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Stir membrane liquid–liquid microextraction

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ABSTRACT

In this article, a novel liquid phase microextraction technique, called stir membrane liquid–liquid microextraction (SM-LLME), is presented. The new approach combines the advantages of liquid phase microextraction and stirring in the same unit allowing the isolation and preconcentration of the analytes in a simple and efficient way. In the construction of the unit, a polymeric membrane is employed to protect the small volume of the extractant phase. The extraction technique is characterized for the resolution of a model analytical problem: the determination of five selected chlorophenols in water. A two-phase extraction mode is used for the extraction of the analytes with an organic solvent in which an in situ derivatization reaction takes place. The analytes are finally analyzed by gas chromatography/mass spectrometry. All the variables involved in the extraction process have been clearly identified and optimized. The new extraction mode allows the determination of chlorophenols with limits of detection in the range from 14.8 ng/L (for 2,4,5-trichlorophenol) to 22.9 ng/L (for 3-chlorophenol) with a relative standard deviation lower than 8.7% (for 2,6-dichlorophenol).

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1. Introduction

The usefulness of membranes for analytes separation, isolation, pre-concentration as well as for the clean-up of complex samples prior to their analysis has been widely described. In this context, polymeric membranes have been extensively used taking into account their high surface to length ratio, availability, wide chemical composition (covering different polarities) and formats (flat sheet, hollow fiber and bag) [1,2]. The use of a hydrophobic membrane for phases separation offers an alternative approach for the application, and even the extension, of the liquid–liquid extraction (LLE) and liquid phase microextraction (LPME) principles [3,4], allowing the proposal of efficient and automated sample pre-treatment techniques, such as supported liquid membrane extraction (SLME) and micro-porous membrane liquid–liquid extraction (MMLLE).

SLME [5–7] is based on a three-phase system with an organic solvent immobilized in the pores of a porous-membrane that acts as a physical barrier between two aqueous phases (the sample and the acceptor phase). The technique, earlier described for industrial applications, was suggested for sample pretreatment by Audunsson [8]. SLME offers high selectivity by obtaining very clean extracts, as well as high enrichment factors, reducing the consumption of organic solvents at the same time. Due to the nature of the acceptor phase, SLME can be easily coupled to conventional analytical techniques like liquid chromatography, electrophoresis and spectroscopy [9,10]. For gas chromatographic analysis, MMLLE is preferred since it is based on a two-phase format where an aqueous phase (the donor) and an organic phase (the acceptor) are separated by a non-porous hydrophobic membrane [11]. This approach has demonstrated possibilities for automation, low solvent consumption, no emulsion formation and greatly reduction of manual labor [12,13].

In the LPME context, Pedersen–Bjergaard and Rasmussen introduced the use of polymeric membranes in 1999 by the description of the hollow-fiber based LPME (HF-LPME) technique [14]. HF-LPME emerged to improve the stability and reliability of LPME. A hollow porous polypropylene fiber of minimal dimensions is then proposed as the container of the acceptor phase. HF-LPME can operate in two different modes depending on the phases involved in the extraction [15,16]. In the two phase mode, the organic extractant is located in the lumen and the pores of the hollow fiber which is immersed in the sample. This mode is mainly used for the extraction of hydrophobic compounds. In the three phase mode, an organic solvent is located in the pores of the fiber acting as a barrier between the sample and the aqueous extractant. This mode is mainly employed for hydrophobic but ionizable compounds since the extraction takes place due to the pH gradient established at both sides of the membrane. Despite its usefulness, HF-LPME develops under passive diffusion which negatively affects to the extraction recovery. In order to improve the kinetics of the extraction process, Pedersen-Bjergaard et al. have proposed a new technique, electrokinetic membrane extraction (EME), based on the electrokinetic migration across a SLM as a result of the application of an

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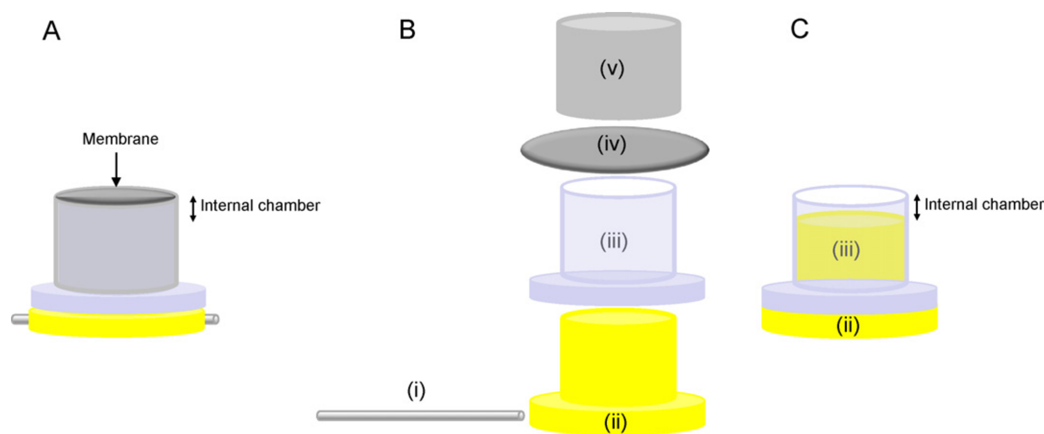

Fig. 1. Description of the extraction device (A) and the main elements employed in its construction (B): (i) iron bar; (ii) a PTFE top-cap; (iii) an internal part; (iv) PTFE membrane and (v) external element. (C) Detail of the combination of elements (iii) and (ii) where the chamber for the extraction solvent is highlighted.

external electrical field [17]. One of the electrodes is placed in the sample while the other electrode is located in the acceptor solution inside the lumen of the fiber. Charged analytes in the sample are drawn across the SLM towards the electrode of opposite charge in the acceptor solution. In EME, the electrical field serves as the driving force for the extraction process improving extraction speed significantly.

As it is the case of any process occurring under the influence of diffusional contributions, HF-LPME is characterized by a decrease of the extraction time with the stirring rate of the sample. In 2004, Jiang and Lee proposed a new and simple solvent microextraction method named solvent bar microextraction (SBME) [18]. The organic solvent is hold within a hollow fiber with its two ends carefully sealed. The solvent bar is then placed in the aqueous solution for extraction. At the same time, the stirrer is switched on and the solvent bar tumbles freely in the aqueous solution. The extracts are finally analyzed by an appropriate instrumental technique. The results show that this technique is stable, reproducible and efficient. In the same way, Yu et al. proposed the dual solvent–stir bars microextraction technique [19] where two hollow fibers are attached to a stir bar in order to favor their agitation.

Recently, stir membrane extraction (SME) [20] has been proposed as new sample treatment technique that combines in the same device the excellent extraction capabilities of polymeric membranes and the well-known beneficial effect of stirring. SME, which is essentially based on a micro-SPE methodology followed by a solvent desorption, has been proved to be an efficient preconcentration tool combined either with chromatographic or spectroscopic techniques [21]. However, adsorption may present, in specific experimental conditions, some disadvantages over absorption such as: limited extraction capacity, incomplete desorption (due to the very strong analyte/adsorbent interaction) and displacement effects, among others [22]. For this reason, in this article a new liquid phase microextraction approach, called stir membrane liquid–liquid microextraction, is proposed for the first time. The new technique involves the advantages of LPME and stirring in the same device. The new proposal, based on a two-phase format, has been evaluated for the determination of five selected chlorophenols in waters using gas chromatography/mass spectrometry as instrumental technique. The variables involved in the extraction process were identified and conveniently optimized.

2. Experimental

2.1. Reagents and samples

All reagents were of analytical grade or better. Methanol, ethyl acetate, trichloromethane, chloroform, hexane and toluene were from Scharlab (Barcelona, Spain). The target chlorophenols (3-chlorophenol, 4-chlorophenol, 2,6-dichlorophenol, 3,4-dichlorophenol and 2,4,5-trichlorophenol) were purchased from Sigma–Aldrich (Madrid, Spain). Stock standard solutions of each analyte were prepared in methanol at a concentration of 2 g/L and stored at 4 °C. Working solutions of the chlorophenols were prepared by dilution of the stocks in Milli-Q water (Millipore Corp., Madrid, Spain) or methanol as required.

The silylating reagent, N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) (98%) was obtained from Supelco (Madrid, Spain). A working solution of BSTFA at 5% (v:v) was prepared in ethyl acetate:toluene 1:1 (v:v) for analytes extraction and derivatization.

PTFE membranes (10 μm of pore size, 100 μm in thickness) were employed for the construction of the extraction unit. The 1 mL empty SPE cartridges and PTFE top-caps, necessary to construct the extraction devices, were obtained from Supelco.

Water samples were collected in amber-glass bottles without headspace. The samples were stored in the dark at 4 °C until their analysis.

2.2. Gas chromatographic/mass spectrometric analysis

Chromatographic analyses were performed using a HP6890 gas chromatograph equipped with an HP5973 (Agilent, Palo Alto, CA) mass spectrometric detector based on a quadrupole analyzer and an electron multiplier detector. System control was achieved with an HP1701CA MS ChemStation (Agilent Technologies). Separations were carried out using a fused silica capillary column (30 m × 0.25 mm i.d.) coated with 5% phenyl–95%-methylpolysiloxane (film thickness 0.25 μm) (Supelco, Madrid, Spain). A column split ratio of 1:10 was selected for the manual injection of 2 μL using a 5 μL microsyringe (Hamilton Co., Nevada, USA). The GC column was operated at an initial temperature of 70 °C, held for 1 min, raised to 115 °C at 15 °C/min and to 155 °C at 3 °C/min, finally ramped to 300 °C at 20 °C/min and maintained at this temperature for 5 min. The quadrupole mass spectrometer detector was operated in selected ion monitoring mode, recording the following m/z ions: 185, 219 and 255. Electron impact ionization (70 eV) was used for analyte fragmentation. The MS source and quadrupole temperatures were maintained at 230 and 150 °C, respectively. The peak areas were used for quantification of individual analytes.

2.3. Extraction unit

The extraction unit, which is depicted in Fig. 1 A, was custom built from five basic elements described in Fig. 1B. These elements involve, namely: (i) an iron bar; (ii) a PTFE top-cap commercially

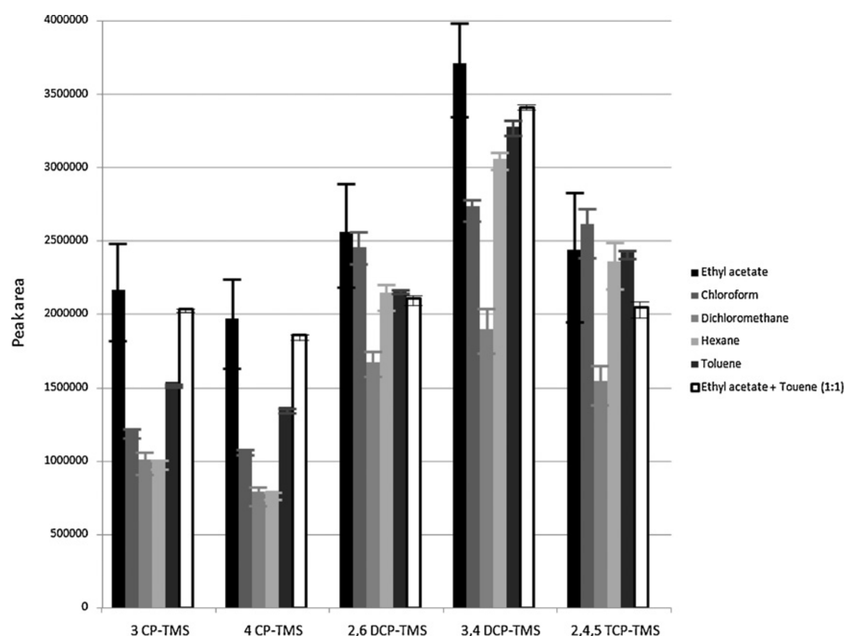

Fig. 2. Comparison of the extraction efficiency for the solvents and mixture of solvents evaluated as extractants in the SM-LLME method. Results are expressed in terms of peak area for each compound with the corresponding error bars. 3 CP, 3-chlorophenol; 4 CP, 4-chlorophenol; 2,6 DCP, 2,6-dichlorophenol; 3,4 DCP, 3,4-dichlorophenol; 2,4,5 TCP, 2,4,5-trichlorophenol; TMS, trimethylsilyl derivatives.

available for the SPE cartridges; (iii) an internal part which is the upper section of a commercial 1 mL SPE cartridge (1 cm internal diameter, 0.6 cm height); (iv) a 100 μm in thickness PTFE membrane and (v) a external element which is cut from a pipette tip (1.2 cm internal diameter, 0.5 cm height). The assembly process is outlined in Fig. 1B. First of all, the internal element (Fig. 1B(iii)) is sealed by means of pressure with the PTFE top-cap (Fig. 1B(ii)) which is previously pierced by the iron bar (Fig. 1B(i)) in order to allow the magnetic stirring. The assembly of elements (ii) and (iii) is crucial since it defines, as depicted in Fig. 1C, the internal chamber where the extraction solvent is located. Later on, the appropriate solvent is introduced in the unit and the membrane (Fig. 1B(iv)) is placed over the unit and fixed to it by displacing the external element (Fig. 1B(v)). The final unit has an internal chamber of ca. 50 μL.

2.4. Analytical procedure

The proposed extraction procedure was as follows: 30 mL of the aqueous standard or sample containing the target analytes were added to a 40-mL extraction vial and placed in a magnetic stirrer. Later on, the extraction unit, containing 50 μL of extraction mixture (ethyl acetate: toluene 1:1 v:v with a 5% of BSTFA), was introduced in the vial and stirred at 850 rpm during 30 min, the extraction of the analytes being performed. Afterward, the extraction unit was withdrawn from the solution by means of tweezers, and two microliters of the extract (accurately measured by using a 5 μL glass microsyringe which pierces the membrane) were analyzed by GC/MS.

After each extraction, the membrane can be replaced by a new one, being the system ready for the next extraction. Moreover, the unit was properly cleaned with fresh volumes of extractant. No carry-over effects between samples were observed after blank analyses.

3. Results and discussion

Recently, stir membrane extraction (SME) has been proposed as a powerful micro-solid phase extraction technique for aqueous samples. As it was previously described, under defined experimental conditions, adsorption may present some shortcomings. To face up these potential limitations a new extraction procedure, called stir membrane liquid–liquid microextraction, is presented in this article. The new approach adapts the SME device for the handling of extraction solvents, including an internal chamber to this purpose. All the variables involved in the procedure have been identified and optimized. Finally, the new extraction technique is characterized in terms of linearity, sensitivity, precision and accuracy.

3.1. Selection of the extractant

The organic solvent plays a key role in any LLE procedure. The optimum solvent should fulfil some requirements. First of all, it must have high affinity for target compounds in order to isolate them from the sample matrix. Moreover, it should be chemically compatible with the membrane employed and it should have a low solubility in water to prevent losses during the extraction. Finally, its compatibility with the instrumental technique must also be taken into account. On the basis of these considerations, hexane, ethyl acetate, toluene, dichloromethane and chloroform (containing in all cases a 5% v:v of BSTFA) were tested as potential extractants. The results obtained for the extraction of aqueous standards containing the analytes at a final concentration of 50 μg/L are presented in Fig. 2. Although ethyl acetate resulted to be the best solvent in terms of sensitivity, the precision of the measurements was too low. For this reason, a mixture of the two best extractants in terms of sensitivity (ethyl acetate) and precision (toluene) was also evaluated. As expected, both analytical properties were clearly improved for the mixture of organic solvents. According to the results, ethyl acetate:toluene (1:1 v/v) was selected as the optimum extractant.

3.2. Derivatization reagent

As it is well described in literature, the derivatization of chlorophenols can improve their determination by gas chromatography. Moreover, this reaction can be exploited for the

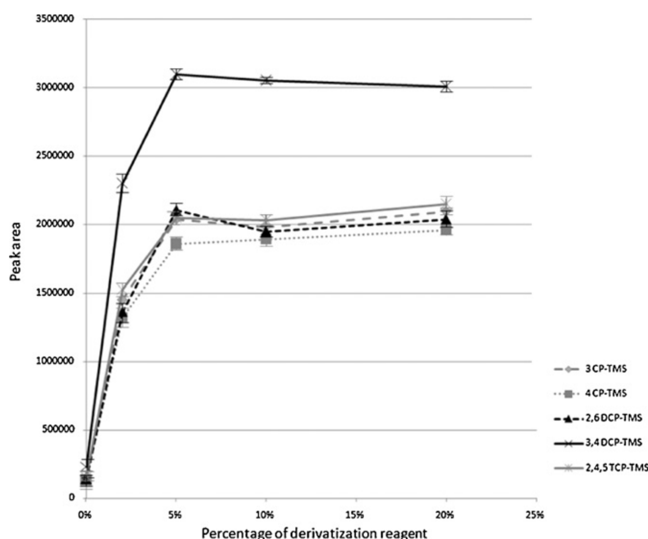

Fig. 3. Influence of the percentage of BSTFA added to the extractant on the analytical signal of the target chlorophenols. 3 CP, 3-chlorophenol; 4 CP, 4-chlorophenol; 2,6 DCP, 2,6-dichlorophenol; 3,4 DCP, 3,4-dichlorophenol; 2,4,5 TCP, 2,4,5-trichlorophenol; TMS, trimethylsilyl derivatives.

improvement of the extraction of these compounds in a LPME procedure. BSTFA is the preferred reagent for trimethylsilylation of alcohols, since it reacts replacing active hydrogens with a trimethylsilyl group. Moreover, BSTFA is more volatile than many other silylating reagents, causing less chromatographic interference. In addition, it is very soluble in a variety of organic solvents. The concentration of BSTFA in the extractant was studied in a wide range from 0 to 20%. The obtained results (see Fig. 3) show that a 5% (v:v) is enough for the complete derivatization of all the analytes.

3.3. Sample pH

The pH of the sample plays a key-role in the extraction of a given analyte since it affects to the chemical state of its ionizable groups. The effect of the sample pH was examined in a wide range (from 2.5 to 11). As expected, the worse extraction values were obtained at alkaline conditions since the analytes are in their ionic form. However, the best extraction results were obtained at neutral pH values instead of under acidic ones as it would be predictable taking into account the pKa of the target analytes. This effect has been also observed for chlorophenols in other extraction techniques [23].

3.4. Ionic strength

In LPME, ionic strength is considered a synergetic factor over the extraction efficiency by a salting-out effect. For this reason the effect of ionic strength was evaluated using sodium chloride as model electrolyte at different concentration levels, within the interval 0–25%. The results showed an increase of the extraction up to the 5% of NaCl while a decrease was observed at higher concentrations. According to Zhao et al. [24], the influence of ionic strength on the extraction can be separated into two simultaneous and different processes. On the one hand, ionic strength increases extraction by a salting out effect. In fact, when salt was added to the solution, water molecules could form hydration spheres around the ions. These hydration spheres reduce the amount of water available to dissolve the analyte molecules; thus it drove additional analytes into the organic solvent. On the other hand, phenol molecules may participate in electrostatic interactions with the salt ions in solution, thereby decreasing their ability to move into the extraction phase. These interactions are possible taking into consideration the working pH. The salting-out effect is predominant up to a concentration of 5%, while the second effect prevails at higher concentrations.

3.5. Effect of the stirring velocity and time

In general, a process occurring under the influence of diffusional contributions is characterized by an increase of the extraction rate with the stirring velocity. This variable was studied in the range from 0 to 1600 rpm using 30 min as extraction time, each point being evaluated in triplicate (see Fig. 4 A). It was found that the peak areas for all chlorophenols increased with the stirring rate from up to 900 rpm. However, at higher velocities a vortex is created directly above the extraction device reducing the contact between sample and extractant. Moreover, this vortex may also induce the evaporation of the solvent, producing a small bubble between the remaining solvent and the membrane. Both effects reduced the extraction efficiency. The membrane breakage was also observed for higher velocities. Consequently, a stirring rate of 850 rpm was chosen for the further work.

The stirring time or extraction time is also an important variable in the extraction procedure. This variable was studied in the interval 5–60 min, the results being depicted in Fig. 4B. For all the studied chlorophenols, the amount extracted markedly increases with the extraction time from 5 to 30 min while from 30 to 60 min the increase was less pronounced. The extraction time was selected as a compromise between sensitivity and sample throughput and therefore 30 min was fixed as the optimal value for further analysis.

The beneficial effects of the stirring-extraction integration in the same unit have been evaluated using the extraction time profile as parameter. This parameter was evaluated under two different conditions, namely: (a) using the proposed device and (b) using a modified device where the stirring takes place externally while the unit remains static during the extraction. For comparison purposes, the modified unit was obtained by removing from the unit body the iron wire which is employed as stirring element. The obtained results, which are similar for all the analytes, are presented in Fig. 5 for 3,4-dichlorophenol. As it can be seen, the proposed device provides superior results indicating the good performance of the integration of stirring and extraction in the same device.

3.6. Effect of the sample and extractant volumes

The enrichment factor of a given extraction technique depends directly on the volume of the donor and the acceptor phases. First of all, the sample volume was evaluated in the range from 10 to 40 mL. The extracted analytes increased in the interval 10–30 mL for all chlorophenols, remaining almost constant for higher volumes. This effect can be ascribed to the limited capacity of the acceptor phase. When higher sample volumes are employed, the acceptor organic phase can be near saturation, the extraction of the analytes being limited. According to these results, 30 mL was used for ensuing studies.

Finally, the volume of extractant was evaluated working with different extraction devices which possess variables volumes in the interval from 50 to 600 μL. As expected, the results indicated that the enrichment factors were better when lower volumes of acceptor phase were used. Therefore, 50 μL was selected as the optimum organic phase volume.

3.7. Analytical figures of merit of the proposed methodology

Once optimized, the method was characterized in terms of linearity, precision, accuracy and sensitivity. In this sense, a calibration graph for each analyte was constructed by extracting 9 working aqueous standards in triplicate containing all the analytes at concentrations in the range from 100 ng/L to 500 μg/L. For all the

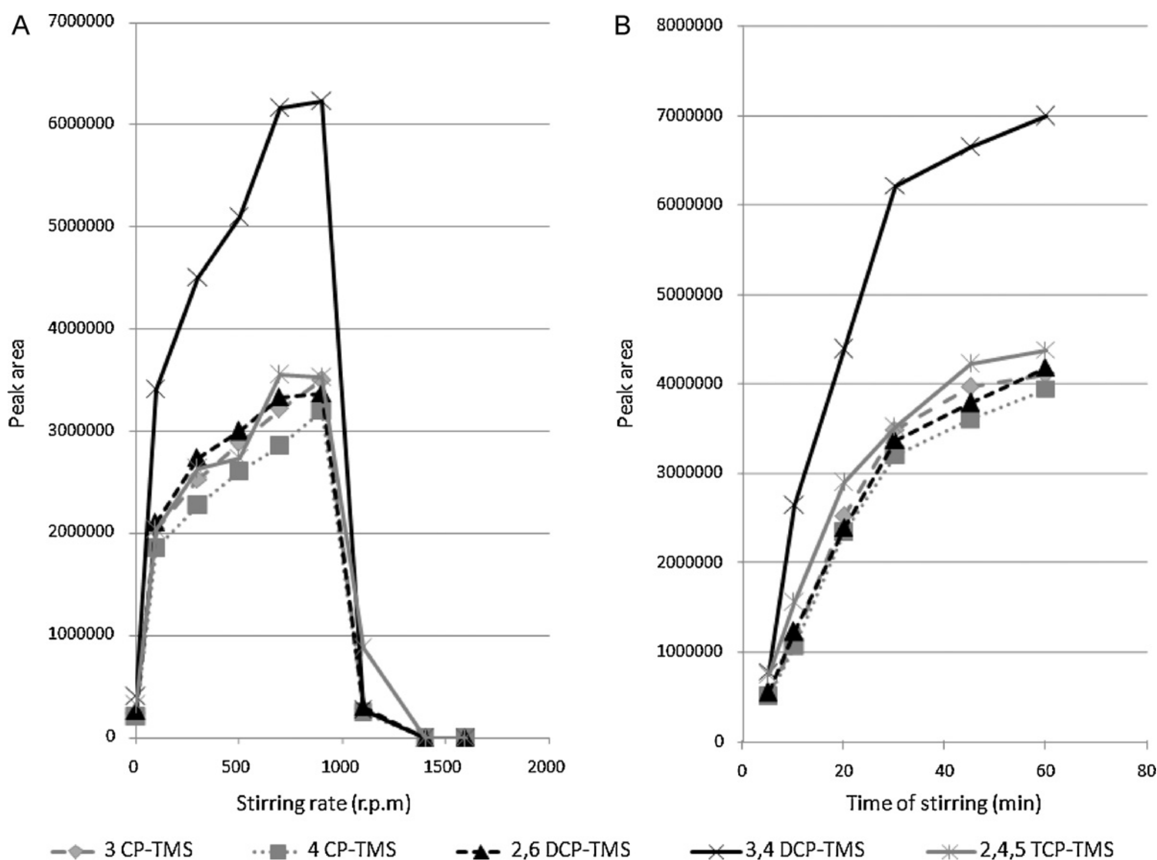

Fig. 4. Effect of the stirring rate (A) and stirring time (B) on the analytical signal of the target chlorophenols. 3 CP, 3-chlorophenol; 4 CP, 4-chlorophenol; 2,6 DCP, 2,6-dichlorophenol; 3,4 DCP, 3,4-dichlorophenol; 2,4,5 TCP, 2,4,5-trichlorophenol; TMS, trimethylsilyl derivatives.

analytes, a good linearity ($R > 0.9999$) was observed. The figures of merit are summarized in Table 1.

The method detection limit (MDL), defined by U.S. EPA, was used to estimate the minimum detectable concentration for the chlorophenols, which varied between 14.8 ng/L (for 2,4,5-trichlorophenol) to 22.9 ng/L (for 3-chlorophenol). These values were concordant with those obtained using a signal to noise ratio of 3.

The repeatability of the method (expressed as relative standard deviation) was evaluated at 100 ng/L by quintuplicate resulting to be in the range from 5.0% (for 3,4-dichlorophenol) to 8.7% (for 2,6-dichlorophenol).

The enrichment factors for all the analytes, which were obtained by comparing the calibration graphs before and after the extraction process, were in the range from 316 (for 3,4-dichlorophenol) and 166 (for 4-chlorophenol). These values highlight the good performance of the new technique.

Table 1
Figure of merit of the proposed method for the determination of chlorophenols in water.

Analyte	RSD[a]	MDL[b]	EF[c]
3-Chlorophenol	7.7	22.9	181
4-Chlorophenol	8.6	20.0	166
2,6-Dichlorophenol	8.7	15.8	296
3,4-Dichlorophenol	5.0	15.0	316
2,4,5-Trichlorophenol	7.2	14.8	246

[a] RSD, relative standard deviation expressed in percentage. Calculated for 5 aliquots at 100 ng/L.
[b] MDL, method detection limit. Expressed in ng/L.
[c] EF, enrichment factor.

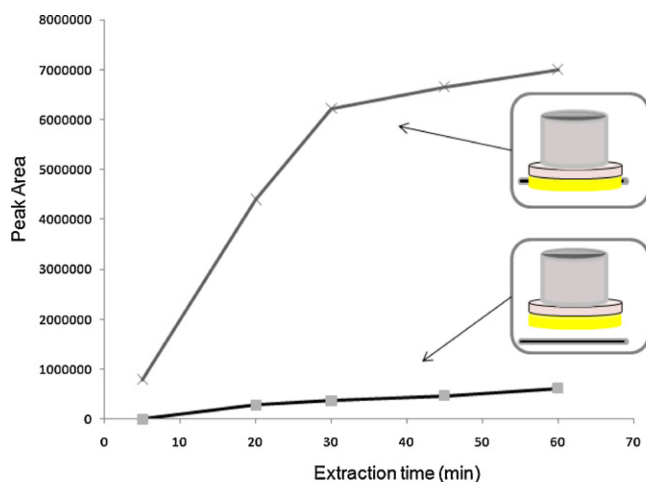

Fig. 5. Comparison of the integration of the stirring in the extraction unit versus the separate configuration. Results are presented for 3,4-dichlorophenol. For details, see text.

Table 2
Recovery study performed using different real samples spiked at a concentration level of 500 ng/L. The results are expressed as percentage ± standard deviation.

Analyte	Tap water 1	Tap water 2	River 1	River 2	River 3
3-Chlorophenol	106 ± 7	103 ± 8	111 ± 9	110 ± 8	109 ± 8
4-Chlorophenol	110 ± 8	108 ± 8	110 ± 9	115 ± 8	109 ± 8
2,6-Dichlorophenol	88 ± 8	92 ± 8	92 ± 8	96 ± 8	96 ± 7
3,4-Dichlorophenol	104 ± 5	85 ± 4	91 ± 5	81 ± 4	76 ± 4
2,4,5-Trichlorophenol	86 ± 5	104 ± 8	99 ± 7	95 ± 7	96 ± 8

Since no positive samples were found, a recovery study was performed spiking water samples with the analytes at a final concentration of 500 ng/L. The data obtained are summarized in Table 2 obtaining excellent recoveries values in all instances.

4. Conclusions

In this article, a new extraction technique, called stir membrane liquid–liquid microextraction, is presented for the first time. The proposal, which was evaluated in the two-phase LPME format, presents excellent features for analytical purposes.

All the variables involved in the SM-LLME process were considered and optimized. The method was finally characterized in terms of linearity ($R > 0.9999$), precision (RSDs lower than 8.7%), sensitivity (MDLs better than 22.9 ng/L), accuracy (mean recovery of 99%) and extraction efficiency (enrichment factors in the range from 166 to 316).

SM-LLME results to be a useful and versatile technique for the extraction of analytes of different nature being easily coupled to conventional chromatographic techniques like GC. Further investigations will be focused on the improvement of the design and the extension of the applicability of the technique into the three-phase LPME mode.

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