drop microextraction.

Repeatability of the results is similar for all the methods examined, except headspace single drop microextraction.

For a selection of the extraction method sample matrix should be regarded. For clean samples all the examined methods can be used. In the case of polluted samples headspace single drop microextraction or hollow fibre liquid phase microextraction is preferred.

4. CONCLUSIONS

1. The possibilities of direct single drop microextraction method to extract underivatized parabens were studied. The optimized extraction conditions were: extraction solvent amyl acetate, internal standard *n*-nonadecane, extraction time 20 min, NaCl concentration 0.2 g/mL.

2. The derivatization of parabens was accomplished using acetic anhidride. Derivatization conditions were optimized It was determined that derivatization of parabens prior to microextraction procedure improves sensitivity of determination of parabens.

3. The possibilities of direct single drop microextraction and headspace single drop microextraction methods to extract derivatized parabens were studied. The optimized extraction conditions were: extraction solvent amyl acetate (direct SDME) or dioctyl phthalate (headspace SDME), internal standard *n*-hexadecane, extraction time 20 min, incubation time 20 min (for headspace SDME), NaCl concentration 0 g/mL (headspace SDME) or 0.2 g/mL (direct SDME).

4. The possibilities of hollow fibre liquid phase microextraction method to extract underivatized and derivatized parabens were studied. The optimized extraction conditions were: extraction solvent chlorobenzene, internal standard *n*-tetradecane (for underivatized parabens) or *n*-hexsadecane (for derivatized parabens), extraction time 40 min (for underivatized parabens) or 30 min (for derivatized parabens), NaCl concentration 0.4 g/mL (for underivatized parabens) or 0 g/mL (for derivatized parabens).

5. The possibilities of dispersive liquid-liquid microextraction method to extract underivatized and derivatized parabens were studied. The optimized extraction conditions were: extraction solvent chlorobenzene, internal standard *n*-nonadecane (for underivatized parabens) or *n*-hexsadecane (for derivatized parabens), dispersion solvent acetone, extraction time few seconds.

6. The quality parameters (detection limits, linear concentration ranges, repeatability of the results) of all the suggested liquid phase microxtraction methods were defined. The methods were applied for the determination of parabens in the tap, river, pool water, urine, cream and facial tonic.

7. It was determined that for all the proposed liquid phase microextraction methods of parabens very small volumes of extraction solvents ((1–20 μL) are required. The fastest is dispersive liquid phase microextraction, the longest is headspace single drop microextraction. Using the same microextraction technique detection limits are lower for derivatized parabens. The highest detection limits and relative standard deviations were obtained using headspace single drop microextraction. For clean water samples all the examined methods can be used. In the case of the samples with complex matrices headspace SDME or HFLPME is preferred.

THE LIST OF ORIGINAL PUBLICATION BY THE AUTHOR

Articles in journals:

1. **A. Prichodko**, K. Jonušaitė, V. Vičkačkaitė. Hollow fibre liquid phase microextraction of parabens. *Central European Journal of Chemistry*, **7**(3) (2009) 285-290.
2. **A. Prichodko**, V. Šakočiūtė, V. Vičkačkaitė. Dispersive liquid-liquid microextraction of parabens. *Chemija*, **21**(2-3) (2010) 112-117.
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4. **A. Prichodko**, E. Janėnaitė, V. Šmitienė, V. Vičkačkaitė. Gas chromatographic determination of parabens after in-situ derivatization and dispersive liquid-liquid microextraction. *Acta Chromatographica*, (2012) 1–13 (online).

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1. **A. Prichodko**, V. Vičkačkaitė. Dispersive liquid-liquid microextraction for parabens gas chromatographic determination in water samples. 5th Conference on Separation and Related Techniques by Nordic Separation Science Society, Tallinn, 2009, p. 127.
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3. **A. Prichodko**, E. Janėnaitė, V. Vičkačkaitė. Dispersive liquid-liquid microextraction for derivatized parabens. 10th International Conference of Lithuanian chemists „Chemistry 2011“, Vilnius, 2011, p. 88.

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SANTRAUKA

Parabenai pasižymi antibakterinėmis bei priešgrybelinėmis savybėmis ir plačiai naudojami kosmetikos, maisto, farmacijos pramonėje kaip konservantai, apsaugantys produktus nuo ankstyvo gedimo ir prailginantys jų galiojimo laiką. Padidėjus įtarimams, jog prasiskverbę per odą parabenai gali sukelti alergines reakcijas, ardyti endokrininę sistemą, skatinti vėžinių ląstelių gamybą, buvo pradėta kontroliuoti jų kiekį aplinkoje, maisto bei kosmetikos produktuose. Tačiau parabenų koncentracijos dažnai yra per mažos, o mėginiai per daug sudėtingi, kad juos būtų galima analizuoti nesukoncentravus ir neizoliavus nuo trukdančios matricos.

Šioje daktaro disertacijoje apibendrintų mokslinių tyrimų tikslas – sukurti parabenų skysčių-skysčių mikroekstrakcijos metodus – mikroekstrakciją tirpiklio lašu, skystafazę mikroekstrakciją kapiliare ir dispersinę skysčių-skysčių mikroekstrakciją – bei pritaikyti juos parabenų nustatymui vandenyje bei kosmetikos produktuose.

Optimizuotos mikroekstrakcijos tirpiklio lašu, skystafazės mikroekstrakcijos kapiliare ir dispersinės skysčių-skysčių mikroekstrakcijos ekstrakcijos sąlygos ir nustatytos pagrindinės analizinės charakteristikos. Ištirta parabenų derivatizacijos įtaka parabenų dujų chromatografinio nustatymo efektyvumui. Paruošti parabenų mikroekstrakcijos metodai pritaikyti vandens ir kosmetikos mėginių analizei.