Monolithic capsule phase microextraction prior to gas chromatography-mass spectrometry for the determination of organochlorine pesticides in environmental water samples

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Abstract: In this study, a capsule phase microextraction (CPME) protocol followed by gas chromatography-mass spectrometry is proposed for the accurate and sensitive monitoring of organochlorine pesticides (OCPs) in environmental water samples. Different monolithic sol-gel encapsulated sorbents were compared and monolithic sol-gel poly(ethylene glycol)-based sorbent incorporated into porous microextraction capsules resulted in the highest extraction efficiency. Following the selection of the microextraction device, the CPME conditions were optimized, while linearity, limits detection (LODs), limits of quantification (LOQs), accuracy and precision were the figures-of-merit measured. Under optimum conditions the LODs for the OCPs ranged between 0.01 ng mL^{-1} and 0.03 ng mL^{-1}. The relative standard deviations were better than 5.3% and 9.2% for intra-day and inter-day study, respectively. The relative recoveries ranged between 90.5-105.2% (intra-day) and 93.0-105.0% (inter-day), demonstrating good method trueness. Finally, the proposed protocol was implemented for the monitoring of OCPs in tap, river, pond, and lake water. The developed method presents better analytical features than existing methods.

Keywords: Organochlorine pesticides; capsule phase microextraction; water; sample preparation, GC-MS, monolithic sorbents

1. Introduction

Pesticides are used in agriculture to repel, prevent, mitigate, or destroy pests [1]. They are classified into different types including insecticides, herbicides, nematicides, rodenticides, fungicides, molluscicides and plant growth regulators [2]. Pesticide residues may constitute a significant source of contamination for the environment since they can be present in air, water and soil [3]. Nowadays, water resources pollution because of the uncontrolled use of pesticides represents a significant environmental and health threat. In order to be able to design and implement strategy plans for environmental and human health protection, the estimation of the type and amount of pesticide residues in water resources is crucial [4].

Organochlorine pesticides (OCPs) are a class of pesticides used for controlling vector-borne diseases (e.g., typhus and malaria) and to destroy pests due to their low cost and high efficiency [5,6]. These compounds were the first major pesticide class that was produced on large scale since the rapid growth of the pesticide industry in the late 1940's [7]. Because of their chemical stability, their high persistence in the natural environment and their low biodegradability, OCPs are ubiquitous among environmental, food and biological samples [3,8]. These compounds are responsible for a wide variety of adverse effects including damages to the human nervous system, cancer predisposition, reproductive disorders, and disruption of the cellular immune system. As a result, their use has been banned by the United Nations Environment Program, while they have been also listed as persistent organic pollutants by the Stockholm Convention [3,9]. Moreover, OCPs have been reported to be toxic by both the World Health Organization (WHO) and the Environmental Protection Agency

(EPA) [8]. The toxicity of these pollutants is clearly related to their chemical structure [5]. Although the use of OCPs has been banned in most industrialized advanced countries and their production has been terminated, their lasting and adverse influence on aquatic biota, human health and wildlife still causes concerns regarding the monitoring of the levels of these compounds in environmental samples [10].

The main difficulties of the determination of these analytes in real-world samples are related to their low concentrations, the sample complexity, and the potential presence of a wide range of interfering compounds. Therefore, an extraction and enrichment step is typically required prior to the determination of the OCPs using an instrumental analytical technique [11,12]. Conventional approaches for the extraction of OCPs include liquid-liquid extraction (LLE) and solid-phase extraction (SPE) that show high consumption of hazardous organic solvents, increased number of complex steps and high waste generation [13].

After the introduction of Green Analytical Chemistry (GAC) [14] that aims to provide the principles for developing of more sustainable and environmentally friendly methodologies, SPE and LLE tend to be progressively replaced by microextraction approaches. Thus, several novel methodologies including solid phase microextraction [15], dispersive solid-phase extraction (d-SPE) [16], magnetic solid-phase extraction (MSPE) [10], fabric phase sorptive extraction (FPSE) [17], stir bar sorptive extraction (SBSE) [18], dispersive liquid-liquid extraction [19] and hollow fiber-liquid phase microextraction [20] have been proposed for the accurate and sensitive monitoring of OCPs in a wide range of samples. An interesting technique that was recently proposed for the monitoring of pesticides in environmental water samples is capsule phase microextraction (CPME) [21].

In CPME, the analytes are extracted by appropriately designed devices that are made of two permeable microporous polypropylene tubes welded together to form a single, bipartite microextraction capsule. One polypropylene capillary tube contains a sol–gel hybrid organic–inorganic sorbent, while the other capillary tube contains a cylindrical magnet that provides to the device the ability to spin when a magnetic field is implemented [22]. The integration of sample stirring can efficiently simplify the extraction procedure to a large extent, while it prevents potential loss of analytes due to their retention on external devices and it results in increased extraction yield [23]. Moreover, the polypropylene membranes exhibit inherent porosity and thus the capsules can be directly employed for the analysis of sample matrices containing insoluble matrix interferants, debris and particulates, without any requirement of sample pretreatment (i.e., filtration) [21]. CPME is based on equilibrium extraction and due to the integration of the stirring mechanism, rapid extraction kinetics can be obtained [24]. An important characteristic of CPME is the utilization of sol-gel technology to prepare hybrid organic–inorganic porous products of various shapes, sizes, and formats. Sol-gel sorbents exhibit good chemical and thermal stability, selectivity, tunable porosity and high purity resulting in the fabrication of powerful microextraction devices [25].

In this work, we aimed to develop a simple and rapid method for the determination of ten OCPs in water samples by CPME combined with gas chromatography-mass spectrometry (GC-MS). Various monolithic sol-gel coated microextraction capsules were evaluated for their performance. Subsequently, the CPME procedure was optimized to ensure that the highest possible extraction efficiency is obtained. After method optimization, the CPME GC-MS protocol was validated. As a final step, the validated methodology was applied for the monitoring of OCPs in different environmental water samples.

2. Experimental

2.1. Reagents and chemicals

Acetonitrile and methanol of LC-MS grade were obtained from Honeywell (Charlotte, North Carolina, USA). HPLC grade acetone (ACE) and reagent grade NaCl were obtained from Merck (Darmstadt, Germany). α-HCH (99.9%), β-HCH (98.4%), γ-HCH (99.7%), alachlor (99.3%), aldrin (98.5%), p,p’-DDE (99.8%), o,p’-DDD (99.9%), p,p’-DDD (99.9%) and methoxychlor (98.7%) were obtained from Supelco (Bellefonte, PA, USA). o,p’-DDE (99.39%) was obtained from Dr. Ehrenstorfer GmbH (Augsburg, Germany). The structures of the target analytes are summarized in Figure S1. Stock solutions (c=1000 mg L^{-1}) for all analytes were prepared in methanol. Multi-analyte working solutions were prepared daily with appropriate dilution in methanol.

Capsule phase microextraction devices were built using Membrana Accurel® porous capillary membranes, which were purchased from 3M Inc. (St. Paul, MN, USA). Cylindrical magnetic rods (1/4” x 1/16”) were purchased from K&J Magnetics Inc. (Pipersville, PA, USA). Sol-gel synthesis materials, namely methyl trimethoxysilane (MTMS), tetramethyl orthosilicate (TMOS), poly(tetrahydrofuran) (PTHF), and polyethylene glycol 300 (PEG 300), were obtained from Sigma-Aldrich (St. Louis, MO, USA). Poly(dimethylsiloxane) (PDMS), octadecyltrimethoxysilane (C_{18}), poly(dimethyldiphenylsiloxane) (PDMDPS) were obtained from Gelest Inc. (Morrisville, PA, USA). Ammonium hydroxide, methylene chloride, isopropanol, and hydrochloric acid were purchased from Fisher Scientific (Milwaukee, WI, USA).

Environmental water samples (*i.e.*, lake, river, pond and tap water) were collected in Vienna, Austria. Amber-glass vials with no headspace were used for sample collection and storage. All samples were stored at 4ºC, while no sample pretreatment was required prior to the CPME GC-MS procedure.

2.2. Instrumentation

A Shimadzu GC-2010 instrument coupled to a QP2010 Plus mass spectrometer (Shimadzu, Kyoto, Japan) was used for the quantification of the OCPs. Separation was achieved using Helium (99.999%) as mobile phase that was delivered at a flow rate of 1.00 mL min^{-1}. Constant linear velocity was employed as flow control mode. An Rtx-5MS (30 m × 0.25 mm, 0.25 μm) column (Restek Corporation, Bellefonte, PA, USA) was used under the following oven temperature program: 100 °C initial temperature (hold time: 2.5 min), increased to 200 °C (rate: 15 °C min^{-1}), then increased to 250 °C (rate: 5 °C min^{-1}) and finally increased to 300°C (rate: 6 °C min^{-1}). The run time and the solvent delay were 27.5 min and 7.0 min, respectively. The injector temperature, the ion source temperature and the interface temperature were 280°C, 220°C and 250 °C, respectively. The injection volume was 2 μL and high-pressure injection (450 kPa) took place. Finally, the OCPs were quantified at the selected ion monitoring (SIM) mode. For each analyte, one target ion was used as quantifier, while two reference ions were used as qualifiers. Table S1 shows the recorded *m/z* ratios for each analyte, as well as their respective retention times.

The CPME procedure was carried out using a magnetic stirrer (Heidolph Instruments GmbH & CO, Schwabach, Germany).

2.3. Preparation of sol-gel monolithic sorbent encapsulated CPME devices

CPME devices with built-in magnet and encapsulated sol-gel PDMS, sol-gel C18, sol-gel PEG 300, sol-gel PTHF and sol-gel PDMDPS monolithic sorbent beds were prepared using a simple protocol which is illustrated in Figure 1.

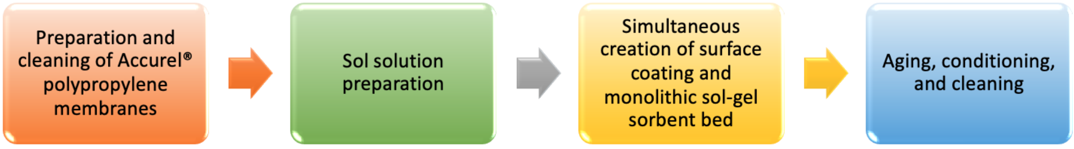

Figure 1. Preparation of the sol-gel monolithic sorbent encapsulated CPME devices

Environmental samples can be collected in large volumes and the target analytes are often at very low concentration levels. As such, a higher sorbent loading is needed to accomplish higher method sensitivity. Thus, CPME media of 3 cm length were used. The synthetical route for the fabrication of the microextraction capsules is described in Supplementary Material.

2.4 CPME procedure

Initially, the CPME capsules were immersed into a vial containing 2 mL of MeOH mixture for 5 min to remove impurities that remained from the material preparation. Accordingly, the capsules were rinsed with water.

Following the activation step, the pre-treated CPME capsules were immersed into 20 mL of sample solution containing 5% *w/v* NaCl and adsorption was carried out within 50 min under stirring at 800 rpm. Following this step, the supernatant was discarded, and the capsule was rinsed with water and dried using lint free tissue. The adsorbed OCPs were eluted by placing the CPME media into Eppendorf tubes containing 250 μL acetone. Finally, the capsules were recovered, and eluent filtration was performed using 0.22 μm polytetrafluoroethylene (Frisenette ApS, Knebel, Denmark). Then, 2 μL was analyzed by GC-MS system. Figure 2 shows a representative chromatogram of a blank river water sample (a) and a spiked river water sample (b) subjected to the herein described protocol.

The monolithic sol-gel PEG 300 CPME device used was immersed in the initial mixture of ACN: MeOH (50:50 v/v) for 5 min. The utilization of the initial solvent mixture meets the requirements of GAC regarding material recycling and reusing [26]. Following this procedure, no carry-over effects were observed. After washing, the clean capsules were left to dry at ambient temperature, and they were stored in airtight sealed vials.

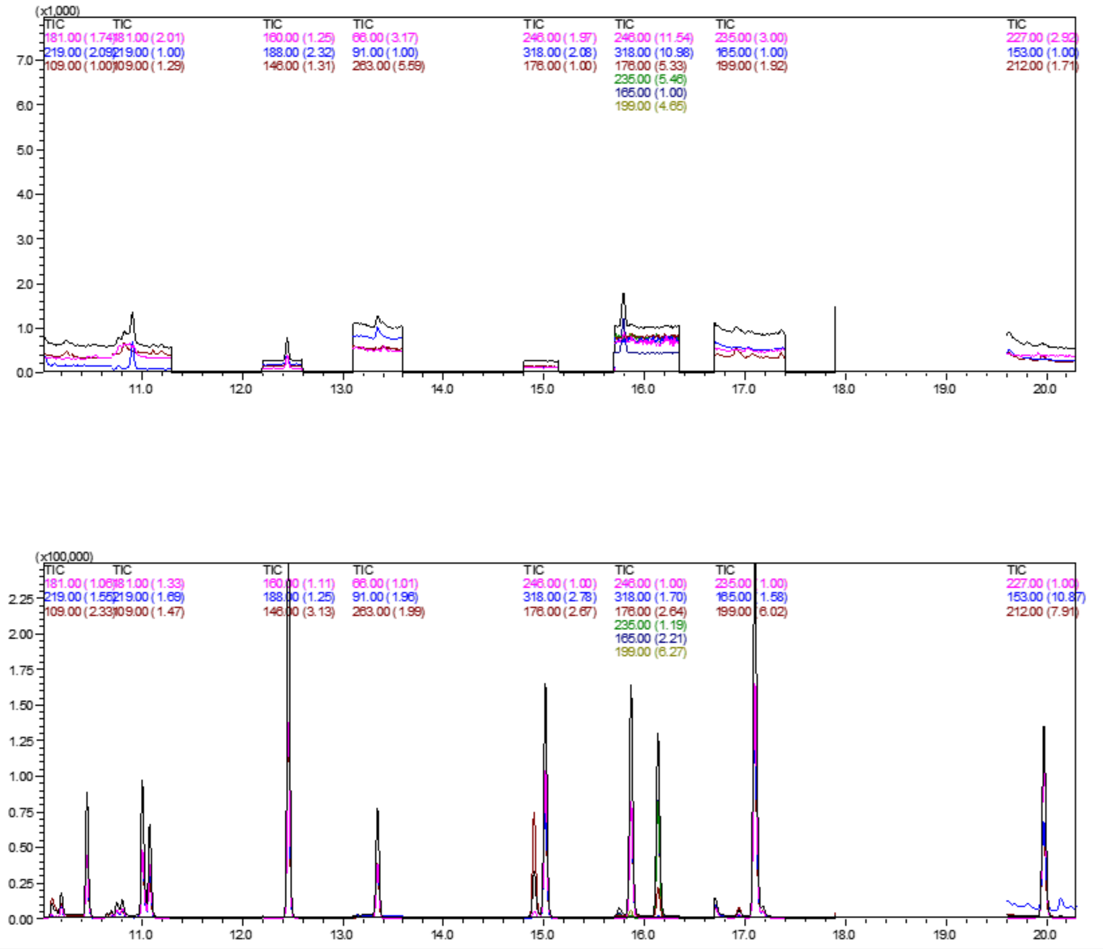

Figure 2. Chromatogram of (a) a blank river water sample and (b) a spiked river water sample (c=20 ng mL^{-1}) after their sample preparation using the monolithic sol-gel PEG 300 CPME device

3. Results and discussion

3.1 Characterization of the CPME media

The characterization of the CPME media by scanning electron microscopy and Fourier transform infrared spectroscopy has been previously conducted [27], with the aim of investigating the functional makeup of the sol-gel sorbents and the surface morphology of the sol-gel sorbent.

3.2 Optimization of CPME method

3.2.1 Selection of sol-gel coated microextraction capsule

Initially, five monolithic sol-gel coated capsules were evaluated to assess the performance of different sorbents and to select the material with the highest affinity towards the target analytes. The examined sorbents were sol-gel PDMS, sol-gel C$_{18}$, sol-gel PEG 300, sol-gel PTHF and sol-gel PDMDPS. As shown, in Figure S2, sol-gel PEG 300 showed the best extraction performance towards the majority of the examined analytes. Higher extraction efficiency was observed for aldrin, o,p’-DDE and p,p’-DDE, only in the case of sol-gel PDMS. However, this sorbent exhibited significantly lower extraction efficiency for α-HCH, β-HCH and γ-HCH and thus, further experiments were conducted using sol-gel PEG 300 as a compromise for all the analytes.

3.2.2 Optimization of the adsorption step

To ensure high extraction efficiency of the OCPs from the water samples, the experimental parameters that influence the performance of the adsorption step (*i.e.*, the stirring rate, the sample volume, the extraction time, and the salt content) were examined under a univariate approach. A spiked water sample solution (c=10 ng mL^{-1}) was used in the optimization study. Table S2 summarizes the experimental conditions before and after the optimization study.

The effect of stirring rate was primarily investigated because it affects the analyte diffusion. For this purpose, four different stirring rates (*i.e.*, 0, 400, 800, and 1000 rpm) were studied. According to the mass transfer theory, sample agitation is important to assist the movement of the analytes to the sol-gel sorbent surface with a reduction in the thickness of the boundary layer in order to shorten the thermodynamic equilibrium time [17]. As shown in Figure S3, sample stirring is critical for the adsorption of the OCPs. Under no stirring (i.e., 0 rpm) negligible adsorption was achieved. The performance of the CPME method increased at 800 rpm for most analytes and it remained constant up to 1000 rpm. Thus, a stirring rate of 800 rpm was chosen.

Accordingly, the sample amount was studied using three different volumes, *i.e.*, 10 mL, 20 mL and 50 mL (Figure S4). A reduction of the extraction recovery was observed by increasing the sample volume from 10 mL to 50 mL. However, the utilization of 10 mL of sample results in lower preconcentration factors (PF) and thus in reduced method sensitivity, Therefore, an amount of 20 mL was used in the CPME method as a compromise between the extraction efficiency and the overall method sensitivity.

The extraction time is an significant factor in equilibrium-based techniques [28]. The extraction time was studied from 10 to 60 min (Figure 3). Equilibrium was achieved at 40 min for aldrin, alachlor, o,p’-DDE, p,p’-DDE, o,p’-DDD and p,p’-DDD while 50 min were required for α-HCH, β-HCH, γ-HCH and methoxychlor. Thus, an extraction time of 50 min was chosen taking into consideration all the analytes.

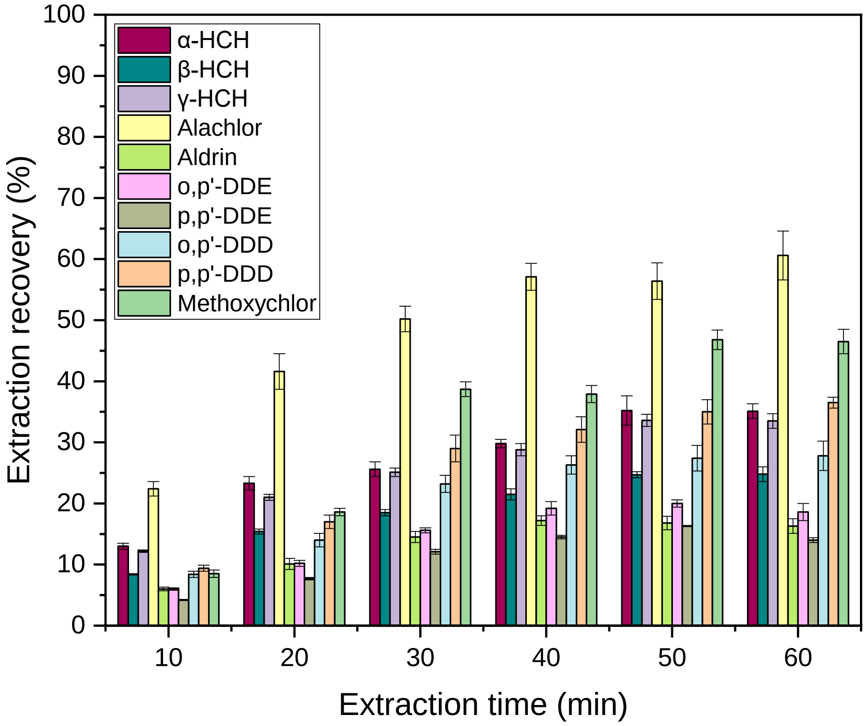

Figure 3. Evaluation of the effect of extraction times. Sample volume: 20 mL, salt content: 0% *w/v* NaCl, eluent: acetonitrile, stirring rate: 800 rpm, volume of eluent: 500 μL, desorption time: 5 min.

As a final step, the effect of salt addition was studied by adding variable concentrations of NaCl (*i.e.*, 0-20% *w/v*). An increase in the extraction recovery was observed for α-HCH, β-HCH, γ-HCH by enhancing the NaCl content up to 5% *w/v* (Figure S5). This phenomenon can be attributed to the salting-out effect, based on which, the addition of salt results in a reduction of the analyte solubility in the sample solution, favoring its interaction with the sorptive phase. However, a further increase from 5% *w/v* to 20% *w/v* had a negative impact on the extraction performance for o,p'-DDD, p,p'-DDD and methoxychlor, probably due to the reduced mass transfer of the OCPs which can be attributed to the enhancement of sample density [21]. Thus, a NaCl content of 5% *w/v* was chosen for further experiments.

3.2.3 Optimization of the elution step

The main parameters that influence the performance of the elution step (*i.e.*, type/volume of eluent and elution time) were also investigated and optimized. Different solvents were examined for their performance to elute the adsorbed analytes from the CPME device. During method optimization, ACN was used as eluent, however its use is not recommended from an environmental aspect [29]. For this purpose, MeOH and ACE were also examined, since these solvents are “preferred” organic solvents according to the Pfizer solvent selection guide [30]. Although the usage of MeOH resulted in decreased elution efficiency, ACE exhibited similar performance as ACN (Figure S6). Thus, ACE was chosen as eluent taking into consideration the principles of GAC regarding the utilization of more environmentally-friendly chemicals [14]. Accordingly, the usage of different aliquots (*i.e.*, 250 μL, 500 μL and 1000 μL) of ACE was evaluated, aiming to reduce the quantity of chemicals used in this study. In principle, it is desirable to use the lowest possible quantity of organic solvent to ensure low waste generation and low cost [14]. Meanwhile, the quantity of the solvent must be enough for the complete analyte elution and for avoiding potential carry over effects. As shown in Figure S7, an aliquot of 250 μL of ACE was sufficient for the elution of OCPs. Lower solvent amounts were not studied to ensure complete immersion of the capsule in the eluent and to ensure sufficient contact between the eluent and the sol-gel sorbent. Thus, further experiments were carried out using this quantity of solvent. Finally, different elution times were studied to ensure the development of a rapid method with high sample throughput. A time span of 2 min was sufficient (Figure 4) for the elution of the OCPs from the CPME device.

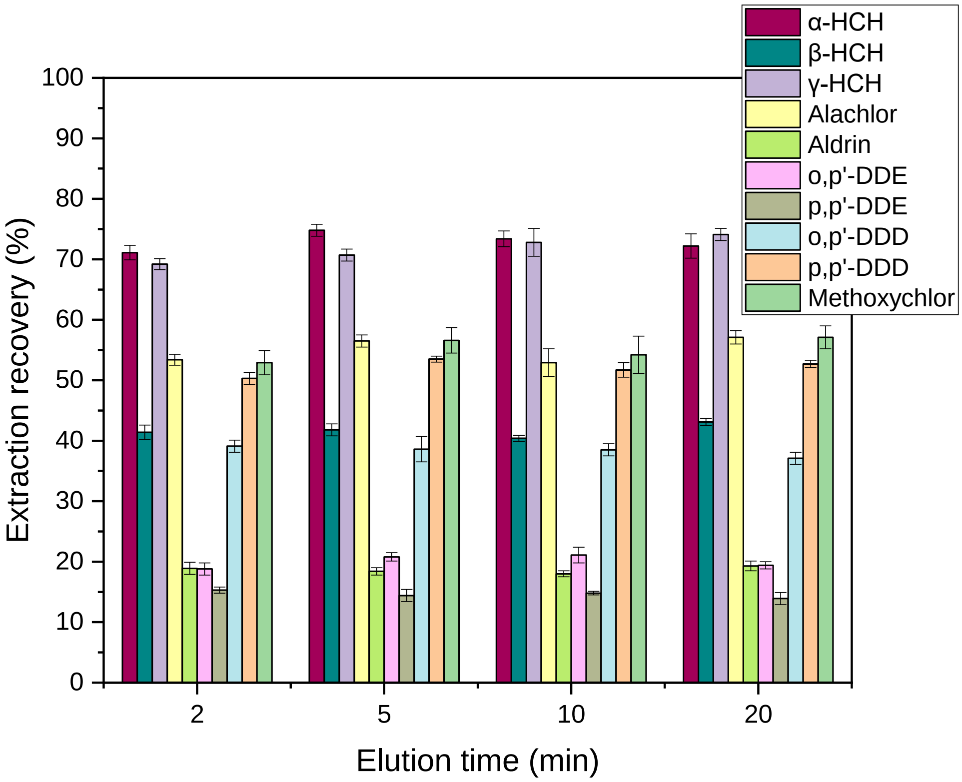

Figure 4. Evaluation of the effect of different elution times. Sample volume: 20 mL, salt content: 5% *w/v*, extraction time: 50 min, stirring rate: 800 rpm, eluent: acetone, volume of eluent: 500 μL.

3.3. Figures-of-merit

In order to assess the linearity of the proposed methodology, spiked samples were subjected to the optimum extraction protocol and linear regression analysis was performed by plotting the peak area of each analyte versus its respective concentration. For each OCP pesticide, the determination coefficient, the slope, and the intercept of the regression lines were calculated. In Table 1, the regression analysis results are presented. The coefficients of determination were 0.9939-0.9993 indicating good method linearity. The lowest point of the calibration curve for each pesticide that had a signal-to-noise ratio higher than 10 was considered to be the limit of quantification (LOQ) and the limit of detection (LOD) was the concentration that corresponded to a signal-to-noise ratio of 3 [31]. For the studied analytes, the LOD values were 0.01-0.03 ng mL^{-1} and the LOQ values were 0.02-0.10 ng mL^{-1}.

Accordingly, the preconcentration factor (PF), the enhancement factor (EF) and the extraction recovery (ER%) were calculated [32]. PFs were calculated as ratio of the sample volume (20 mL) compared to the eluent amount (250 μL). Thus, the theoretical PF for each analyte is 80. The EF values of each analyte were calculated as the ratio of the slope derived from the calibration curve of the respective analyte prior and after the CPME method. Finally, the ER% values were calculated by dividing the EF with the theoretical PF *100. As shown in Table 1, the EF values for each analyte were in the range 11.5-59.9. Finally, the ER% values were obtained by dividing the EF values by the PF values and multiplying with 100. The ER% values of the OCPs were in the range of 14.4-74.8%

Table 1. Figures-of-merit for the proposed CPME GC-MS protocol

OCP	**Regression Analysis**	**R^2**	**Linear range (ng mL^{-1})**	**LOD[1] (ng mL^{-1})**	**LOQ[2] (ng mL^{-1})**	**ER[3] (%)**	**EF[4]**
α-HCH	y = 4884.6x + 765.51	0.9993	0.05-50.0	0.02	0.05	74.8	59.9
β-HCH	y = 3808.1x + 2789.5	0.9975	0.10-50.0	0.03	0.10	41.8	52.9
γ-HCH	y = 3722.5x + 550.9	0.9991	0.10-50.0	0.03	0.10	70.7	59.4
Alachlor	y = 14054x – 1809.6	0.9989	0.05-50.0	0.02	0.05	56.5	45.2
Aldrin	y = 2887x + 2850.8	0.9939	0.05-50.0	0.01	0.02	18.4	14.7
o,p’-DDE	y = 10197x + 1204.2	0.9986	0.02-20.0	0.01	0.02	20.8	16.6
p,p’-DDE	y = 6404.8x + 1222	0.9970	0.02-20.0	0.01	0.02	14.4	11.5
o,p’-DDD	y = 5885.3x + 3022.2	0.9949	0.02-50.0	0.01	0.02	38.6	30.9
p,p’-DDD	y = 20404x + 5194.9	0.9973	0.02-50.0	0.01	0.02	53.5	42.8
Methoxychlor	y = 33202x – 11634	0.9989	0.05-50.0	0.02	0.05	56.6	45.3

[1] LOD: Limit of detection

[2] LOQ: Limit of quantification

[3] ER: Extraction recovery

[4] EF: Enhancement factor

Method accuracy and method precision was investigated by analyzing spiked samples (*i.e.*, c=2.00 and 10.00 ng mL^{-1}). For the intra-day studies, five replicate measurements (*n*=5) of each spiked concentration level were conducted in the same day, while for the inter-day studies triplicate analysis of each spiked concentration level were performed on four consecutive days (*n*=3 × 4) [33]. Method accuracy was expressed in terms of relative recovery (RR%) between the found and added concentration of each pesticide. Method precision was expressed in terms of relative standard deviation (RSD%). The results of the assessment of method trueness and method precision are summarized in Table 2. As it can be observed, the RR% values for intra-day study were between 90.5% and 105.2% and the RSD% values were less than 5.3% for all analytes. As for the inter-day study, the RR% values were 93.0% and 105.0% and the RSD% values were less than 9.2%, indicating good method trueness and precision.

Table 2. Intra-day (*n*=5) and inter-day (*n*=4 ×3) performance studies of the CPME GC-MS method

Analyte	**Added ($ng\ mL^{-1}$)**	**Intra-Day (*n*=5)**			**Inter-Day (*n*=4 ×3)**		
		Found ($ng\ mL^{-1}$)	**RSD%[1]**	**RR%[2]**	**Found ($ng\ mL^{-1}$)**	**RSD%**	**RR%**
α-HCH	2.00	1.99 ± 0.04	1.8	99.5	2.09 ± 0.14	6.7	104.5
	10.00	9.74 ± 0.21	2.1	97.4	9.31 ± 0.56	6.0	93.1
β-HCH	2.00	1.95 ± 0.07	3.6	97.5	2.03 ± 0.08	3.9	101.5
	10.00	9.78 ± 0.24	2.4	97.8	9.30 ± 0.45	4.8	93.0
γ-HCH	2.00	2.03 ± 0.06	3.2	101.5	2.06 ± 0.09	4.2	103.0
	10.00	9.78 ± 0.30	3.1	97.8	9.36 ± 0.54	5.8	93.6
Alachlor	2.00	1.96 ± 0.07	3.5	98.0	2.02 ± 0.11	5.3	101.1
	10.00	9.66 ± 0.30	3.1	96.6	9.61 ± 0.35	3.6	96.1
Aldrin	2.00	1.81 ± 0.06	3.3	90.5	1.95 ± 0.09	4.8	97.5
	10.00	9.88 ± 0.28	2.9	98.8	9.51 ± 0.58	6.1	95.1
o,p-DDE	2.00	1.82 ± 0.08	4.5	91.0	1.94 ± 0.07	3.7	97.0
	10.00	9.85 ± 0.24	2.4	98.5	9.62 ± 0.47	4.9	96.2
p,p-DDE	2.00	1.94 ± 0.08	4.2	97.0	2.10 ± 0.15	7.2	105.0
	10.00	10.11 ± 0.14	1.4	101.1	9.79 ± 0.42	4.3	97.9
o,p-DDD	2.00	1.99 ± 0.07	3.5	99.5	2.00 ± 0.13	6.3	100.0
	10.00	10.00 ± 0.16	1.6	100.0	9.88 ± 0.67	6.7	98.8
p,p-DDD	2.00	2.03 ± 0.05	2.7	101.5	1.96 ± 0.14	7.4	98.0
	10.00	9.97 ± 0.14	1.4	99.7	9.84 ± 0.32	3.2	98.4
ethoxychlor	2.00	2.10 ± 0.06	2.7	105.0	2.02 ± 0.06	3.1	101.0
	10.00	9.42 ± 0.50	5.3	94.2	9.84 ± 0.90	9.2	98.4

[1]RSD: Relative standard deviation

[2]RR: Relative recovery

3.4. Reusability of the sol-gel PEG 300 CPME media

In a further step, the reusability of the sol-gel PEG 300 CPME media was studied to provide a more comprehensive assessment regarding the performance of the proposed method. In green sample preparation, the utilization of reusable materials over those of disposable nature is of high importance to promote the reduction of waste aiming to develop more environmentally-friendly and low-cost methods [34]. For this study, one capsule was used for 20 repeated extraction cycles using a spiked sample (c= 10 ng mL^{-1}) and the criterion of a reduction of ≥ 10% of the recovery compared to the initial recovery was set. As shown in Figure S8, the performance of the CPME device was unaffected after 20 consecutive extraction cycles. Thus, the capsules are reusable for at least 20 times.

3.5. Evaluation of method's green character and comparison with other approaches

The herein developed method was compared with previously reported methods for the extraction of OCPs, as shown in Table 3.

Table 3. Comparison of the proposed method with other methodologies.

Sample preparation[1]	**Instrumentation**[2]	**Sample amount (mL)**	**Filtration**	**Extraction time (min)/Elution time(min)**	**Eluent**	**Evaporation/ reconstitution**	**RSD%**[3]	**LODs**[4] **(ng mL^{-1})**	**Ref.**
HS-SBSE using PDMS	GC-MS	15	No	120/15	1.5 mL of toluene: acetonitrile (20:80 v/v)	Required	<14.8	0.02-0.38	[18]
DMIP-SPE	GC-MS	100	No	-	12 mL of dichloromethane	Required	<6.69	0.007-0.126	[35]
d-SPE using SWCNTs	GC-ECD	20	No	10/15	5 mL of ethyl acetate	Required	<5.6	0.025-0.049	[36]
μ-SPE using TiO$_2$ nanotube arrays	GC-ECD	10	Required	40/7	dichloromethane	Required	<9.88	0.0076-0.10	[37]
MSPE using (M-M-ZIF-67)	GC-MS	5	Required	20/5	4 mL of acetonitrile	Required	<8.5	0.07-1.03	[38]
MSPE using GO/Fe$_3$O$_4$@Au	GC-μECD	10	Required	10/2	250 μL of acetonitrile	No	<7.3	0.4-4.1 x 10^{-3}	[39]
CPME	GC-MS	20	No	50/2	250 μL of acetone	No	<5.3 (intra-day) <9.2 (inter-day)	0.01-0.03	This study

[1] HS-SBSE: Headspace-stir bar sorptive extraction, DMIP: Dummy template molecularly imprinted polymer, SWCNTs: single-walled carbon nanotubes, M-M-ZIF-67: zeolitic imidazolate framework based on magnetic multi-walled carbon nanotubes, RGO/Fe_3O_4@Au: reduced graphene oxide/ Fe_3O_4@gold nanocomposite,

[2] GC-ECD: Gas chromatography-electron capture detector, GC-μECD: Gas chromatography- micro electron capture detector

[3] RSD: Relative standard deviation

[4] LODs: Limits of detection

The sample amount used during the extraction procedure was higher than the sample amount used in refs. [18,37–39], similar to the sample amount used in ref. [36] and lower than the sample amount used in ref. [35]. The overall extraction time was comparable with the extraction time required in ref. [37], higher than the extraction time required in refs. [36,38,39] but lower than the extraction time required in ref. [18]. Moreover, the sensitivity of the proposed method (in terms of LOD values) was comparable to those of refs. [18,35–37], higher than the sensitivity of ref. [38] but lower than the sensitivity of ref. [39].

A significant advantage of the proposed procedure is the utilization of a small amount of organic solvent as eluent. In this work, elution is performed using 250 μL of acetone, while the organic solvent requirements in most of the other studies are above 1.5 mL (*i.e.*, refs. [18,36,38] and they range up to 12 mL (*i.e.*, ref. [35]). Only in ref. [39] the same amount (*i.e.*, 250 μL) of organic solvent is employed; however acetonitrile is used which is not recommendable from an environmental perspective [29]. On the other hand, acetone is considered to be a “preferred” solvent, as already discussed in section 3.2.3 [30]. The proposed method does not require acetonitrile (used in ref. [18] and [38]), toluene (used in ref. [18]) and chlorinated solvents (used in refs. [35] and [37]) which are more hazardous chemicals. Thus, the proposed method meets the requirements of GAC [14] regarding the low consumption of organic solvents and the replacement of chemicals with less hazardous ones.

Another advantage of CPME is that it overcomes the need for sample filtration prior to the extraction procedure and the need for sample evaporation following the extraction procedure. Sample filtration was required in refs. [37–39], while sample evaporation and reconstitution were required in refs. [18,35–38]. In principle, a multi-step sample preparation procedure may result in reduced precision and accuracy, while it can be time-consuming and demand high expenditures of chemicals and energy [34]. Thus, the reduction of sample preparation steps is a significant factor towards the development of greener methods. An additional benefit of CPME is the increased simplicity of the method, because the microextraction capsules can be removed from the eluent and the sample solution using tweezers. Thus, they overcome the need of magnetic separation that is necessary in MSPE [38,39] and centrifugation that is necessary in d-SPE [36] processes.

A usefool tool to make the greenness of an analytical method visible and comparable are ComplesGAPI pictograms [40]. In this tool, the environmental friendliness of an analytical method is assessed by evaluating the sample preparation procedure, the instrumentation used for the analytical determination, the reagents and chemicals used and the overall method type. Moreover, the hexagonal field of the ComplexGAPI pictogram examines the impact of the yield and conditions, chemicals, instrumentation purification and workup used during the manufacturing of extraction materials which in this case includes the CPME device. Figure 5 depicts the ComplexGAPI pictogram that corresponds to the herein developed CPME GC-MS method, as well as to two of the other existing methodologies for the monitoring of OPCs in water samples found in the literature. With regard to the preparation of the microextraction capsules most of the assessment criteria are met (green colour). The synthesis was characterized by a high process yield and reduced waste generation, as well as a low E-factor. As for the extraction, the proposed scheme is characterized by low chemical consumption and waste generation since microextraction is used. Future recommendations towards the reduction of the environmental impact of the herein developed method include the utilization of more environmentally-friendly chemicals (*i.e.*, deep eutectic solvents, DESs) instead of conventional organic solvents.

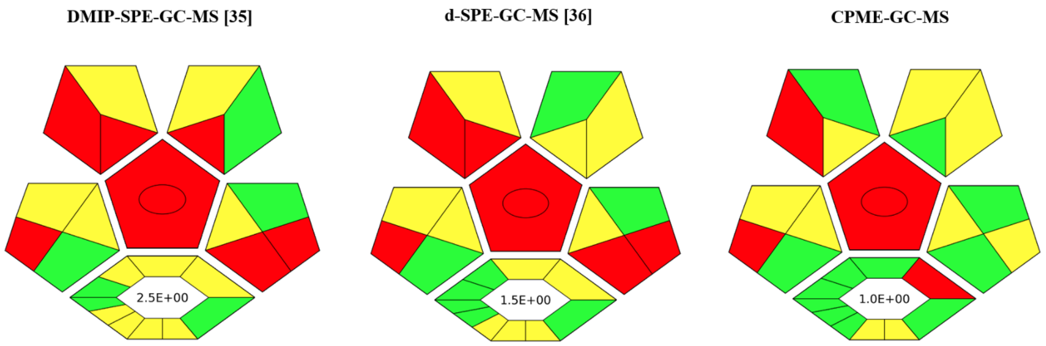

Figure 5. ComplexGAPI pictogram of the developed method (right), compared to other selected methods (left and middle) [35, 36]

3.6. Analysis of real-world water samples

Following method development and measurement of the figures-of-merit of the proposed method, water samples of different origin (*i.e.*, tap, river, pond and lake water) were analysed. Each sample was spiked at two different concentration levels (*i.e.*, c=2.00 ng mL^{-1} and 10.00 ng mL^{-1}) to investigate the applicability of the proposed methodology to different water samples. As shown in Table 4, the relative recoveries in the examined spiked levels ranged between 80.1-112.5% indicating good method applicability of the proposed scheme in different environmental water samples. The absence of interferences in the blank samples shows that the proposed method is characterized by specificity, while no contamination occurred during sample analysis.

Table 4. Analysis of environmental water samples through CPME GC-MS.

Analyte	**Added (ng mL^{-1})**	**Lake water 1**		**Lake water 2**		**Pond water**		**River water**		**Tap water**	
		Found (ng mL^{-1})	**RR%[1]**	**Found (ng mL^{-1})**	**RR%**	**Found (ng mL^{-1})**	**RR%**	**Found (ng mL^{-1})**	**RR%**	**Found (ng mL^{-1})**	**RR%**
α-HCH	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	2.01±0.04	100.3	1.82±0.04	91.0	1.71±0.01	85.5	2.22±0.09	111.0	1.98±0.02	99.1
	10.00	10.16±0.06	101.6	9.57±0.18	95.7	10.22±0.38	102.2	9.89±0.16	98.9	9.92±0.18	99.2
β-HCH	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	1.90±0.02	95.2	1.80±0.03	90.2	1.75±0.02	87.4	1.77±0.03	88.6	1.92±0.02	96.1
	10.00	10.52±0.12	105.2	9.28±0.34	92.8	10.38±0.22	103.8	9.97±0.22	99.7	10.12±0.25	101.2
γ-HCH	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	1.97±0.02	98.3	1.85±0.07	92.4	2.06±0.02	103.0	2.21±0.04	110.5	1.91±0.04	95.4
	10.00	9.71±0.09	97.1	9.25±0.07	92.3	9.77±0.28	97.7	9.88±0.17	98.8	9.23±0.27	92.3
Alachlor	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	1.64±0.05	82.0	1.96±0.05	98.1	1.95±0.05	97.4	2.03±0.01	101.3	2.01±0.03	100.5
	10.00	9.74±0.44	97.4	9.14±0.28	91.4	9.89±0.30	98.9	9.58±0.60	95.8	10.73±0.24	107.3
Aldrin	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	1.62±0.02	81.2	2.01±0.01	100.6	1.93±0.06	96.4	1.97±0.02	98.6	1.98±0.03	99.0
	10.00	10.51±0.04	105.1	10.25±0.15	102.5	8.90±0.37	89.0	9.65±0.01	96.5	10.25±0.27	102.5

Analyte	Added (ng mL^{-1})	Lake water 1		Lake water 2		Pond water		River water		Tap water	
		Found (ng mL^{-1})	RR%[1]	Found (ng mL^{-1})	RR%	Found (ng mL^{-1})	RR%	Found (ng mL^{-1})	RR%	Found (ng mL^{-1})	RR%
o,p-DDE	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	1.72±0.01	86.0	1.91±0.06	95.5	1.60±0.01	80.1	1.76±0.06	87.8	2.10±0.11	105.1
	10.00	10.98±0.05	109.8	9.95±0.07	99.5	10.05±0.19	100.5	9.51±0.13	95.1	10.25±0.27	102.5
p,p-DDE	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	1.97±0.01	98.7	1.75±0.05	87.6	1.70±0.07	85.2	1.74±0.01	87.1	2.15±0.05	107.3
	10.00	9.53±0.14	95.3	9.68±0.17	96.8	8.87±0.45	88.7	9.25±0.20	92.5	10.87±0.15	108.7
o,p-DDD	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	1.85±0.01	92.7	2.11±0.03	105.3	2.00±0.09	99.8	2.06±0.02	102.8	2.07±0.05	103.4
	10.00	10.34±0.15	103.4	11.17±0.16	111.7	8.91±0.20	89.1	8.51±0.07	85.1	11.25±0.16	112.5
p,p-DDD	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	1.81±0.04	90.4	1.93±0.02	96.4	1.81±0.10	90.6	1.94±0.03	97.2	1.98±0.06	98.8
	10.00	8.79±0.02	87.9	8.24±0.30	82.4	8.04±0.02	80.4	8.61±0.01	86.1	10.72±0.16	107.2
ethoxychlor	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	2.00	1.70±0.0.03	85.1	1.82±0.03	90.9	1.74±0.07	87.1	1.93±0.05	96.5	1.96±0.02	98.2
	10.00	9.15±0.90	91.5	8.43±0.82	84.3	8.89±1.05	88.9	8.79±0.10	87.9	9.94±0.81	99.4

[1] RR: Relative recovery

4. Conclusions

In this work, CPME was used for the extraction of OCPs in environmental water samples. Among the examined sorbents, the monolithic sol-gel poly(ethylene glycol)-based CPME device resulted in the highest extraction efficiency. Under optimum sample preparation conditions, the proposed method showed good linearity, accuracy, precision, and sensitivity. Moreover, the capsules could be reused for at least 20 times. The proposed scheme exhibits multiple benefits including handling simplicity, rapid extraction kinetics, and low consumption of organic solvents. CPME efficiently overcomes the need for sample pretreatment (*i.e.*, filtration) prior to sample preparation, while it also reduces the need for sample manipulation (*e.g.*, evaporation/reconstitution) after the sample preparation. Moreover, the integration of stirring mechanism results in a less error prone and more powerful extraction device, that prevents potential loss of analytes due to their retention on external devices (*e.g.*, magnetic rods).

Declaration of Competing Interest

The authors declare no conflict of interest

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Monolithic capsule phase microextraction prior to gas chromatography-mass spectrometry for the determination of organochlorine pesticides in environmental water samples

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Preparation of the capsule phase microextraction devices

First, Accurel® polypropylene S6/2 porous membranes were cut into 3 cm pieces. The porous capillary membranes were then cleaned with methylene chloride for 30 min under sonication and subsequently, air dried at room temperature for 30 min. A cylindrical magnet (3/4" x 1/16") was used in each of the CPME device. The magnet was inserted into an empty polypropylene capsule. Subsequently, one empty capsule and a capsule containing the magnet were fused together by the ends using an impulse heat-sealing machine. As a result, both the capsules were connected to each other by their ends. The CPME devices were then ready for the sol-gel sorbent coating process.

Sol solutions for in situ creation of sol-gel PDMS/sol-gel PEG 300/ sol-gel C_{18}/sol-gel PDMDPS monolithic sorbent bed within the lumen of the empty propylene capsule were prepared by the sequential addition of tetramethyl orthosilicate (TMOS), methyl trimethoxysilane (MTMS), polymer, isopropanol, hydrochloric acid catalyst and deionized water at a molar ratio: 1: 1: 0.2: 30: 0.04: 8, respectively in a 50mL amber glass reaction container. The mixture was kept at room temperature for 12 h so that acidic hydrolysis of the sol-gel precursors moves towards completion. Subsequently, the sol solution was centrifuged and the supernant particle free fraction was transferred into a wide-mouth glass reaction vessel. Successively, NH_4OH (1 M) was added to the solution in droplets at a molar ratio between TMOS and NH_4OH at 1: 0.10 with continuous stirring to achieve a homogeneous mixture. The process allows creation of batch of 30 units of CPME devices at once that can be even expanded by extending the size of the reaction vessel. A batch of 30 CPME devices were submerged into the sol solution and then at the reaction vessel containing the submerged CPME devices was sonicated for 5 min to remove air bubbles from the system. The gelation of the sol solution begins with the addition of the base catalyst and the sol solution turns into solid gel in 1 h at room temperature. The sol solution formed a solid monolithic bed within the lumen of the capsules and a mesh-like network on the surface of the porous polypropylene capsules and inside the pores of its thick walls. The CPME devices were then subjected to aging and thermal conditioning at 50°C for 24 h. The CPME devices were subsequently cleaned by scrubbing the sol-gel sorbent from their outer surface and rinsing with a mixture of methanol: methylene chloride (50:50 v/v) under sonication for 30 min. The monolithic bed of the sol-gel sorbent was disintegrated into fine microparticles by sonication. The CPME devices were then dried in an oven at 50°C. Finally, the CPME devices were ready for the analyte extraction.

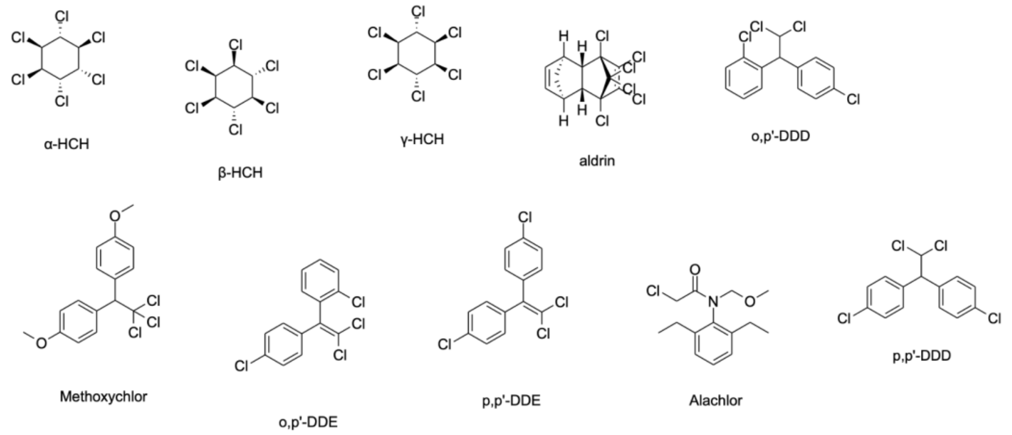

Figure S1. Chemical structures of the target analytes

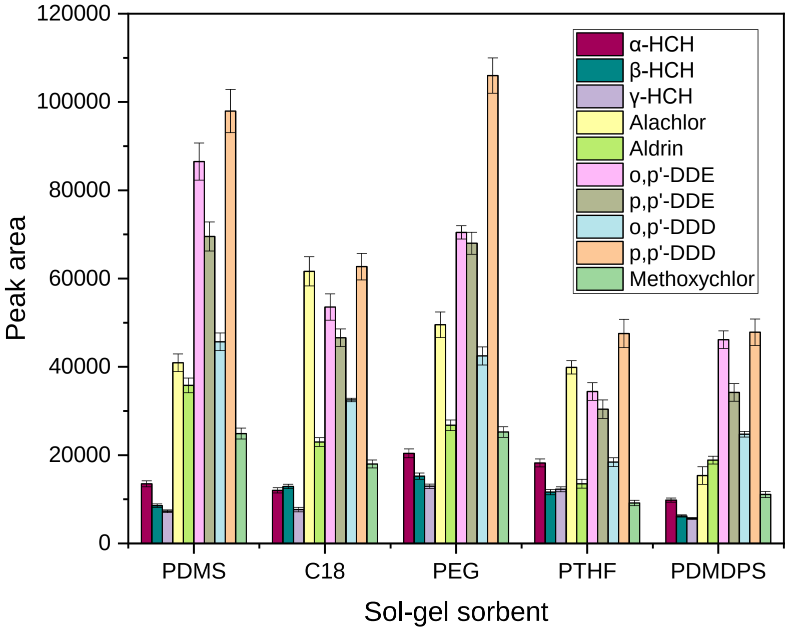

Figure S2. Evaluation of the effect of different monolithic sol-gel coated microextraction capsules. Sample volume: 20 mL, extraction time: 30 min, stirring rate: 800 rpm, salt content: 0% *w/v* NaCl, eluent: methanol, volume of eluent: 1000 μL, desorption time: 5 min.

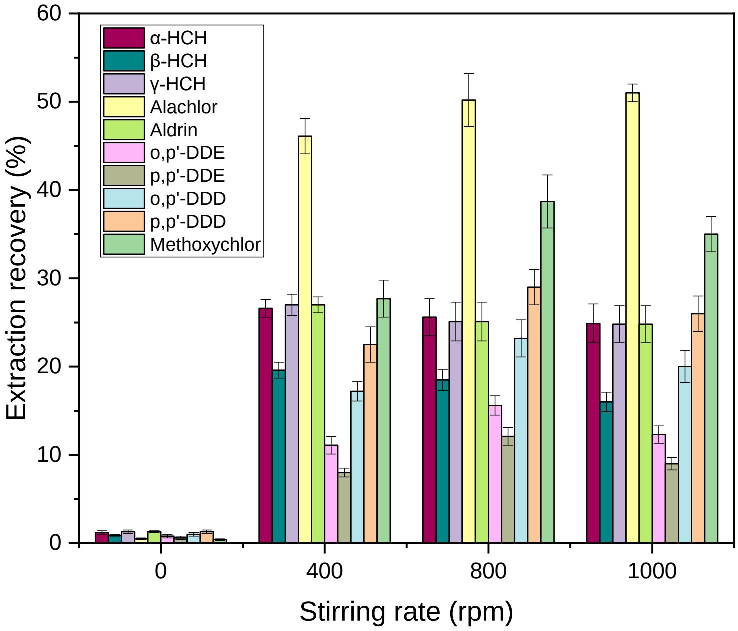

Figure S3. Evaluation of the effects of different stirring rates on extraction recovery. Sample volume: 20 mL, extraction time: 30 min, salt content: 0% *w/v* NaCl, eluent: acetonitrile, volume of eluent: 500 µL, desorption time: 5 min.

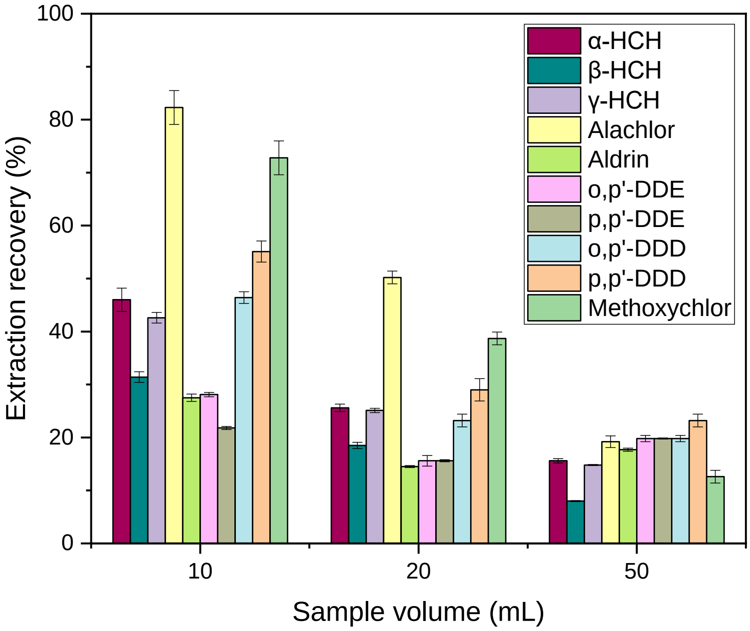

Figure S4. Evaluation of the effect of different sample volumes on extraction recovery. Extraction time: 30 min, salt content: 0% *w/v* NaCl, eluent: acetonitrile, stirring rate: 800 rpm, volume of eluent: 500 µL, desorption time: 5 min.

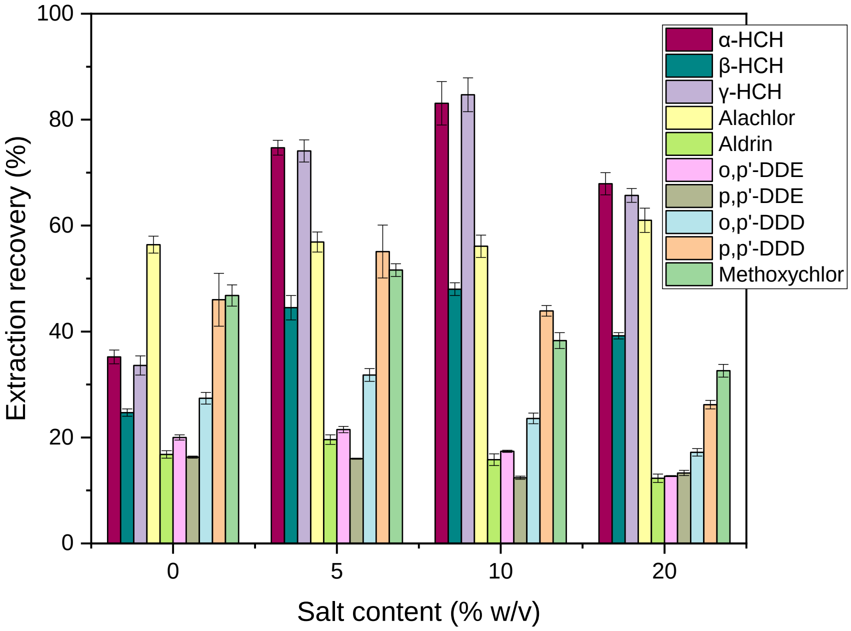

Figure S5. Evaluation of the effect of salt content on extraction recovery. Sample volume: 20 mL, extraction time: 50 min, eluent: acetonitrile, stirring rate: 800 rpm, volume of eluent: 500 µL, desorption time: 5 min.

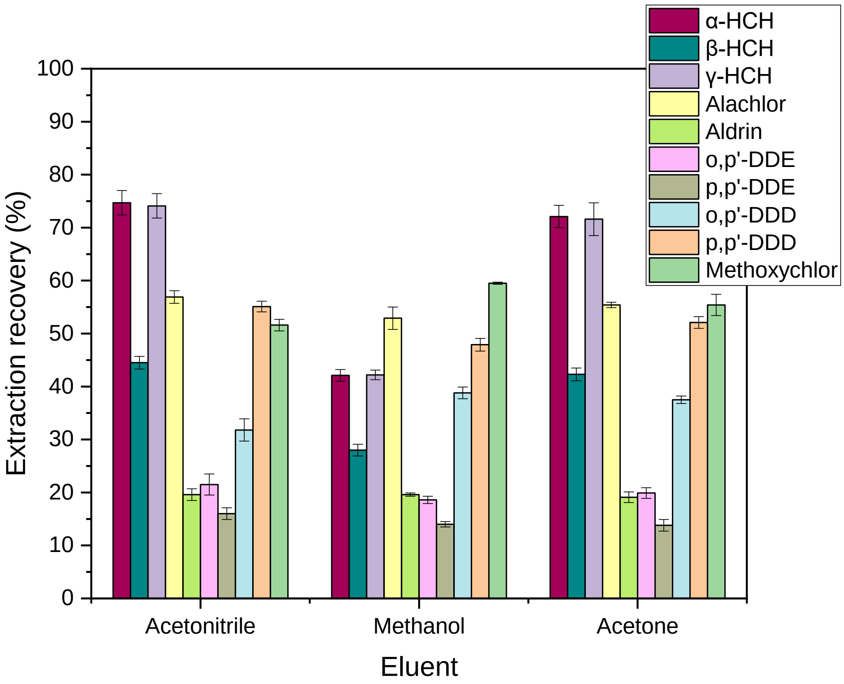

Figure S6. Evaluation of the effect of different eluents. Sample volume: 20 mL, salt content: 5% *w/v*, extraction time: 50 min, stirring rate: 800 rpm, volume of eluent: 500 µL, desorption time: 5 min.

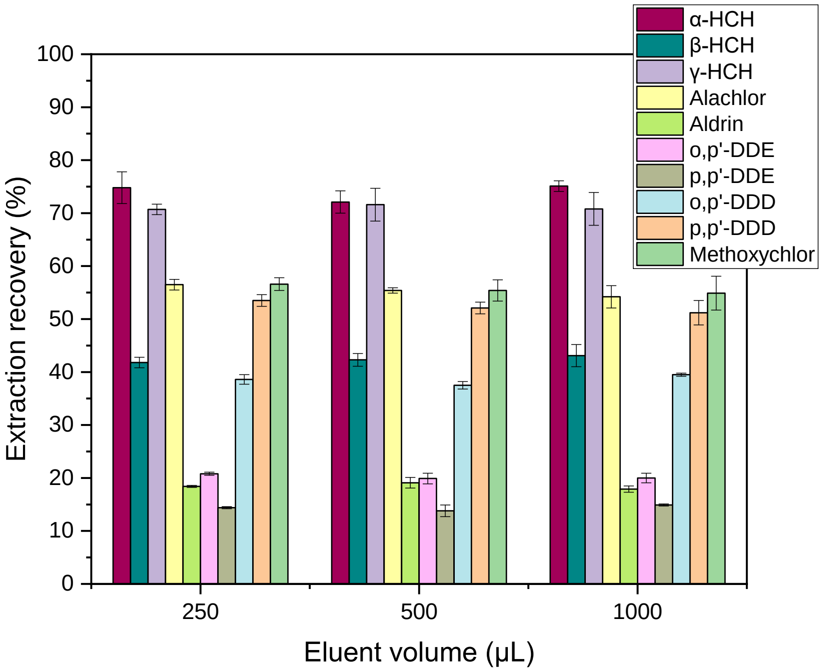

Figure S7. Evaluation of the effect of eluent volume on extraction yield. Sample volume: 20 mL, salt content: 5% *w/v*, extraction time: 50 min, stirring rate: 800 rpm, eluent: acetone, desorption time: 5 min.

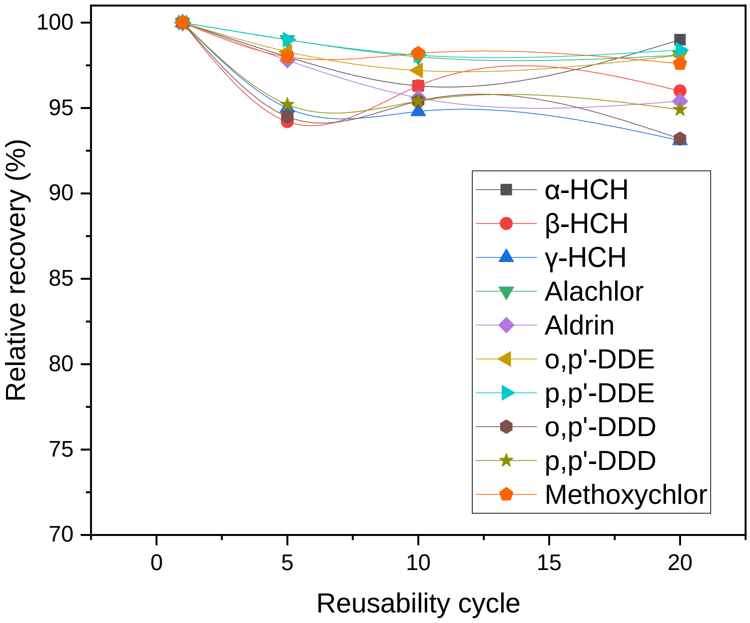

Figure S8. Results of the reusability study of sol-gel PEG 300 microextraction capsules

Table S1. Retention times and *m/z* values used for the OCPs.

Analyte	Retention time (min)	Target Ion (m/z)	Reference Ions (m/z)
α-HCH	10.45	181	109 219
β-HCH	11.00	181	109 219
γ-HCH	11.80	181	109 219
Alachlor	12.46	160	146 188
Aldrin	13.46	66	91 263
o,p’-DDE	15.02	246	318 176
p,p’-DDE	15.87	246	318 176
o,p’-DDD	16.14	235	165 199
p,p’-DDD	17.11	235	165 199
Methoxychlor	19.98	227	153 212

Table S2. Initial parameters, interval studies and optimum/selected values for the CPME method using monolithic sol-gel PEG 300 microextraction capsules.

Variable	Initial value	Interval studied	Optimum/selected value
Adsorption step			
Sample amount (mL)	20	10-50	**20**
Stirring rate (rpm)	800	0-1200	**800**
Extraction time (min)	30	10-60	**50**
Salt content (% w/v)	0	0-20	**5**
Elution step			
Eluent[1]	ACN	ACN, ACE, MeOH	**ACE**
Volume of eluent (µL)	500	250-1000	**250**
Elution time (min)	5	2-20	**2**

[1] ACN: Acetonitrile, ACE: Acetone, MeOH: Methanol