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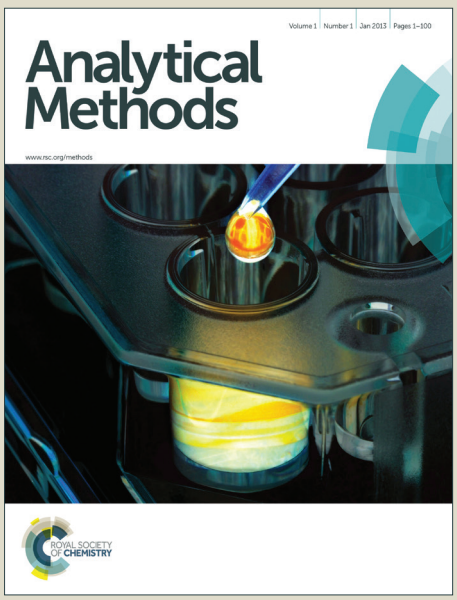

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FULL PAPERS

Droplets-based microextraction assisting solid phase microextraction for gas chromatography of polar compounds as clopyralid in water

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For the first time, we assessed the performance of liquid phase microextraction (LPME) with droplets of organic solvent that assists solid phase microextraction (SPME) with chemically bonded polydimethylsiloxane (PDMS) fiber for analysis by gas chromatography-mass spectrometry of trace amounts of polar compounds in water. Clopyralid was used as target analyte. LPME with droplets was performed with dichloromethane and was compared with dispersive liquid-liquid microextraction (DLLME) by addition of acetone or methanol as disperser solvent to dichloromethane. The main factors potentially affecting the microextraction were optimized. The optimal volume of dichloromethane was 17 µL per mL of aqueous sample. The relative enrichment factor for LPME in the presence of dichloromethane droplets was 200 and decreased by addition of disperser solvent. Consequently, DLLME cannot be applied with this SPME fiber. A characteristic of the method is that LPME and SPME can be conducted simultaneously or in two steps in the same vial. The limit of detection and limit of quantification were 0.02 µg L^{-1} and 0.07 µg L^{-1}, respectively for 7-µm chemically bonded PDMS fiber and mass spectrometric detection.

Keywords: Droplets-based liquid phase microextraction; Solid phase microextraction with fiber; Disperser solvent; Clopyralid; Water sample; Gas chromatography-mass spectrometry.

1. Introduction

Clopyralid (3,6-dichloropyridine-2-carboxylic acid) is an herbicide that is used to kill unwanted plants, especially thistles and clover in lawn, pasture, sugar beets, wheat, and mint. Clopyralid acts as a growth hormone, altering plant growth by causing proliferation of abnormal growth that interferes with nutrient transport. Clopyralid is unavoidable scattered into the surrounding vicinity of the application and it is ubiquitously in soil, water and food. Chronic studies with laboratory animals have identified effects on the stomach, liver, blood and body weight and acute exposure to clopyralid is severely irritating to eyes lasting up to 21 days after exposure[1] and may cause irreversible eye damage. Because there are no biomonitoring reports of clopyralid exposure for workers, little is known about the dermal absorption of clopyralid in humans. The commercial clopyralid is very soluble in water and very mobile in soil and has the potential to leach in the ground water and/or to contaminate surface water. Depending on soil type and climate, clopyralid can persist up to 14 months in soil[1]. Despite of its low level of use in the United States, clopyralid was found in two of the twenty river basins[1]. The requirements for drinking water are very strict in the European Community[2] and the concentration of pesticides must not exceed 0.1 µg L^{-1}.

The regulatory analytical methods for the determination of clopyralid from water samples, soil, and compost include gas chromatography (GC)[3-10] and liquid chromatography (LC)[11-15]. Since clopyralid has a carboxylic group, the GC analysis required also the derivatization of the analyte as methyl ester[4,6], 1-butyl ester[3,5,7], pentafluorobenzyl ester[8] or silyl derivatives[10]. LC could be an attractive method because no derivatization is required, but the sensitivity of the UV detector is not enough to detect and quantify clopyralid at trace level in a quality control lab without mass spectrometer.

GC is one of the most common techniques for the analysis of the thermostable compounds. The introduction of aqueous samples directly into the gas chromatograph is undesirable because the column is degraded, the sensitivity of the apparatus is significantly decreased, and the resolution is lost. A few sample preparation techniques are required prior the GC analysis of clopyralid in soil and water[16]. These techniques involve cleanup procedures, sample concentration, and derivatization. The optimization of sample preparation is a very important part of the method development that can reduce the analysis time, the amount of solvent, and the size of samples.

Usually, the extraction performs clean up and concentration in one step. The most applied extraction technique of clopyralid from water with organic solvents was in the presence of sodium chloride[4,5], sodium hydroxide[6,8,9] or tetrabutylammoniumhydroxide [7]. An aliquot was acidified and then was partitioned with an organic solvent. The classic liquid extraction requires high amounts of toxic solvents, is time consuming, and most of the analytes can be lost during the extraction procedures. The volume of solvent was reduced and the sensitivity for trace analysis was improved by solid phase extraction of clopyralid in drinking water[15] and solid phase microextraction (SPME) of clopyralid in atmospheric samples[10]. The above reported methods for clopyralid analysis in several matrices proved to be insufficient for analysis in soil and drinking water or require the use of critical chemicals and are too complicated for routine analysis.

Recently, in order to increase the extracted quantity of analytes and to overcome the disadvantages of the above mentioned techniques, we developed SPME with immobilized PDMS fiber assisted by droplets-based LPME, which improved the extraction efficiency of the volatile organic hydrocarbons with low polarity[17]. In this system, the presence of a small volume of organic solvent into the sample matrix had a swelling effect on the immobilized PDMS sorbent increasing the absorption volume. Moreover, the sorbent can adhere to the surface of solid sorbent generating a thin layer of solvent with pre-extracted analytes, enhancing the amount of analytes extracted by fiber.

The goal of this study is the improvement of the extraction efficiency of polar compounds as clopyralid in water by SPME with chemically bonded PDMS fiber for gas chromatography–mass spectrometry (GC-MS) analysis. For this propose, SPME is assisted by LPME with droplets of organic solvent and the results are compared to simple SPME and to SPME assisted by dispersive liquid-liquid microextraction (DLLME) achieved by addition of a disperser solvent. Clopyralid was analyzed without derivatization in order to see its behavior as polar compound.

2. Experimental

2.1. Chemicals and Materials

Clopyralid (99.4%) was provided from Riedel de Haen (Seelze, Germany). All of the other solvents and chemicals were purchased from Merck (Darmstadt, Germany). All these reagents were at least of analytical grade and were used without further purification. High purity water obtained with a Milli-Q water purification system (Millipore, Bedford, USA) was used throughout the experiments. Commercially available 7-µm bonded film thickness PDMS on 0.1-mm fused silica fiber was from Supelco (Belafonte, USA). Only this 7-µm chemically bonded PDMS fiber has been available commercially. Other commercial SPME sorbents such as 100-µm PDMS, 30-µm PDMS, 65-µm PDMS/Divinylbenzene, 65-µm Carbowax/Divinylbenzene, 75-µm Carboxen/ PDMS, 50/30-µm Divinylbenzene/Carboxen/PDMS, 85-µm Polyacrilate, etc are not chemically bonded to the silica fiber and they can be destroyed at a long contact with dichloromethane.

The stock solutions at different concentrations were prepared by addition of deionized water to known amounts of clopyralid up to fill 250 mL volumetric bottle. The mixture was magnetically stirred at room temperature for 1 h. A volume of 12 mL was carefully drawn out with a syringe from each bottle and was transferred into the extraction vial.

2.2. Apparatus

GC-MS analysis of clopyralid was performed with a Trace GC Series 2000 gas chromatograph coupled to a quadrupole ion trap GCQ^{plus} mass spectrometer from Thermo (Austin, TX, USA). High purity helium was used as carrier gas at constant flow of 1 mL min^{-1}. The GC was equipped with a DB-5 fused capillary column (30m x 0.25mm i.d.) with 0.25 µm film thickness of PDMS with 5% phenyl from J&W Scientific (Folsom, CA, USA). The injector was in the splitless mode at 300°C. The GC oven temperature was started at 180°C and was increased to 240°C at a rate of 15°C min^{-1}.

The mass spectra were recorded in positive mode by electron ionization (EI) within the scan range of 40-300 m/z. The temperature in the transfer line was 290°C. Identification of the peak was performed by the comparison of the retention times and by the interpretation of the fragmentation patterns as well as spectra with mass spectra of standards.

Agitation was carried out with a magnetic stirrer using a PTFE-coated magnetic bar (15 mm x 5mm) at 500 rpm and pH was measured using a Mettler-Toledo S 400 pH-meter (Greifensee, Switzerland).

2.3. Microextraction Procedure

All the microextractions were performed in 12 mL glass vials with PTFE-lined septa and screw caps. The stirring bar was firstly introduced into the sample vial and then the aqueous solution was added until the vial was completely filled. Consequently, the vial had no free space and the headspace was practically avoided.

SPME assisted by LPME can be performed in one step or in two steps. One step procedure was already presented[17]. In two steps microextraction, small volumes of organic solvent (dichloromethane) were introduced under agitation into the sample vial with a Hamilton syringe. The organic solvent was turned into droplets in the aqueous matrix and the microextraction with organic solvent began. For SPME assisted by DLLME, a few microliters of disperser solvent were injected rapidly into the agitated solution with organic solvent. The SPME with PDMS fiber was started after a few seconds when the immobilized PDMS fiber was immersed into the aqueous sample under agitation at room temperature. When the microextraction with PDMS fiber was completed (10 min), the fiber was retracted into the protection needle, was removed from vial, and then was immediately introduced into the GC injector for thermal desorption. Each experiment was repeated five times. All experiments were performed at 20°C in a themostated water bath.

3. Results and Discussion

This method involves SPME with immobilized PDMS fiber assisted by LPME with droplets of organic solvent. The general mechanism of this method has been described before [17]. Under agitation, the organic solvent was transformed in small drops. Consequently, the interface between the organic solvent and the aqueous sample was very large and a very fast mass transfer of analytes from the aqueous sample to the organic solvent occurred. Liquid-liquid equilibrium was achieved very quickly. The limiting step in the general extraction process will be the solid-liquid equilibrium. For this reason, the simultaneous starting of the LPME and SPME will give the same extraction time as for two steps extraction when first is started LPME and after a few seconds SPME.

The analytes from the aqueous sample are partially isolated and concentrated by LPME into a small volume of organic solvent. The PDMS fiber inserted into the aqueous solution comes in contact with both the aqueous phase and the organic phase. The droplets of organic solvent have a higher concentration of analytes than the aqueous solution and adhere very quickly to the surface of the PDMS fiber. Then the solvent spreads on the surface of the PDMS fiber, generating a thin layer of organic solvent with analytes on the surface of the immobilized PDMS.

The difference between LPME with droplets and DLLME is given by the size of the droplets and how they are generated. In DLLME, the organic solvent in the presence of dispersive solvent generates a stabile colloidal solution in water with particles that become equally dispersed throughout the liquid sample. The particles of the colloidal solution are in the range of nanometers and can be seen only under a microscope. In LPME with droplets, the organic solvent is divided in small drops only by agitation. These drops are in the range of millimeters and can be viewed with the free eye. They have different sizes and are not equally distributed into the sample.

The extraction process depends mainly on the selection of the extraction solvent, the volume of solvent, the presence of a disperser solvent, pH, agitation, temperature, and extraction time. The effect of agitation, temperature, and extraction time were previously discussed [17] and their influence on extraction efficiency had a similar variation. The optimum value selected in this experiment was 500 rpm for agitation, 20°C for temperature, and 10 min for extraction time.

3.1. Selection of the organic solvent and its volume.

The selection of suitable extraction solvent is very important in order to ensure the highest extraction efficiency for analyte. As the principle"like dissolves like", the organic solvent should have a high affinity for analyte and low solubility in water. Since clopyralid has a carboxylic group, the organic solvent should possess a relative high polarity. The solvent should have higher density than water in order to create easily small drops by magnetic agitation. For a good chromatographic behavior, the organic solvents should have a high volatility and should not be strongly retained by the PDMS fiber.

The solvent selection has been made based on the above requirements. Table 1 shows boiling point, density, solubility in water, and relative polarity to water of a few potential organic solvents for extraction. Hydrocarbons, aromatic hydrocarbons and diethylether have smaller density than water and a relative low polarity. Moreover, diethylether has relatively a high solubility in water. They cannot be used as extraction solvents. Chlorinated organic solvents have the higher density. Among these solvents, dichloromethane has relatively the highest polarity, a high density, and demonstrated the maximum extraction efficiency. Tetrachloromethane is suitable for apolar compounds and was strongly retained by the PDMS sorbent giving carry-over.

Table 1. Properties of organic solvents potentially used in LPME.

Solvent	Boiling point[18], °C	Density[19], g mL^{-1}	Solubility[20] at 20°C, g in 100g water	Relative polarity [18]
Dichloromethane	39.6	$1.326^{20°C}$	1.4	0.309
Trichloromethane	61.2	$1.478^{25°C}$	0.82	0.259
Tetrachloromethane	76.7	$1.594^{20°C}$	0.07	0.052
Benzene	80.1	$0.876^{20°C}$	0.17	0.111
Toluene	110.6	$0.867^{20°C}$	0.05	0.099
n-Hexane	68.7	$0.655^{20°C}$	0.011	0.009
Cyclohexane	80.8	$0.779^{25°C}$	0.008	0.006
Diethyl ether	34.5	$0.713^{20°C}$	7.5	0.117
Acetone	56.1	$0.789^{20°C}$	miscible	0.355
Methanol	64.6	$0.791^{20°C}$	miscible	0.762

The relative enrichment factor (REF) was defined as the ratio between the amount of extracted analyte by SPME-LPME with PDMS fiber (three phase extraction) and the amount of extracted analyte by SPME with PDMS fiber (two phase extraction) at equilibrium. The REF was 200 with dichloromethane and 73 with trichloromethane. Consequently, dichloromethane was selected as organic solvent in this experiment.

The effect of the dichloromethane volume was also investigated. Experiments were performed with different volume of dichloromethane. Figure 1 shows the influence of the volume of dichloromethane added in 12 mL of aqueous sample on the peak area of clopyralid. The peak area is direct proportional with the amount of clopyralid extracted by SPME-LPME. The first point of the graph is for extraction without organic solvent when a simple SPME occurred. The amount of clopyralid extract by simple SPME is extremely low because the fiber sorbent is non-polar and clopyralid is a relative polar compound. By increasing the volume of dichloromethane from zero to its half solubility limit, the extracted amount of clopyralid by PDMS fiber is practically constant at a very low value. Dichloromethane has the solubility limit of 126 µL in 12 mL of water at 20°C (Table 1). Increasing the volume of dichloromethane over its half solubility limit, the extraction efficiency increased slowly until its solubility limit and then increased rapidly to a maximum. This was

corresponding to the formation of the small drops of dichlormethane which extracted clopyralid and then adhered to the surface of PDMS. The optimum volume of dichloromethane is around the maximum point of the graph (200 ± 10 µL). Consequently, 200 µL dichloromethane in 12 mL of aqueous sample was used as extraction solvent.

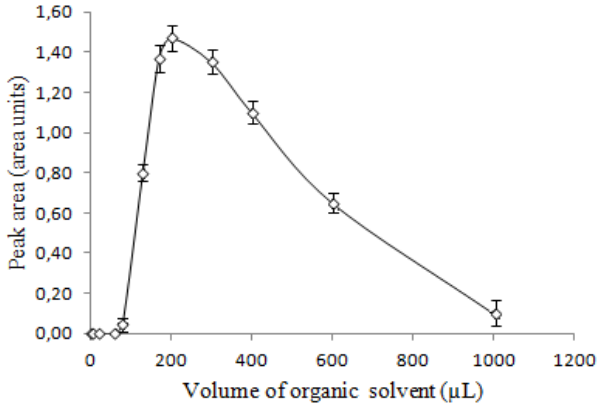

Fig. 1. Influence of the volume of organic solvent on the amount of clopyralid extracted by LPME–SPME. Conditions: extraction time 10 min; concentration of 3.30 µg L^{-1} at pH=1; temperature of 20˚C; stirring rate of 500 rpm; sample volume of 12 mL.

3.2. Influence of the disperser solvent

The disperser solvent is an organic solvent that is miscible in extraction solvent and also in aqueous sample. The disperser solvent should have no interference with the analyte peak in chromatogram. Acetone and methanol have these abilities and were selected for this purpose. By addition of the disperser solvent in aqueous sample with extraction solvent, it was generated a cloudy solution of tiny droplets. This cloudy state was stable for a long time.

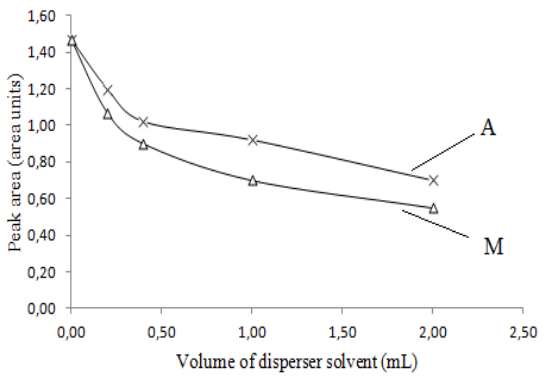

Fig. 2. The influence of the volume of disperser solvent (A-acetone; M-methanol) on the amount of clopyralid extracted by LPME–SPME. Conditions: 200 µL of dichloromethane. For other conditions see Fig. 1.

Figure 2 shows that increasing the volume of acetone and methanol added to sample solution in the presence of dichloromethane as extraction solvent, the peak area of clopyralid decreases for both disperser solvents. The amount extracted in the presence of methanol is less. The first point of the graph is for extraction with dichloromethane without disperser solvent. A possible explanation of this decrease could be the influence of the relative polarity of the disperser solvents on the solubility of clopyralid in the extraction solvent and on the thickness of the layer of extraction solvent on the surface of SPME sorbent. We found that the solubility of clopyralid at 20°C in methanol (10.5 g/100g) is less than in acetone (15.8 g/100g). Therefore, the partition coefficient is less with methanol, generating a smaller amount of extracted clopyralid in the presence of this disperser solvent. PDMS is non-polar and the presence of the disperser solvent with high polarity will lower the extraction solvent affinity for PDMS sorbent. Methanol has a higher polarity compared to acetone and its adherence to the surface of PDMS is less. Consequently, the layer of extraction solvent becomes thinner with methanol and the amount extracted less. This results show that the disperser solvents have no favorable effect in SPME assisted by droplets-based LPME of clopyralid and were not used further for method validation.

3.3. Effect of pH

The pH value of the sample solution affects the protonation equilibrium of the acidic analyte and has a main effect on the extraction efficiency because can influence the clopyralid solubility in the organic solvent. The ionized form of clopyralid is less soluble in organic solvents. Clopyralid[15] has pKa = 2.01. When the pH is low, the acid-base equilibrium for clopyralid shifts toward the neutral form and clopyralid becomes soluble in dichloromethane. The pH effect on extraction was studied within the range of 1-9. The pH values higher than 9 may destroy the PDMS fiber. The pH sample solution was adjusted with solutions of HCl and NaOH using a pH-meter. The results can be seen in Figure 3. In the pH range within 6 and 9, clopyralid is totally ionized form and is not extracted. From pH 5, the clopyralid equilibrium is shifted to neutral form. At this pH value, the presence of the salts had an insignificant influence on the extraction process because in the sample solution are already the ions from the dissociation of the acid. Moreover, an acid pH can release clopyralid from any type of chemical combination of the matrix. The best extraction efficiency was obtained at pH=1 and this pH value was chosen in the all experiments. The 7-µm chemically bonded PDMS fiber is a cross-linked polymer that has been chemically bonded to the surface of the silica fiber. Such a material is not affected by immersion in concentrated hydrochloric acid[21]. No change was observed in the extraction efficiency and in the PDMS sorbent surface at a microscopic inspection, even after 150 extractions. Polar and chemically unbounded sorbents are not stable in the presence of dichloromethane and at pH=1.

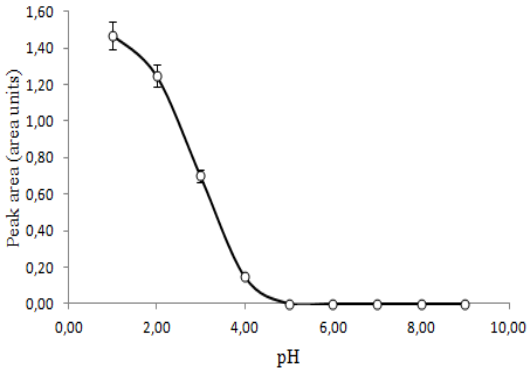

Fig. 3. Influence of the sample solution pH on the amount of clopyralid extracted by LPME–SPME. Conditions as in Fig. 2.

3.4. Method validation

Quantitative evaluation in the proposed microextraction method was carried out by the external standard method[22] under optimal conditions using GC–MS. The optimal experimental conditions selected for the validation of the method performance were 12 mL of aqueous sample, 200 µL dichloromethane, 500 rpm, 20°C, pH = 1, and 10 min as extraction time.

The method was validated in terms of reproducibility, linearity, limit of detection and limit of quantification. The reproducibility, expressed as relative standard deviation (RSD), was studied for five replicate experiments with clopyralid concentration of 3.30 µg L^{-1} and was 14.65%. This high RSD value is caused by the tailing of the chromatographic peak because the analyte was not derivatized. The linearity of the method was tested in the range of 1.0-10.0 µg L^{-1} and is satisfactory with correlation coefficient of 0.978. The limits of detection (LOD) and quantification (LOQ) were experimentally estimated from the injections of standard solutions serially diluted until the signal-to-noise ratio for clopyralid reached a value of 3 for LOD and 10 for LOQ[17]. The LOD was 0.02 µg L^{-1} and LOQ was 0.07 µg L^{-1} for a 7-µm immobilized PDMS fiber. Due to the presence of the organic phase, the LOD by SPME-LPME is 207 times higher than by simple SPME, which had a LOD of 4.2 µg L^{-1}.

The recovery of the method was verified by the analysis of real samples of groundwater and river water spiked with known amounts of analytes at optimal experimental conditions. The recoveries, defined as the ratio between concentration of analyte found to concentration of spiked analyte of the samples are presented in Table 2. The recoveries for the spiked real samples are good and varied between 89.7% and 92.2%. Clopyralid was not found in blank samples. No significant difference was found in the recoveries obtained for groundwater and river water. These results demonstrate that the matrix of groundwater and river water had little effect on the quantitative analysis with this method.

Table 2. Recoveries obtained in the analysis of clopyralid by SPME-LPME from spiked groundwater and river water samples.

Sample	Spiked quantity (µg L^{-1})	Found Concentration (µg L^{-1})	Recovery (%)
Groundwater	0.00	0.00	n/a
	2.00	1.82	91.06
	5.00	4.55	90.82
Riverwater	0.00	0.00	n/a
	2.00	1.82	90.98
	5.00	4.57	89.44

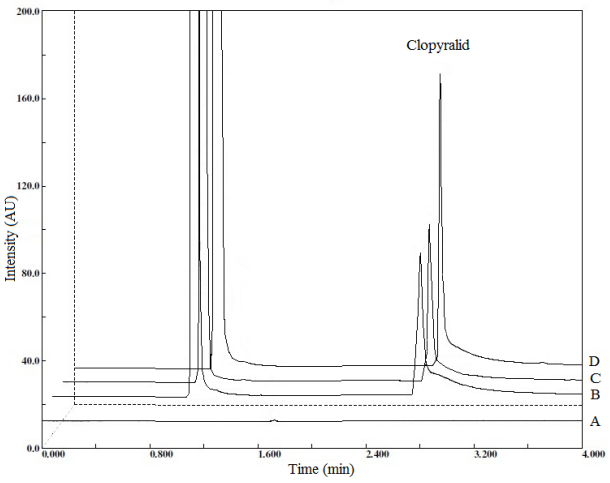

Fig.4. GC-MS total ion current chromatograms of clopyralid in aqueous solution. (A) SPME, (B) SPME-LPME with methanol as disperser solvent, (C) SPME-LPME with acetone as disperser solvent, (D) SPME-LPME without disperser solvent. Conditions in Experimental Section.

Figure 4 shows four overlayed GC-MS chromatograms of clopyralid extracted from aqueous solutions in different conditions. We compared the SPME assisted by droplets-based LPME with simple SPME and SPME assisted by dispersive liquid-liquid microextraction (DLLME) in order to see when SPME has the highest efficiency. The first peak is very broad and is given by solvent. Clopyralid has the highest peak in chromatogram (D) when the extraction was performed by SPME assisted by LPME with droplets of dichloromethane and without disperser solvent. In chromatogram (C) and (B), the peak area lowered by addition of acetone and methanol, respectively, as disperser solvent to SPME-LPME. Chromatogram (A) was performed by simple SPME with 7-µm immobilized PDMS fiber and a very small amount of clopyralid was extracted. Similar results than in chromatogram (A) were obtained for simple SPME with 100-µm PDMS without organic solvent. The 100-µm PDMS fiber has a higher volume than 7-µm immobilized PDMS fiber and therefore theoretically a higher recovery. However, since clopyralid without derivatization is practically not soluble in PDMS, the extracted amounts of clopyralid are practically very

similar. Consequently, SPME with PDMS for analysis of polar compounds as clopyralid in water can be performed only assisted by LPME.

4. Conclusion

SPME with PDMS fiber assisted by LPME with droplets of organic solvent was developed in this study as an approach for preconcentration of a polar compound as clopyralid in aqueous samples prior to GC-MS analysis. The results of the SPME assisted by LPME with droplets of organic solvent were compared to simple SPME and to DLLME achieved by addition of a disperser solvent. DLLME decreased the amount of extracted analyte. This decrease could be generated by the influence of the disperser solvent polarity on the solubility of the analyte in the extraction solvent and on the reduction in affinity between extraction solvent and PDMS fiber. The relative enrichment factor for SPME-LPME method was 200 times higher than for simple SPME. Consequently, the LOD for the proposed method was 0.02 μg L^{-1} and for simple SPME was 4.2 μg L^{-1}. The method was reproducible and linear over a wide range. The recoveries were good. The volume of organic solvent was very low (ca. 17 μL for 1 mL of sample solution). This study demonstrated that SPME with bonded PDMS fiber assisted by LPME with droplets of organic solvent is a simple, fast, and convenient approach for sample preparation of polar compounds as clopyralid in water samples.

Notes and references

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