

1 **Green capsule phase microextraction employing hydrophobic monolithic sol-gel**
2 **octadecyl siloxane platforms for the monitoring of organophosphorus pesticides**
3 **in environmental water samples**

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28 **Abstract:** In this study, a novel, facile and green capsule phase microextraction
29 (CPME) method is presented for the extraction and preconcentration of
30 organophosphorus pesticides (i.e., chlorpyrifos, disulfoton, ethoprophos, fenclorphos,
31 prothiofos, and parathion-methyl) from environmental water samples. Monolithic sol-
32 gel octadecyl siloxane (sol-gel C₁₈) sorbent encapsulated within porous polypropylene
33 capsules was synthesized, characterized, and evaluated for its efficiency towards the
34 adsorption of the target organophosphorus pesticides. CPME was combined with gas

35 chromatography-mass spectrometry (GC-MS) for the monitoring of the target analytes.
36 The method was optimized to ensure high method sensitivity and it was fully validated.
37 The limits of detection of the CPME-GC-MS method for the OPPs were 0.02-0.15 ng
38 mL⁻¹. The relative standard deviations were 1.5-8.7% for intra-day study and 5.4-9.6%
39 for inter-day study, demonstrating satisfactory precision. Moreover, good method
40 accuracy was obtained, since the relative recoveries were within the range 92.6-107.0%
41 and 90.8-107.6% for intra-day and inter-day (c=5.00 and 20.0 ng mL⁻¹), respectively.
42 The absence of interferences in the blank samples demonstrate that the proposed
43 method is selective. The sol-gel C₁₈ sorbent encapsulated CPME media could be reused
44 for at least 25 adsorption/desorption cycles. In addition, the methodology presents
45 advantageous features in comparison to existing methods. The final protocol was used
46 for analyzing four different water sample types (i.e., lake water, river water, pond water
47 and tap water sample).

48

49 **Keywords:** organophosphorus pesticides; water samples; capsule phase
50 microextraction; GC-MS

51

52 1. Introduction

53 Organophosphorus pesticides (OPPs) comprise a big and diverse class of
54 compounds used to control pests and increase the production of crops (Hu et al., 2013;
55 Mangas et al., 2017). The exposure of humans to OPPs can cause serious health
56 problems and may lead to distinct neurotoxic effects, depending on the type of
57 pesticide, the dose and the frequency of exposure (Čadež et al., 2021). The mechanism
58 of action of OPPs in the human body involves the de-activation of acetyl-cholinesterase
59 that could cause accumulation of acetylcholine and acetylcholine receptors' disorder
60 (Hu et al., 2013). Moreover, individual OPPs may exhibit carcinogenic, teratogenic,
61 mutagenic and cytotoxic effects (Xie et al., 2013). These compounds are among the
62 most widely used insecticides (Singh and Walker, 2006). The occurrence of OPPs in
63 rivers, soil, air, plants and groundwater remains a concern for public health, because of
64 their toxicity and their widespread use (Čadež et al., 2021). Particularly for
65 environmental water systems, OPPs can enter to it through many sources, and serve as
66 a threat both for animals and for humans (Gao and Pan, 2020). Thus, the development
67 of sensitive and accurate methodologies for the monitoring of these pesticides in
68 environmental samples is of paramount importance.



69 High-performance liquid chromatography (HPLC) (Harshit et al., 2017),
70 capillary electrophoresis (Li et al., 2010), and gas chromatography (GC) (Hu et al.,
71 2013; Lambropoulou et al., 2000) can be employed for monitoring the OPPs levels in
72 environmental water samples. Among these instrumental techniques, GC coupled to
73 various detection systems including nitrogen phosphorus detector (NPD) (Ballesteros
74 and Parrado, 2004), electron capture detector (ECD) (Oliva et al., 2000), flame
75 ionization detector (FID) (Amiri et al., 2019), flame thermionic detector (FTD)
76 (Lambropoulou et al., 2000) and mass spectrometers (MS) (Lambropoulou et al., 2000)
77 comprises the main analytical strategies for the monitoring of OPPs, due to their good
78 performance. In order to enable the chromatographic determination of OPPs, sample
79 preparation is necessary to provide sufficient clean up and preconcentration (Kaur et
80 al., 2019). Solid-phase extraction (SPE) (Brito et al., 2002; Gillespie and Walters, 1991;
81 Harshit et al., 2017) and liquid-liquid extraction (LLE) (Brito et al., 2002; Harshit et
82 al., 2017) are between the most common methods used for the extraction of OPPs.
83 However, LLE is considered to be a time-consuming technique and it requires high
84 quantities of hazardous solvents. Similarly, SPE requires sample pretreatment and
85 elution can be a tedious task, particularly with samples that have a high fraction of
86 suspended matter (Ahmadi et al., 2006).

87 Following the development of Green Analytical Chemistry (GAC) principles
88 that was an outcome of Green Chemistry, large efforts have been made by the scientific
89 community to develop greener sample preparation methods (Anastas, 1999; Armenta
90 et al., 2015). As a result, multiple miniaturized techniques have been proposed and
91 successfully employed for the preconcentration and extraction of OPPs. Typical
92 paradigms of these techniques include single drop microextraction (SDME) (Pinheiro
93 et al., 2011), dispersive liquid-liquid microextraction (DLLME) (Cacho et al., 2018),
94 pipette-tip solid phase extraction (Esrafilı et al., 2020), solid-phase microextraction
95 (SPME)(Delińska et al., 2022), dispersive solid-phase extraction (d-SPE) (Amiri et al.,
96 2019), stir bar sorptive extraction (SBSE) (Hu et al., 2013), QuEChERS extraction
97 (Alcântara et al., 2019), magnetic solid-phase extraction (MSPE) (Liu et al., 2020; Xie
98 et al., 2013) and fabric phase sorptive extraction (FPSE) (Kaur et al., 2019). At the same
99 time, various novel materials were introduced for the extraction of pollutants from
100 complex samples (Li et al., 2021; Xu et al., 2022). In the above-mentioned sorbent-
101 based extraction techniques, extraction takes place either by directly adding the sorbent
102 in the sample (e.g., MSPE, d-SPE) or after the immobilization of the sorbent in suitable



103 substrates (e.g., FPSE). Undoubtedly, the exploration of novel extraction techniques
104 and materials is critical for the miniaturization of the extraction of OPPs from water
105 samples.

106 Capsule phase microextraction (CPME) is an extraction/preconcentration
107 technique that aims to simplify the sample preparation procedure of complex food,
108 biological and environmental samples. CPME utilizes specially designed capsules that
109 include three parts: (a) a permeable microporous membrane from polypropylene, (b) a
110 magnet with cylindrical shape and (c) a sol–gel sorbent (Manousi et al., 2022). Because
111 of the inherent porosity of the membranes, the CPME devices integrate a filtration
112 mechanism and, thus, this technique may be directly used for analyzing complex
113 matrices without pretreatment. At the same time, the device integrates a stirring
114 mechanism, resulting in rapid extraction kinetics. As a result, CPME overcomes
115 potential losses of the target analytes during sample pretreatment as it eliminates further
116 external steps of sample preparation, or potential sample contamination due to the
117 addition of external magnets (Georgiadis et al., 2019). An advantageous feature of
118 CPME is the utilization of a monolithic sol-gel sorbent. Sol-gel technology comprise
119 an efficient vehicle for preparing advanced hybrid inorganic–organic polymer sorbents
120 that are characterized by high chemical and thermal stability, remarkably high surface
121 area as well as tunable selectivity and porosity (Lazaridou et al., 2020). Using sol-gel
122 technology, a wide variety of sorptive phases including non-polar, polar, medium polar,
123 negatively- or positively-charged, zwitterionic multi-mode sorbents can be prepared to
124 fabricate coated microextraction capsules, resulting in increased selectivity towards a
125 wide range of target analytes with diverse chemical properties (Samanidou et al., 2018).
126 Until now, CPME has found to be a great analytical tool for the monitoring of various
127 environmental pollutants, such as polycyclic aromatic hydrocarbons (N. Manousi et al.,
128 2021b), basic and acidic compounds (Carles et al., 2020), and triazine herbicides in
129 water (N. Manousi et al., 2021a).

130 The purpose of this work was to develop an efficient CPME method combined
131 with GC-MS for the simultaneous extraction and preconcentration of six representative
132 OPPs (chlorpyrifos, disulfoton, ethoprophos, fenchlorphos, parathion-methyl and
133 prothiofos) from environmental water. Different coated CPME devices were evaluated
134 for their performance to find the most efficient sorptive phase in order to find the best
135 compromise for the studied OPPs. Subsequently, the main factors (i.e., extraction time,
136 sample volume, salt content, stirring rate, eluent, mode of elution, volume of eluent and



137 desorption time) were optimized. Following method optimization and validation, the
138 herein developed scheme was validated and used for analyzing tap, pond, lake, and
139 river.

140

141 **2. Experimental**

142 **2.1. Reagents, chemicals, and samples**

143 LC-MS grade acetonitrile and methanol were obtained from Honeywell
144 (Charlotte, North Carolina, USA), while HPLC grade acetone and GC-MS grade
145 toluene were obtained from Merck (Darmstadt, Germany). Ultrapure water was
146 provided by a Milli-Q system Plus purification system (Millipore, Bedford, MA, USA)
147 and it was used throughout the study. Reagent grade NaCl was also obtained from
148 Merck (Darmstadt, Germany). Chlorpyrifos ($\geq 98.0\%$), disulfoton ($\geq 98.0\%$),
149 ethoprophos ($\geq 95.0\%$), fenchlorphos ($\geq 98.0\%$), parathion-methyl ($\geq 98.0\%$) and
150 prothiofos ($\geq 98.0\%$) were from Supelco (Bellefonte, PA, USA). The chemical
151 structures of the target analytes are shown in Figure S1. A stock solution of the each
152 analyte (1000 mg L^{-1}) was made in hexane:acetone (9:1, v/v) and were kept at 4°C . On
153 a daily basis, working standards were made through serial dilutions in acetone at a
154 concentration range of 0.05 and 1000 ng mL^{-1} .

155 Building blocks of the microextraction devices such as porous polypropylene
156 capillary membranes (nominal pore size is 0.2 micrometer), Accurel® was obtained
157 from 3M Inc. (St. Paul, MN, USA). Magnets of cylindrical shape ($1/4'' \times 1/16''$) were
158 obtained from K&G Magnetics Incorporated (Pipersville, PA, USA). Tetramethyl
159 orthosilicate (TMOS), poly(tetrahydrofuran) (PTHF), and poly(ethylene glycol) 300
160 (PEG 300) were obtained from Sigma Aldrich (St. Louis, MO, USA). Isopropanol,
161 methylene chloride, methanol, HCl and NH_4OH were purchased from Fisher Scientific
162 (Milwaukee, WI, USA). Poly(dimethyl siloxane) (PDMS), poly(caprolactone)-
163 poly(dimethylsiloxane)-poly(caprolactone) (PCAP-PDMS-PCAP) and octadecyl
164 trimethoxysilane (C_{18}) were from Gelest, Inc. (Morrisville, PA, USA). A tabletop
165 impulse heat sealer (Uline Corp, Pleasant Prairie, WI, USA) was used to heat seal both
166 the ends of the CPME devices.

167 The CPME-GC-MS methodology was employed for the analysis of different
168 water samples. All samples were collected from Vienna, Austria in amber-glass vials
169 with no headspace. Until their analysis, all samples were stored at 4°C (Roldán-Pijúan

170 et al., 2015; Zohrabi et al., 2016). No sample pre-treatment steps (e.g., filtration) were
171 required prior to the microextraction procedure.

172

173 **2.2. Instrumentation**

174 A GC-2010 gas chromatograph and a QP2010 Plus mass spectrometer (MS)
175 from Shimadzu (Kyoto, Japan) equipped with a Rtx-5MS (30 m × 0.25 mm, 0.25 μm)
176 column (Restek Corporation, Bellefonte, PA, USA) was used in this study. The mobile
177 phase used was helium (99.999%) and it was delivered at a constant gas flow rate of
178 1.05 mL min⁻¹. The injector was operated at 280°C. Splitless high pressure injection
179 was performed at 300 kPa for 0.50 min using an injection volume of 3 μL. The oven
180 temperature was: 80 °C initial temperature (hold time 2 min), raised to 280 °C at a ramp
181 rate of 8 °C min⁻¹ and raised to 350 °C at a ramp rate of 50 °C min⁻¹. The analysis time
182 was 28.4 min and a solvent delay of 7 min was used. The ion source was operated at
183 220 °C and the interface was operated at 250 °C. The quantification was conducted in
184 the selected ion monitoring (SIM) mode to ensure good sensitivity and selectivity. For
185 this purpose, one target ion was used as quantifier and two reference ions were used as
186 qualifiers for each analyte taking into consideration their abundance. The selected m/z
187 values for the OPPs are presented in Table S1, along with their retention times.

188 A Philips XL30 Scanning Electron Microscope equipped with an EDAX
189 detector, an Agilent Cary 670 FTIR Spectrometer, a RIGAKU diffractometer model
190 SmartLab II, and a dynamic sorption surface area analyser Flowsorb III from
191 Micrometrics Instrument Corporation were used for the characterization of the sol-gel
192 C₁₈ sorbent.

193

194 **2.3. Preparation of microextraction capsules**

195 CPME devices encapsulating sol-gel sorbents were created using an in-situ
196 gelation of sol solutions where the microextraction capsules were kept submerged
197 during the phase transition, from liquid sol to solid gel. The overall CPME device
198 fabrication process involves several sequential steps: (a) preparing porous
199 polypropylene capillary membranes for the device fabrication; (b) preparation and
200 design of sol solutions; (c) in-situ creation of the coating on the porous polypropylene
201 wall and the monolithic bed inside the lumen; and (d) aging/conditioning/cleaning of
202 the CPME devices. Seven sorbents were prepared to study their efficiency towards the
203 extraction of selected organophosphorus pesticides. The sol-gel sorbents include: (1)

204 sol-gel PTHF; (2) sol-gel sol-gel PDMS; (3) sol-gel poly(dimethyldiphenylsiloxane)
205 (sol-gel PDMDPS); (4) sol-gel poly(caprolactone)-poly(dimethylsiloxane)-
206 poly(caprolactone) (sol-gel PCAP-PDMS-PCAP); (5) sol-gel PEG 300; (6) sol-gel
207 Carbowax 20 M (sol-gel CW 20M); and (7) sol-gel C₁₈.

208 All CPME devices were built at three-centimeter-long size. Capsule phase
209 microextraction devices were prepared for surface coating/creating monolithic bed,
210 Accurel® S6/2 membranes were cut into 3-centimeter-long sections, followed by
211 cleaning and drying. Two capillary membranes were impulse heat sealed using the
212 tabletop impulse heat sealer. A magnet was then placed into one of the capillary
213 membranes. Subsequently, the open ends of the two capillary membranes were
214 impulses sealed and the CPME media are ready for the creation of monolithic bed/ sol-
215 gel sorbent coating.

216 Design of the sol solution for the preparation of sol-gel coating and/or
217 monolithic bed is the most important and challenging task in the CPME device
218 fabrication process with a goal to have high efficiency and to minimize sample
219 preparation time, with least possible sample handling. As such, the sol solution
220 preparation process was streamlined utilizing the same molar ratio between the reagents
221 for a different sol solutions. The molar ratio between TMOS, methyl trimethoxysilane,
222 polymer, solvent, hydrochloric acid, and water were kept at 1:1:0.2:30:0.04:8,
223 respectively. The reagents were sequentially added to a 50-milliliter reaction vessel
224 with vortexing after adding each ingredient. Then, the sol solution remained for 12
225 hours at room temperature. to enable the sol-gel precursor(s)hydrolysis. Subsequently,
226 1 M ammonium hydroxide was added at a molar ratio at 1:0.18 (TMOS:ammonium
227 hydroxide) under constant stirring. Twenty capsule units were then immersed in the
228 solution that was sonicated and transformation of the solution into solid gel occurred
229 within an hour. During the phase transition, a solid network was formed in the pores of
230 the walls of the capillary membrane, while a monolithic bed was created inside of the
231 capillary membranes' lumen. The capsules were then aged and conditioned for 24 h at
232 50 °C. The capsules were washed with dichloromethane:methanol (50:50 v/v) for 30
233 min under ultrasonic irradiation. During the ultrasonic irradiation process, the sol-gel
234 sorbent monolithic bed is crashed into micro particles, leading to significant expansion
235 of the overall surface area. Prior to their use for analytical experiments, all capsules
236 were dried for 2 h at 50°C.

237



238 **2.4 CPME procedure**

239 Prior to the microextraction procedure, sol-gel C₁₈ CPME devices were placed
240 in an Eppendorf tube that contained 2 mL of methanol for 5 min for the removal of
241 potential residues of the sol-gel synthesis process and to activate the surface of the
242 sorbent. Subsequently, the capsules were rinsed with H₂O for the removal of traces of
243 organic solvents from the sorptive phase that could potentially hinder the adsorption of
244 the OPPs.

245 Initially, twenty millilitres of sample was placed in a vial and extraction took
246 place within 60 min under a stirring rate of 500 rpm. Then, the CPME device was
247 isolated and cleaned with H₂O. Prior to the desorption of the adsorbed OPPs, the CPME
248 device was wiped and dried thoroughly using tissue (lint free). Desorption of the target
249 analytes took place in Eppendorf tubes by adding a volume of 250 µL acetone. No
250 stirring was required during this step and complete elution was achieved in 1 min. The
251 eluent was filtered using PTFE filters (0.22 µm) and analysed by GC-MS.

252 Washing of the used capsules was performed by immersion in 2 mL of methanol
253 for 5 min. The clean sol-gel C₁₈ CPME device was left to dry at room temperature, and
254 they were placed in airtight sealed vials for storage until their next application. Figure
255 S2 shows the main steps of the CPME-GC-MS method.

256

257

258 **3. Results and discussion**

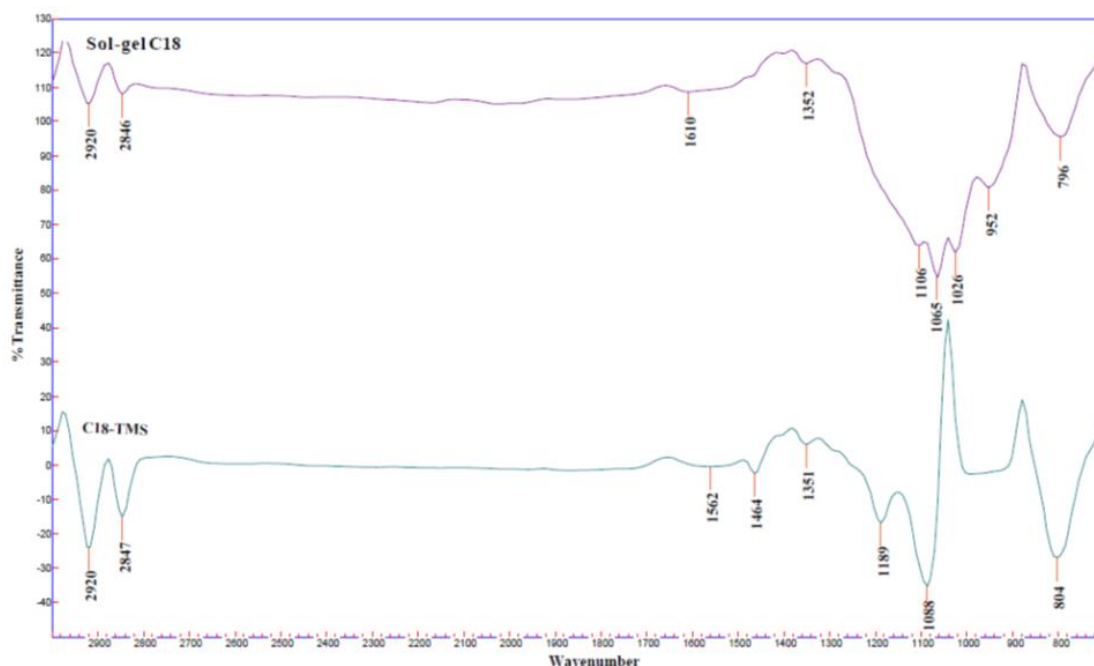
259 **3.1. Characterization of coated CPME devices**

260 The sol-gel C₁₈ sorbent was characterized using scanning electron microscopy
261 (SEM), Brunauer-Emmett-Teller (BET) adsorption isotherm, Fourier transform
262 infrared spectroscopy (FT-IR), and X-Ray diffraction analysis (XRD). The
263 characterization study was performed as a basis for understanding the composition and
264 structure of the herein used sorbent. The preparation procedures, obtained results and
265 characterization data regarding the other examined sorbents included in this study have
266 been previously reported elsewhere (N. Manousi et al., 2021b, 2021a; Manousi et al.,
267 2022).

268

269 **3.1.1 Characterization of the sol-gel C₁₈ by FT-IR**

270 The functional composition of the sorbent and their building blocks were
271 evaluated using FT-IR Spectrometry. Figure 1 shows the FT-IR spectrum of sol-gel C₁₈
272 (up) and C₁₈-TMOS (bottom).



273

274 **Figure 1.** FT-IR spectra of sol-gel C₁₈ (up) and C₁₈-TMOS (bottom)

275

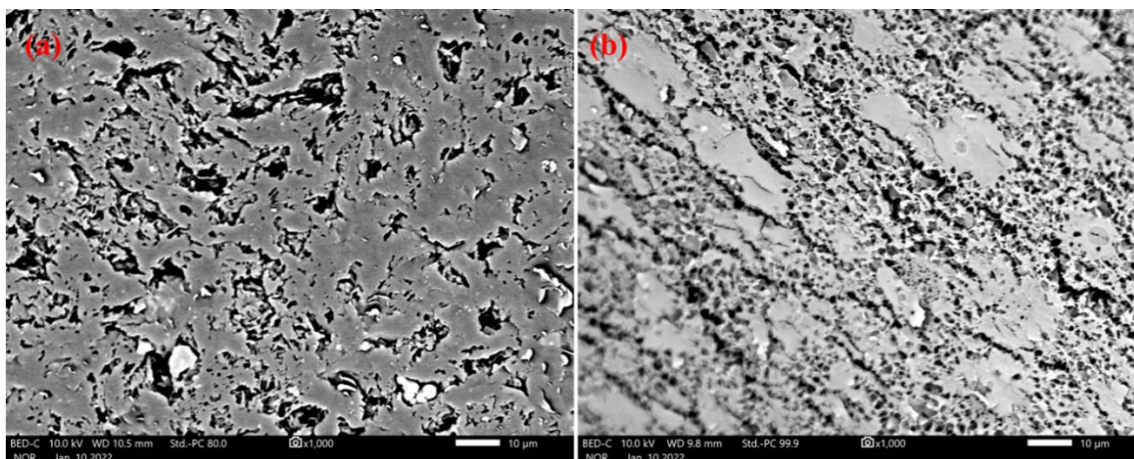
276 The spectrum of C₁₈-TMOS (Figure 1, bottom) demonstrates characteristic
277 bands at 2920 cm⁻¹ and 2846 cm⁻¹ that correspond to C-H stretching (Einati et al., 2009).
278 The band at 1190 cm⁻¹ corresponds to the asymmetric bending of C-H bonds. The band
279 at 1075 cm⁻¹ corresponds to Si-O-C bonds. Similar bands are also seen in the FT-IR
280 spectrum that is shown in Supplementary Figure S3 as both C₁₈-TMOS and TMOS have
281 the same base unit. The spectrum of sol-gel octadecyl siloxane reveals many features
282 presented either in the spectrum of C₁₈-TMOS or that of TMOS or common to both,
283 suggesting the integration of both the sol-gel precursors into the network of the sol-gel
284 sorbent.

285

286 3.1.2 Characterization of the sol-gel C₁₈ by SEM

287 The SEM images of porous polypropylene capillary membrane surface, before
288 and after the sol-gel sorbent coating, are presented in Figure 2, both at ×1,000
289 magnification.

290



291

292 **Figure 2.** Scanning electron microscope images at $\times 1,000$ magnification of the surface
 293 of porous polypropylene capillary membrane before coating (a) and after coating (b).

294

295 The polypropylene capillary membranes are porous with a $0.2 \mu\text{m}$ nominal pore
 296 size. The SEM image of surface before the coating procedure shows the opening of the
 297 pores almost evenly distributed on the surface. The SEM image representing sol-gel C_{18}
 298 coated capillary membrane surface is very different from that of the uncoated one, with
 299 a distinct layer of the sorbent coating. However, the pores on the surface remain intact,
 300 although the pore opening seems to be reduced. The polypropylene capillary membrane
 301 has thick walls of $450 \mu\text{m}$. The sol solution can permeate without any difficulty through
 302 the walls during the coating process and transform into a polymeric gel within the
 303 porous channels. Consequently, the thick walls of the CPME device behaves like a
 304 solid-phase extraction disk.

305

306 **3.1.3 X-ray diffraction analysis (XRD)**

307 The XRD pattern of sol-gel C_{18} is presented in Figure S4. The sample was run
 308 at 40 mA, 40 KV, 2 degrees/min, 0.02 step size. A broad peak at theta $\sim 22.5^\circ$ in the
 309 diffraction pattern represents a signature marker of amorphous solid that have been
 310 reported in the XRD patterns of amorphous silica obtained from several studies (Liu et
 311 al., 2008; Tanev and Pinnavaia, 1995).

312

313 **3.1.4 Brunauer-Emmett-Teller adsorption isotherm**

314 The average pore width, the pore volume and the specific surface area of sol-
 315 gel C_{18} were carried out. For the comparison purpose, the same characterizations were
 316 performed on a commercial C_{18} sorbent. The BET nitrogen adsorption isotherm data

317 obtained for sol-gel C₁₈ and commercial C₁₈ are distinctly different. Sol-gel C₁₈ has a
318 specific surface area of ~650 cm²/g, whereas the specific surface area for commercial
319 C₁₈ sorbent is ~346 cm²/g. Sol-gel C₁₈ sorbent was created by the polycondensation of
320 hydrolysed TMOS with hydrolysed octadecyl trimethoxysilane. The sol-gel synthesis
321 process allows changing the molar ratio between the functional precursor (C₁₈-TMS)
322 and the networking precursor (TMOS) that may be exploited to achieve higher carbon
323 loading in the synthesized sorbent. As the commercial C₁₈ sorbents utilize spherical
324 silica particles as the substrate to bind C₁₈ moieties on their surfaces, carbon loadings on
325 commercial C₁₈ sorbents are limited and primarily determined by the size of substrate
326 silica particle. The pore volume of sol-gel C₁₈ was found as 0.43 cm³/g compared to
327 0.72 cm³/g for commercial C₁₈. The average pore width for sol-gel C₁₈ was calculated
328 as 26.9 Å whereas the average pore width for the commercial C₁₈ was 83.7 Å.

329

330 **3.2 Optimization of the CPME procedure**

331 The effect of the experimental parameters that may affect the CPME method
332 were thoroughly investigated and optimized. Initially, different CPME devices (i.e.,
333 different sol-gel sorbents and different dimensions) were tested for the extraction of the
334 OPPs from the environmental water samples. Subsequently, the adsorption and
335 desorption steps were individually studied by means of the one-variable-at-a-time
336 (OVAT) approach. As such, all variables that could have an influence on the
337 performance of the CPME method were independently examined, and the other
338 parameters remained constant.

339

340

341 **3.2.1 Selection of the sol-gel coated CPME device**

342 Firstly, the seven sol-gel sorbent encapsulated CPME devices (see section 2.3)
343 were evaluated. The length of the capsules was 3 cm. These capsules were initially
344 tested under the following experimental conditions: salt content: 0% w/v NaCl,
345 extraction time: 30 min, sample volume: 20 mL, stirring rate: 500 rpm, eluent: acetone,
346 volume of eluent: 1 mL, desorption time: 5 min. Table S2 presents the results of the
347 investigation of the different sol-gel sorbents. Sol-gel C₁₈ exhibited the best adsorption
348 performance taking into consideration all the examined analytes. C₁₈ is a powerful
349 sorbent for the extraction of OPPs from water samples (Ballesteros and Parrado, 2004;
350 Harshit et al., 2017; Xie et al., 2013).



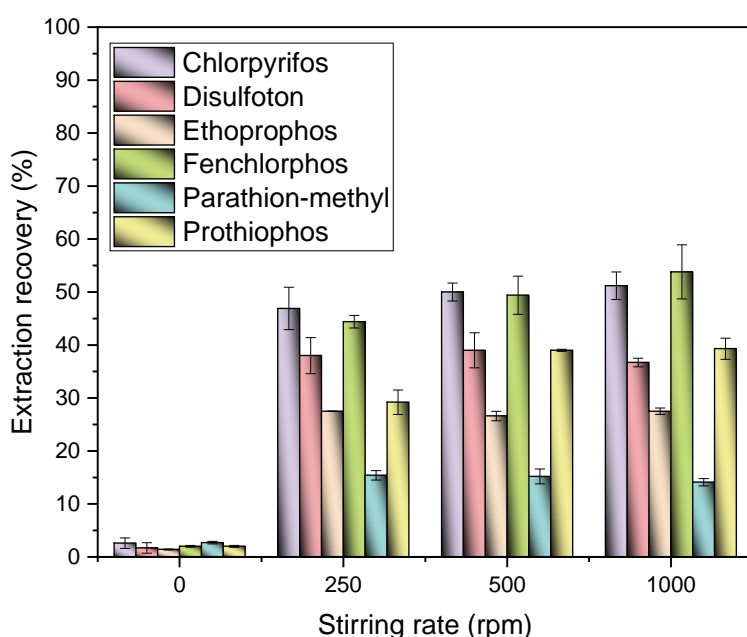
351 Subsequently, two different dimensions of sol-gel C₁₈ encapsulated CPME
352 devices (i.e., 1 cm and 3 cm) were evaluated (Figure S5). The 3 cm microextraction
353 capsules showed higher extraction performance, due to the higher sorbent loading.
354 Thus, further experiments were conducted using of sol-gel C₁₈ encapsulated CPME
355 devices of 3 cm.

356

357 3.2.2 Optimization of adsorption conditions

358 The parameters that can affect the adsorption step were optimized. The
359 optimization of the adsorption conditions was conducted starting from the following
360 experimental conditions: sol-gel sorbent: C₁₈, length of microextraction capsules: 3 cm,
361 salt content: 0% w/v NaCl, extraction time: 30 min, sample volume: 20 mL, stirring
362 rate: 500 rpm, eluent: acetone, volume of eluent: 1 mL, elution time: 5 min.

363 In equilibrium-based microextraction techniques, the implementation of
364 external stimuli (e.g., stirring, shaking or sonication) can enhance the diffusion of the
365 target analytes and result in lower extraction time and enhanced recovery (N. Manousi
366 et al., 2021a). CPME integrates a stirring mechanism, since it contains a magnetic rod
367 and, thus, sample stirring can be employed to assist the adsorption step. Four different
368 stirring rates between 0 and 1000 rpm were investigated. Figure 3 shows the effect of
369 stirring rate on the extraction recovery. It is noteworthy that without constant stirring,
370 negligible extraction recoveries were obtained for all the target analytes.



371

372 **Figure 3.** Evaluation of the effect of different stirring rates.

373

374 An increase of stirring rate up to 500 rpm had a positive impact on the CPME
375 procedure. Moreover, the extraction recoveries of all analytes remained constant up to
376 a stirring rate of 1000 rpm. Thus, extraction was conducted using a stirring rate of 500
377 rpm.

378 Subsequently, sample volume was examined in the range of 10-50mL. Higher
379 recoveries were obtained when 10 mL of water sample were utilized (Figure S6).
380 However, regarding sample enrichment the operation of higher sample amount (e.g., 20
381 mL or 50 mL) could result in higher PFs and, thus, enhanced method sensitivity.
382 Therefore, as a compromise between ER% and PF values, further experiments were
383 performed using 20 mL of sample.

384 Extraction time is a factor that is important for the performance of equilibrium-
385 based techniques like CPME, since it is necessary to find a time span sufficient for all
386 analytes to reach equilibrium (N. Manousi et al., 2021a). During the investigation of
387 the extraction time, five different time spans between 15 and 75 min were examined.
388 As shown in Figure S7, most analytes reached an equilibrium at 60 min. Only for
389 parathion-methyl the recovery was enhanced for an extraction time up to 75 min.
390 However, since adequate sensitivity was obtained for all analytes and in order to avoid
391 prolonging of the extraction time and to ensure method rapidity, an extraction time of
392 60 min was chosen.

393 Finally, the impact of the ionic strength of the water sample was investigated.
394 Therefore, different amounts of sodium chloride between 0 and 20% w/v) were
395 evaluated. Salt addition may have either a positive effect (i.e., by decreasing the target
396 analytes' solubility and thus favoring their interaction with the adsorbent, known as
397 salting-out effect) or a negative effect (i.e., by increasing the density of the aqueous
398 sample and lowering the mass transfer of the target analytes) in the microextraction
399 process (N. Manousi et al., 2021b). An increase of the ionic strength up to 5% w/v did
400 not have an impact on the efficiency of extraction for the target analytes (Figure S8).
401 However, an enhancement of the NaCl content up to 10% w/v had a negative impact
402 for chlorpyrifos, fenchlorphos and prothiophos. Moreover, at 20% w/v NaCl the
403 extraction performance for most analytes was significantly reduced. As a compromise
404 for all OPPs, further experiments were carried out with no salt addition.

405



406 3.2.3 Optimization of desorption conditions

407 Following the optimization of the adsorption step, the effect of the main
408 parameters affecting the elution (i.e., eluent, mode of elution, eluent amount and
409 desorption time) were studied. Adsorption optimization was conducted using the
410 following initial experimental conditions: sol-gel sorbent: C₁₈, dimensions of
411 microextraction capsules: 3 cm, stirring rate: 500 rpm, extraction time: 60 min, sample
412 volume: 20 mL, salt content: 0% w/v NaCl, eluent: acetone, volume of eluent: 1 mL,
413 desorption time: 5 min.

414 The effect of eluent was examined by evaluating the performance of four
415 different solvents, i.e., acetone, methanol, acetonitrile, and toluene for the desorption
416 of the adsorbed OPPs. An appropriate eluent must provide effective desorption of the
417 analytes with enhanced recovery (Kaur et al., 2019). As shown in Figure S9, similar
418 results were obtained for most analytes using acetone, methanol, and acetonitrile.
419 However, acetone exhibited better performance compared to the other solvents for
420 prothiophos, while it also characterized by low toxicity. Thus, acetone was chosen as
421 eluent.

422 Accordingly, the elution mode was investigated. Since the CPME device
423 contain a magnetic rod, the device can spin when a magnetic stirrer is employed. The
424 need for stirring during the elution process was studied to ensure sufficient desorption
425 of the analytes and two different modes of elution (i.e., with and without stirring) were
426 evaluated. As it can be observed from Figure S10, stirring was not required during the
427 elution of the target analytes. This is probably because of the sponge-like morphology
428 and the inherent porosity and of sol-gel sorbents that enables the diffusion of the eluent
429 during the desorption process, thus overcoming the need for any external energetic
430 stimulus during this step (Kabir and Samanidou, 2021). Therefore, elution of the OPPs
431 from the sol-gel C₁₈ coated CPME device was carried out without stirring.

432 The desorption time is another important factor that must be investigated during
433 the optimization of the CPME protocol to find the optimum time span that is required
434 for elution system to exhaustively scavenge the adsorbed analytes and to ensure high
435 sample throughput (Kabir and Samanidou, 2021). In this study, the desorption time was
436 investigated in the range of 1-15 min. As it can be observed in Figure S11, 1 min was
437 sufficient for the desorption of most of the adsorbed OPPs and it was chosen for further
438 experiments. Only for chlorpyrifos, a slight increase of the extraction efficiency was
439 observed by increasing the desorption time at 5 min. However, in order have increased



440 sample throughput and a rapid sample preparation protocol a desorption time of 1 min
441 was finally chosen.

442 Finally, the amount of acetone was investigated. For this purpose, aliquots (250-
443 1500 μL) were used during the elution step. The amount of the desorption solvent is
444 associated with the enriching ability of the method and thus the utilization of small
445 amounts of eluent can provide enhanced method sensitivity. Moreover, the use of low
446 solvent amount complies with GAC regarding the reduction of the consumption of
447 hazardous chemicals. In this case, sufficient recovery was obtained using small amount
448 of acetone (Figure S12). Only for chlorpyrifos, the ER% was improved by using a
449 higher solvent amount (1500 μL). However, taking into consideration the requirements
450 of GAC, the elution of the OPPs was conducted using 250 μL of eluent.

451

452 3.3. Figures of merit

453 Method validation is thoroughly described in the Supplementary Material. The
454 figures of merit of the proposed method are presented in Table 1. Good linearity was
455 achieved for the OPPs and the coefficients of determination were 0.9912-0.9996. The
456 LODs of the CPME-GC-MS methodology for the target analytes were 0.02-0.15 ng
457 mL^{-1} and the LOQs were 0.05-0.50 ng mL^{-1} . The PF of the proposed method was 80 for
458 all OPPs taking into consideration that the initial volume of sample was 20 mL and the
459 final volume after elution was 250 μL . Moreover, the EF values for the target analytes
460 ranged between 15 and 47, while the ER% values were 19-59%.

461

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

OPP	Regression Analysis	R ²	Linear range (ng mL ⁻¹)	LOD (ng mL ⁻¹)	LOQ (ng mL ⁻¹)	ER%	EF
Chlorpyrifos	y = 11696x + 5981.8	0.9982	0.20-100.0	0.06	0.20	59	47
Disulfoton	y = 32847x - 41670	0.9912	0.05-50.0	0.02	0.05	48	39
Fifthoprophos	y = 8734.8x + 9309.8	0.9985	0.20-50.0	0.06	0.20	34	27
Enchlorphos	y = 23013x + 14285	0.9969	0.05-50.0	0.02	0.05	57	46
Parathion- methyl	y = 5819.1x - 1159.3	0.9996	0.50-100.0	0.15	0.50	19	15
Prothiophos	y = 9119.1x + 33918	0.9982	0.20-100.0	0.06	0.20	53	42

463

464 The results for the evaluation of method precision and accuracy are presented
465 in Table S3. The RR% for the target analytes ranged between 92.6% and 107.0% for
466 the intra-day study and between 90.8% and 107.6% for the inter-day study, indicating
467 good method trueness. Furthermore, the RSDs were 1.5-8.7% and 5.4-9.6% for the
468 intra-day and inter-day study, respectively. Thus, the method exhibits good precision.
469 At a final step, the capsule-to-capsule reproducibility was examined utilizing six (n=6)
470 different sol-gel C₁₈ encapsulated microextraction capsules. The CPME media were
471 used for the extraction of OPPs (c=5.00 ng mL⁻¹) from standard solutions prepared in
472 deionized water. As shown in Table S3, the RSDs were better than 3.2%, indicating
473 good capsule-to-capsule reproducibility.

474

475 **3.4. Reusability of the sol-gel C₁₈ capsules**

476 During the evaluation of the performance of the sol-gel C₁₈ encapsulated
477 microextraction capsules, their potential reusability was examined. For this purpose, a
478 single CPME device was used in 25 continuous adsorption/elution cycles of the target
479 analytes from tap water. The reusability was evaluated taking into consideration the
480 RR% value derived from the initial performance of the sol-gel C₁₈ coated capsule and
481 the performance after consecutive microextraction cycles. As such, a threshold of ≥
482 10% of performance loss was set. The results are summarized in Figure S13. Since no
483 important performance's reduction was seen after continuous adsorption/elution cycles,
484 it can be concluded that the capsules are reusable for at least 25 times.

485

486 **3.5. Comparison with other studies**

487 A comparison of the herein proposed CPME-GC-MS method with other studies
488 published in the literature is shown in Table 2.

489

490

491 **Table 2.** Comparison with other studies

Extraction	OPPs	Instrumentation	Sample volume (mL)	RSD%	Relative Recoveries %	Enhancement factors	LODs (ng mL ⁻¹)	Ref.
MSPE	Chlorpyrifos methyl, diazinon, malathion, parathion, parathion-methyl, pirimiphos-methyl	GC-MS	10	≤ 10.7 %.	NA ¹	NA	1.8-5.0	(Xie et al., 2013)
DLLME	Parathion-methyl, phoxim	HPLC-UV	10	2.5-2.7	88.2-103.6	50	0.17-0.29	(Zhou et al., 2008)
PT-SPE	Malathion, parathion	GC-MS	2	≤ 6.37	89.37-101.22	42.7-47.3	0.10	(Esrafil et al., 2020)
Continuous SPE	Diazinon, dimethoate, fenthion, fenthion sulfoxide, malathion, methidathion, parathion ethyl, parathion methyl	GC-NPD	10	2.9-4.3	93.8-104.5	95.0-98.6	0.05-0.13	(Ballesteros and Parrado, 2004)
SPME	Bromophos ethyl, bromophos methyl, dichlofen- thion, ethion, fenamiphos, fenitrothion,	GC-MS and GC-FTD	2-5	7-14 (for GC-MS) 3-10 (for GC-FTD)	86.2-119.7	NA	0.01-0.05 (for GC-MS)	(Lambropoulou et al., 2000)



Extraction	OPPs	Instrumentation	Sample volume (mL)	RSD%	Relative Recoveries %	Enhancement factors	LODs (ng mL ⁻¹)	Ref.
	fenthion, malathion, parathion-ethyl, parathion-methyl						0.01-0.02 (for GC-FTD)	
d-SPE	Diazinon, fenitrothion, fenthion, phosalone, profenofos	GC-FID	20	4.9-8.5 (intra-day) 5.9-8.8 (inter-day)	91.9-99.5	803-914	0.03-0.21	(Amiri et al., 2019)
CPME	Chlorpyrifos, disulfoton, ethoprophos, fenchlorphos, parathion-methyl and prothiofos	GC-MS	20	1.5-8.7 (intra-day) 5.4-9.6 (inter-day)	92.6-107.0 (intra-day) 90.8-107.6 (inter-day)	15-47	0.02-0.15	This study

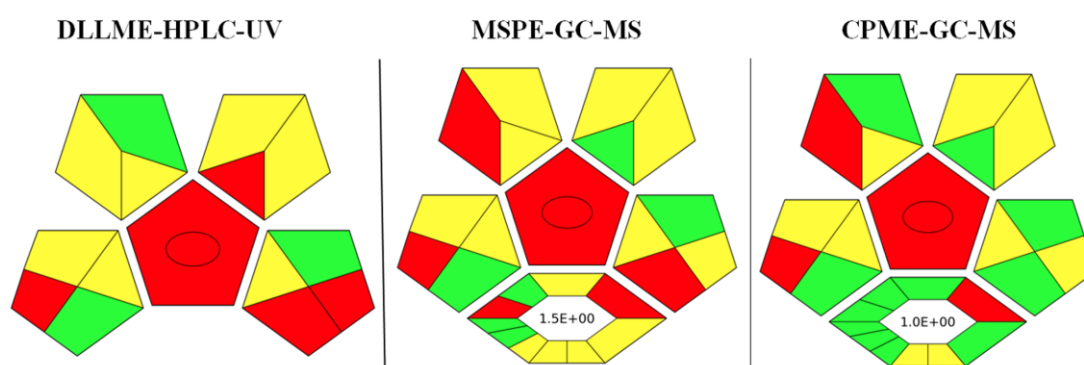
492

493 ¹ N.A.: Not available

494 As it can be observed, the developed approach permitted the utilization of higher
495 amount of sample compared to those in literature (Ballesteros and Parrado, 2004;
496 Esrafilı et al., 2020; Lambropoulou et al., 2000; Xie et al., 2013; Zhou et al., 2008). In
497 addition, the accuracy (in terms of RR% values) and the precision (in terms of RSD%
498 values) of the proposed method is satisfactory, compared to other studies. The
499 enhancement factors of the proposed method were similar to those of ref. (Esrafilı et
500 al., 2020; Zhou et al., 2008) but lower to those of ref. (Amiri et al., 2019; Ballesteros
501 and Parrado, 2004). The LODs for the OPPs were better than those reported in ref.
502 (Esrafilı et al., 2020; Xie et al., 2013; Zhou et al., 2008) and comparable to those in refs.
503 (Amiri et al., 2019; Ballesteros and Parrado, 2004; Lambropoulou et al., 2000). In case
504 that further enhancement of method sensitivity is required, the herein developed
505 microextraction protocol can be combined with more sensitive systems (e.g., GC-
506 MS/MS instruments).

507 Besides the analytical performance parameters, the green nature of the selected
508 procedures was also compared by application of ComplexGAPI (Płotka-Wasyłka and
509 Wojnowski, 2021). This tool enables the evaluation of the different analytical methods
510 according to the principles of GAC. ComplexGAPI index takes into consideration the
511 procedures, reagents, and instrumentation that are employed in an analytical method,
512 while it also considers all the processes before the analysis (Płotka-Wasyłka and
513 Wojnowski, 2021). A green colour indicates the compliance with the respective
514 requirements. From the GAPI pictogram in Figure 4, it can be concluded that the
515 synthesis of the capsules shows high process yield and reduced waste generation, while
516 it also shows a low E-factor, supporting green economy. Moreover, reduced
517 consumption of chemicals and reduced waste generation can be also considered among
518 the benefits of the technique since microextraction is used. As it can be seen, the
519 proposed CPME-GC-MS method shows a greener character compared to previously
520 reported protocols.





521

522 **Figure 4.** ComplexGAPI pictograms obtained for procedures based on DLLME-
 523 HPLC-UV (Zhou et al., 2008), MSPE-GC-MS (Xie et al., 2013), and CPME-GC-MS
 524 (this study)

525

526 Considering other advantages, CPME offers the benefits of fast and easy
 527 isolation of the sorptive phase, since the CPME device can be easily handled by using
 528 tweezers resulting in ease in isolation from the sample solution. On the contrary, the
 529 separation of the adsorbent in d-SPE (or MSPE) processes can be a time-consuming
 530 step and it may require additional instrumentation (e.g., centrifugation).

531 Additionally, in comparison with conventional SPE and LLE approaches,
 532 CPME offers the ability to use reduced amount of organic solvents and to simplify the
 533 overall procedure. When compared to a procedure based on HPLC-UV (Zhou et al.,
 534 2008), the same conclusion can be made, meaning, reduction of the solvent
 535 consumption and production of waste. Considering MSPE-GC-MS method (Xie et al.,
 536 2013) in which also additional processes are required prior to analysis, it is visible at
 537 first glance that the CPME-GC-MS method is greener, mainly in terms of the conditions
 538 used for the synthesis of required elements (sorbents, devices).

539 All features considered, CPME is a powerful technique for the monitoring of
 540 OPPs in environmental water samples.

541

542

543

544

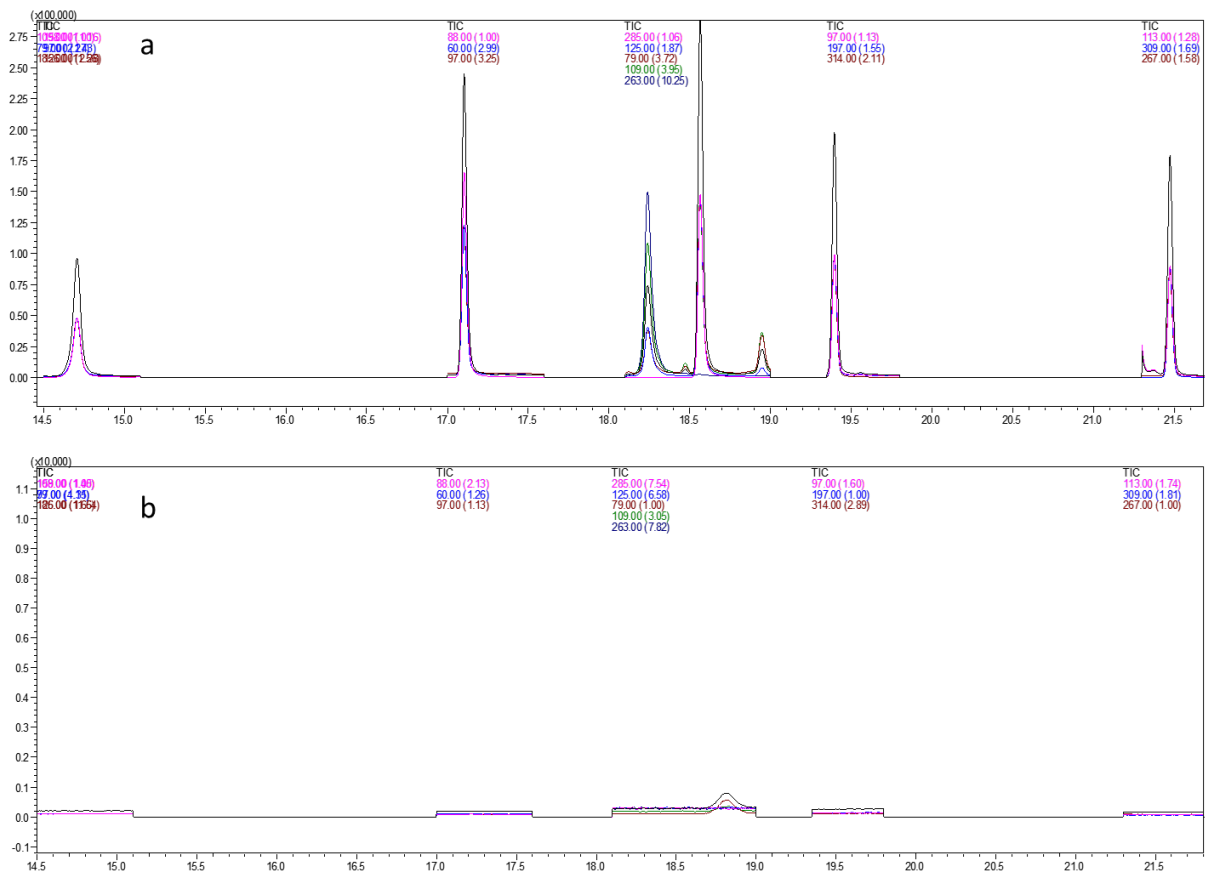
545



546 **3.6. Analysis of real samples**

547 The CPME-GC-MS protocol was finally employed for the determination of
548 OPPs in real water samples. Chromatograms of a spiked and a blank water sample are
549 shown in Figure 5.

550



551

552 **Figure 5.** Chromatograms of (a) spiked river water sample ($c=2.00 \text{ ng mL}^{-1}$) and (b)
553 blank river water.

554

555 For the assessment of the potential method applicability in different types of
556 water samples, spiked sample solutions ($c=5.00$ and 20.0 ng mL^{-1}) were prepared and
557 analysed. Table 3 presents the obtained results for the real samples.

558

559 **Table 3.** Determination of OPPs by CPME-GC-MS in real water samples (n=2)

Analyte	Added (ng mL ⁻¹)	Lake water		Pond water		River water		Tap water	
		Found (ng mL ⁻¹)	Relative Recovery (%)	Found (ng mL ⁻¹)	Relative Recovery (%)	Found (ng mL ⁻¹)	Relative Recovery (%)	Found (ng mL ⁻¹)	Relative Recovery (%)
Chlorpyrifos	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	5.00	5.58±0.49	111.6	5.73±0.40	114.6	5.18±0.39	103.6	4.77±0.20	95.4
	20.0	18.2±1.2	91.0	20.4±1.2	102.0	17.6±1.4	88.0	20.4±0.1	102.0
Disulfoton	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	5.00	5.18±0.34	103.6	5.34±0.30	106.8	5.32±0.45	106.4	5.20±0.29	104.0
	20.0	20.4±0.9	102.0	19.0±0.1	95.0	19.0±0.8	95.0	18.0±1.6	90.0
Ethoprophos	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	5.00	4.87±0.33	97.4	5.05±0.36	101.0	5.32±0.45	106.4	5.71±0.31	114.2
	20.0	20.5±1.5	102.5	19.3±0.2	96.5	18.9±0.4	94.5	18.5±1.3	92.5
Fenclorphos	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	5.00	4.54±0.19	90.8	5.02±0.18	100.4	5.71±0.21	114.2	4.32±0.15	86.4
	20.0	21.3±0.3	106.5	20.6±1.0	103.0	20.5±0.7	102.5	18.1 ± 0.2	90.5
Parathion- methyl	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	5.00	4.27±0.15	85.4	4.49±0.34	89.8	5.11±0.08	102.2	4.08±0.09	81.6

Analyte	Added (ng mL ⁻¹)	Lake water		Pond water		River water		Tap water	
		Found (ng mL ⁻¹)	Relative Recovery (%)	Found (ng mL ⁻¹)	Relative Recovery (%)	Found (ng mL ⁻¹)	Relative Recovery (%)	Found (ng mL ⁻¹)	Relative Recovery (%)
Prothiophos	20.0	21.8±1.0	109.0	21.4±1.4	107.0	19.8±0.2	99.0	20.9±0.4	104.5
	0	<LOD	-	<LOD	-	<LOD	-	<LOD	-
	5.00	5.27±0.51	105.4	4.69±0.37	93.8	4.75±0.41	95.0	4.82±0.25	96.4
	20.0	19.3±0.9	96.5	17.6±1.5	88.0	19.2±1.4	96.0	18.8±1.0	94.0

560

561 The OPPs were not detected in the real samples. Thus, either there were no
562 residues of these compounds in the samples, or their concentrations were lower
563 compared to their respective LOD values. The RR% values for all analytes were found
564 to be 81.6-114.6%. The average value 99.0% demonstrates that no significant matrix
565 effect exists between the examined matrices. Thus, the proposed analytical scheme can
566 be used for the analysis of lake, river, pond and tap water samples with good accuracy.
567 Finally, the absence of interferences in the real samples confirm method selectivity.

568

569 **4. Conclusions**

570 A simple and efficient CPME-GC-MS protocol was developed for the monitoring of
571 OPPs in environmental water samples. Sol-gel C₁₈ encapsulated microextraction media
572 were proved to be the most efficient CPME device for extracting and preconcentrating
573 the target analytes. The analytical scheme exhibited good linearity, accuracy,
574 sensitivity, and precision. The sol-gel C₁₈ coated CPME devices were able to extract
575 the target analytes from water samples for at least 25 continuous adsorption/desorption
576 cycles. Moreover, the proposed method showed a greener character compared to
577 previously reported protocols. A disadvantage of this methodology is that extraction
578 was not *in situ* performed. However, by utilizing CPME and portable magnetic stirring,
579 extraction can be carried out directly in the field aiming to reduce sample
580 transport/storage costs. All features considered, CPME is an efficient and simple novel
581 sample preparation which can be utilized for monitoring pollutants in environmental
582 water. Future directions towards the utilization of CPME for OPPs extraction include
583 its application for the sample preparation of other complex samples (e.g., food samples)
584 and the expansion of its application for the extraction of multi-class of pesticides.

585

586 **Declaration of Competing Interest**

587 The authors declare no conflict of interest

588

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