Insights in the analytical performance of neat metal-organic frameworks in the determination of pollutants of different nature from waters using dispersive miniaturized solid-phase extraction and liquid chromatography

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Abstract

Five metal-organic frameworks (MOFs), specifically HKUST-1, MOF-5(Zn), MIL-53(Al), UiO-64 and MOF-74(Zn) are synthetized, characterized, and utilized in a miniaturized solid-phase extraction method under dispersive mode (D-μSPE) for the determination of six pollutants of different nature, including one polycyclic aromatic hydrocarbon, two hormones, two drugs, and one disinfectant, from environmental waters (tap water and wastewater). A discussion of possible interactions justifying the partitioning of target analytes to the MOFs is included, considering not only the analytes' physicochemical characteristics but also those of MOFs: metal nature, structural environment of MOF pores, pore size and pore aperture, among others. MIL-53(Al) is selected for its versatility and high extraction efficiency for the target compounds. The D-μSPE method using MIL-53(Al) is optimized and used in combination with high-performance liquid chromatography (HPLC) with diode array detector (DAD) or liquid-chromatography with time-of-flight mass spectrometric detector (LC-TOF). Under optimum conditions, only 5 mg of MIL-53(Al) are required for 10 mL of water, with the aid of 5 min of vortex and 5 min of centrifugation. Elution is accomplished with 200 μL of acetonitrile (3 times), and evaporation down to 100 μL before LC injection. Detection limits down to 0.040 μg L^{-1} for triclosan and 0.013 μg L^{-1} for atrazine are obtained for the entire method using HPLC-DAD and LC-TOF, respectively. The method, operating at low spiked levels (2 μg·L^{-1} for HPLC-DAD and 0.7 μg·L^{-1} for LC-TOF), is also characterized for average relative recoveries of 109% and 105%; relative standard deviation values lower than 8.7% and 7.5%; and average extraction efficiencies of 41.2% and 49.1%; using HPLC-DAD and LC-TOF, respectively; while demonstrating adequate analytical performance with complex samples such as wastewaters.

Keywords: metal-organic frameworks; dispersive miniaturized solid-phase extraction; sample preparation; pollutants; environmental waters

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1. Introduction

Metal-organic frameworks (MOFs) are structurally diverse, porous materials that are composed of metal nodes bridged by organic linkers [1]. Using rational design, the chemical and physical properties of MOFs can be tuned elegantly to generate materials with very high surface areas (from ~200 to ~7000 m^2 g), high porosity, and adequate chemical and thermal stability [2,3]. Furthermore, the possibility of performing in pore functionalization and outer-surface modifications have made MOFs outstanding materials in a variety of fields (sensing, catalysis, gas storage, energy applications…) [4-7]. Recent attention has also arisen around them in analytical chemistry [8-11].

MOFs have been successfully used as sorbents in a variety of microextraction methods [8-10,12], with the higher number of applications devoted to their use in dispersive miniaturized solid-phase extraction (D-µSPE) approaches [8,10]. D-µSPE is gaining a lot of attention nowadays in sample preparation from an environmental-friendly point of view, due to impressive decrease in the amounts of sorbents required (<500 mg) together with the assurance of an adequate partitioning of the target analytes to the solid sorbent (normally favored by the strength of the sorbent dispersion into the sample) [13]. Appropriate sorbents for D-µSPE should present ideally an adequate chemical and mechanical stability under extraction/elution conditions (water stability, stability *versus* extreme pH and salt content values, maintaining of integrity under the presence of several organic solvents…) [14], reusability, fast kinetics, ability to disperse properly in liquid samples, large specific surface area (~400 m^2 g^{-1})… [8]. Given these considerations, it is not a surprise that applications of MOFs in this strategy constitute a sample preparation trend [8,10].

In D-μSPE applications involving neat MOFs as novel sorbents, analytes belonging to the same family of compounds have been the focus of the strategies: polycyclic aromatic hydrocarbons (PAHs) [15,16], polychlorinated biphenyls (PCBs) [17], phenols [18], triazine herbicides [19], hormones [20], phenylurea herbicides [21], and parabens [22], among others. Clearly, it is interesting the development of MOFs for task-specific applications [23] as those reported but it would be also of interest to find successful MOFs performing as generic sorbents for a wide variety of compounds (and thus not exclusively associated to a specific family of compounds). At the same, it is important to gain knowledge regarding MOF structure-extraction performance activity [24], with the purpose of increasing the tools for MOFs design intended for sample preparation.

This study intends to find a versatile MOF able to extract contaminants with different chemical and physical properties, and, if possible, to establish relationships between MOF structure – analyte nature considering the analytical performance of the microextraction. In this sense, five different MOFs will be tested in a D-μSPE method for determining six emerging pollutants of quite different nature (two pharmaceutical drugs, one disinfectant, one polycyclic aromatic hydrocarbon, and two hormones) in water samples (tap water and wastewater). Specifically: HKUST-1, with Cu as metal and benzene-1,3,5-tricarboxylic acid as ligand; MOF-5(Zn), with Zn and terephthalic acid; MIL-53(Al), with Al and terephthalic acid; UiO-64, with Zr and fumaric acid; and MOF-74(Zn), with Zn and 2,5-dihydroxyterephthalic acid; will be the MOFs under consideration. The microextraction method will be used in combination with high-performance liquid chromatography (HPLC) and diode array detection (DAD), and with ultrahigh-performance liquid chromatography (UHPLC) and time-of-flight (TOF) mass spectrometry detection. Within all MOFs evaluated in this study, HKUST-1 and MOF-

5(Zn) are the only ones previously reported as neat sorbent materials in D-μSPE [22,25], whereas MIL-53(Al), UiO-64 and MOF-74(Zn) have been not reported yet as extraction sorbents in D-μSPE.

2. Experimental

2.1. Chemicals, reagents, materials, and samples

Six pollutants of quite different nature were subjected to study. Carbamazepine (99.0%) and atrazine were purchased from Sigma-Aldrich (Steinheim, Germany); progesterone (>99.99%) and triclosan (>99.99%) were obtained from US Pharmacopoeia Reference Standard (Basel, Switzerland); estrone was purchased from European Pharmacopoeia Reference Standard (Strasburg, France); and fluorene was obtained from Supelco (Bellefonte, PA, USA). All these compounds were obtained as solid products. A standard solution containing all pollutants was prepared in acetonitrile (ACN) HiPerSolv Chromanorm liquid chromatography (LC) grade, purchased from VWR (Llinars del Vallés, Spain), at a concentration of 10 $mg \cdot L^{-1}$, and stored at 4 ºC. Working standard solutions for the calibrations were weekly prepared in ACN.

Deionized water (Milli-Q, ultrapure grade) was obtained by a water purification system A10 MilliPore (Watford, UK). Methanol was of LC grade (Chromasolv®, purchased to Sigma-Aldrich).

HPLC mobile phases were always filtered with Durapore® membrane filters of 0.45 μm, supplied by Sigma-Aldrich. UHPLC mobile phase were always filtered with the same brand of filters but of 0.22 μm. Samples were also filtered with 0.22 μm of Durapore® before application of the d-μSPE method.

0.2 μm syringe filters Whatman™ PVDF (polyvinylidene fluoride) were purchased from GE Healthcare (Buckinghamshire, UK), and used to filter all eluates before HPLC or UHPLC injection.

Pyrex® centrifuge tubes (Staffordshire, UK) were used in the microextraction procedure, with dimensions of 10×2.6 cm and volume of 30 mL. Parr Instrument Company (Moline, IL, USA) supplied solvothermal reactors (composed by Teflon) and stainless steel autoclaves.

Copper(II) nitrate hemi(pentahydrate), zinc(II) acetate dihydrate, aluminum(III) nitrate nonahydrate, zirconium(IV) chloride, 2,5 dihydoxyterephthalic acid (98%), fumaric acid (<99%), imidazole (99%), triethylamine (TEA), benzene-1,3,5-tricarboxylic acid (95%) (H_3btc) and terephthalic acid (H_2bdc) (98%), were purchased from Sigma-Aldrich and used to synthetize the MOFs. Formic acid ACS reagent was supplied by Merck (Darmstadt, Germany). Ethanol absolute (99.5%) and chloroform ($CHCl_3$, 99%) were purchased to Panreac (Barcelona, Spain), whereas dimethylformamide (DMF) 99.9% HPLC grade and ammonium acetate were acquired to Fluka-Sigma Aldrich.

Tap water was taken at the laboratory. Three wastewater samples were supplied by an environmental monitoring laboratory. They were sampled in different areas of Tenerife Island (Canary Islands, Spain) using amber glass recipients properly cleaned, avoiding the formation of bubbles during sampling. They were kept in fridge until reaching the lab, and then they were filtered through 0.45 μm filters and kept in the dark at 4 ºC until analysis.

2.2. Synthesis of MOFs

146 The MOFs used in this study were synthetized according to previous reports with
147 minor modifications: HKUST-1 [26], UiO-64 [27], MOF-5(Zn) [28], MOF-74(Zn) [29]
148 and MIL-53(Al) [30]. Once prepared, all MOFs were activated by heating at reduced
149 pressure in order to remove any possible guest molecule from the pores of the crystalline
150 structure. Proper activation temperatures were obtained through thermogravimetric
151 analysis/differential thermal analysis (TG/DTA) for each MOF.
152 HKUST-1 was prepared by adding dropwise 15 mL of an aqueous solution (using
153 ultrapure water) of $Cu(NO_3)_2 \cdot 5H_2O$ (1.255 g, 5.4 mmol) to 15 mL of an ethanol solution
154 of H_3btc (0.630 g, 3 mmol), followed by stirring for 20 min. Afterwards, the mixture was
155 transferred to the solvothermal reactor (45 mL), and heated to 110 ºC during 1 day. After
156 cooling down the system, the deep blue powder was filtered, washed with ethanol and
157 dried at room temperature (getting a yield of 90%, based on Cu). The activation
158 temperature of HKUST-1 was 150 ºC.
159 UiO-64 was synthetized dissolving first fumaric acid (0.081 g, 0.7 mmol) and
160 $ZrOCl_2$ (0.23 g, 0.7 mmol) in a solution formed by a mixture of DMF and formic acid (35
161 mL and 5.3 mL, respectively), while being magnetically stirred for 20 min. Afterwards,
162 the mixture was transferred to the solvothermal reactor (45 mL), and heated to 120 ºC
163 during 1 day. The white powder obtained was filtered, washed with fresh DMF, and air
164 dried (getting a yield of 65%, based on Zr). The activation temperature of UiO-64 was
165 150 ºC.
166 MOF-5(Zn) was prepared dissolving terephthalic acid (0.506 g, 3 mmol) and
167 triethylamine (0.85 mL) in 40 mL of DMF. Then, 50 mL of a DMF solution containing
168 $Zn(OAc)_2 \cdot 2H_2O$ (1.673 g, 7.6 mmol) was slowly added to the previous solution under
169 continuous stirring at room temperature. A precipitate was formed, and the suspension
170 was stirred for 2.5 h at room temperature. The precipitate was then filtered and immersed

171 in DMF overnight. Afterwards, it was filtered and immersed in $CHCl_3$. The $CHCl_3$ solvent
172 was renewed two times over 4 days. Finally, the white powder of MOF-5(Zn) was filtered
173 and stored under argon atmosphere (getting a yield of 60%, based on Zn). MOF-5(Zn)
174 required activation at 120 ºC under reduced pressure conditions.

175 MOF-74(Zn) was prepared by firstly dissolving the organic ligand, 2,5
176 dihydroxyterephthalic acid (0.155 g, 0.8 mmol) in DMF under stirring for 20 min, while
177 the $Zn(OAc)_2 \cdot 2H_2O$ (0.550 g, 2.5 mmol) was dissolved in ethanol:water (1:1, v/v). Both
178 solutions were mixed and the final solvent ratio was 15:1:1 (v/v/v), DMF:ethanol:H_2O.
179 The solution was then placed in a solvothermal reactor (45 mL), and heated at 120 ºC
180 overnight. The yellow-orange powder obtained was washed with fresh DMF and ethanol,
181 and then it was filtered and air dried (getting a yield of 70%, based on Zn). This MOF
182 was heated at 150 ºC during 24 h under reduced pressure for its activation.

183 MIL-53(Al) was prepared by dissolving H_2bdc (0.288 g, 1.7 mmol) and
184 $Al(NO_3) \cdot 9H_2O$ (1.3 g, 3.5 mmol) in 15 mL of ultrapure water. The solution was then
185 transferred to a solvothermal reactor (23 mL), and kept at 220 ºC for 3 days. Then, the
186 autoclave was cooled down to room temperature and the obtained white product was
187 isolated by filtration, washed with water, and air dried at 50 ºC (getting a yield of 45%,
188 based on Al). The MOF was finally heated at 400 ºC during 16 h for the activation.

189 All as synthetized MOFs were properly characterized by X-Ray Diffraction
190 (XRD), TG/DTA, and Scanning Electron Microscopy (SEM), and their sorption capacity
191 was evaluated with a nitrogen adsorption isotherm.

192

193 *2.3. Instruments and equipment*

194

195 The HPLC was a ProStar 230 Varian (Palo alto, CA, USA) in combination with a
196 diode array detector (DAD) ProStar 330 Varian. The quantification wavelengths of the
197 DAD were set at 220 nm for carbamazepine, atrazine, estrone and triclosan, 254 nm for
198 fluorene, and 236 nm for progesterone. The HPLC system includes a Rheodyne injection
199 valve with an injection loop of 20 µL, supplied by Supelco. The ACE Ultra Core 5
200 SuperC18 (5 µm, 150×4.6 mm) analytical column was obtained from Symta (Madrid,
201 España), with a safeguard column Pelliguard LC-18, purchased to Supelco. ACN and
202 ultrapure water were employed as mobile phases using a linear gradient at a constant flow
203 rate of 1 $mL \cdot min^{-1}$, starting from 40 to 100% of ACN (v/v) in 14 min, being then kept
204 isocratic for another 3 min.
205 The UHPLC was the model 1290 from Agilent (Agilent Technologies, Santa
206 Clara, CA, USA), connected to a time-of-flight mass spectrometer (MS/TOF) Agilent
207 6230 and equipped with an orthogonal ESI inter-face (Agilent Jet Stream, AJS). The ESI
208 parameters were the following: sheath gas temperature at 350 ºC, sheath gas flow at 11
209 $L \cdot min^{-1}$, nebulizer pressure at 40 psi, capillary voltage at 4000 V for positive mode and
210 3500 V for negative mode, nozzle voltage at 250 V, drying gas temperature at 350 ºC and
211 drying gas flow at 6 $L \cdot min^{-1}$. The sheath gas was nitrogen obtained by a Peak nitrogen
212 generator (Peak Scientific, Scotland, UK). The Agilent reference standard introduced by
213 an automatic reference sprayer system was used for mass correction with 121.050873 m/z
214 and 922.009798 m/z as the lock masses for the positive mode, and 68.9957 m/z, 112.9855
215 m/z, 119.036 m/z and 1033.9881 m/z for the negative mode. Data were collected from
216 100–1000 m/z in the centroid mode and the data acquisition rate was 0.7 s/scan. The Mass
217 Hunter Workstation software 4.0 from Agilent was used. The ZORBAX Eclipse Plus C18
218 column (1.8 µm, 2.1×50 mm) was obtained from Agilent. Carbamazepine, atrazine and
219 progesterone were determined under positive mode using as mobile phase: water with

220 0.1% (v/v) formic acid as phase A, whereas phase B was ACN with 0.1% (v/v) formic
221 acid. Regarding estrone and triclosan, their determination was performed in negative
222 mode using water with 0.03% (v/v) ammonium hydroxide as phase A, and ACN with
223 0.03% (v/v) in ammonium hydroxide as phase B. For all analytes, the chromatographic
224 separation was performed with a flow of 0.5 $mL \cdot min^{-1}$, starting in all cases with 40% of
225 phase B and being linearly increased up to 100% in 8 min.

226 A vortex from Reax-Control Heidolph GMBH (Schwabach, Germany) and a
227 centrifuge model 5720 Eppendorf (Hamburg, Germany) were utilized in the D-μSPE
228 procedure.

229 Phase identification of the as synthetized MOFs was carried out by X-ray powder
230 diffraction on a X'Pert Diffractometer, supplied by Panalytical (Eindhoven, Netherlands)
231 operating with Bragg-Brentano geometry. Data collection was carried out using Cu K_α
232 radiation (λ = 1.5418 Å) over the angular range from 5.01º to 80.00º (0.02º steps) with a
233 total exposure time of 30 min. The microscopic morphology of the material was examined
234 by a JSM6300 scanning electron microscope, from JEOL company (Tokyo, Japan). The
235 nitrogen adsorption isotherms were measured on a Gemini V 2365 Model, supplied by
236 Micromeritics (Georgia, USA) surface area analyzer at 77 K in the range $0.02 \leq P/P_0 \leq$
237 1.00. The Brunauer, Emmet and Teller (BET) method was used to calculate the surface
238 area. TG/DTA analysis was performed in a thermal analysis instrument Perkin Elmer
239 Pyris Diamond TGA/DTA (Waltham, MA, USA).

240

241 *2.4. Dispersive miniaturized solid-phase extraction procedure (D-μSPE)*

242

243 All conditions of the miniaturized solid phase extraction method using MOFs as
244 sorbents were carefully optimized. Under generic conditions, a certain amount of MOF

is added to a water sample of 10 mL, followed by vortex, centrifugation, removal of the supernatant, and elution of trapped analytes in the MOF by addition of certain amount of elution solvent. Under optimum conditions, 5 mg of MIL-53(Al) is added to 10 mL of water sample contained in a Pyrex® centrifuge tube. The tube is then subjected to vortex during 5 min, followed by centrifugation for 5 min at 3500 rpm. The supernatant aqueous phase is then removed with a Pasteur pipette. Afterwards, 200 µL of ACN are added to the MIL-53(Al) containing extracted analytes to perform its desorption, while applying vortex for another 5 min followed by centrifugation (5 min, 3500 rpm). The elution solvent is filtered through 0.2 µm PVDF syringe filters. The elution step with 200 µL of ACN was repeated two more times. The total elution volume of 600 µL of ACN containing extracted analytes was then subjected to dryness using a current of air assisted by a vacuum, down to 100 µL, and injected in the chromatographic system after proper filtration.

3. Results and discussion

3.1. Chromatographic methods

The determination of the six pollutants studied in this work was first achieved using HPLC-DAD, using proper quantification wavelengths for each analyte. The optimum conditions for the separation were summarized in Section 2.3. The overall separation took less than 11 minutes, as it can be observed in Figure ESM-1 of the Electronic Supplementary Material (ESM).

Table ESM-1 of the ESM shows several quality analytical parameters of the calibrations obtained by HPLC-DAD. Calibration curves were constructed by plotting the

chromatographic peak-area *versus* the pollutant concentration (in $\mu g \cdot L^{-1}$), using standards in ACN. Calibration curves were linear, with correlation coefficient values (R) higher than 0.9994. The limits of detection (LOD) and the limits of quantitation (LOQ) were calculated as the signal to noise (S/N) ratio of 3 and 10, respectively; and verified by preparation of standards at such concentration levels. LOQs varied from 9.30 $\mu g \cdot L^{-1}$ for fluorene to 49 $\mu g \cdot L^{-1}$ for estrone. The precision of the chromatographic method was evaluated using two standards at concentration levels not prepared when constructing the calibration curve, but included within the calibration range (See Table ESM-1). In all cases, RSD (in %) values for the peak areas were lower than 6.8% for the lowest concentration level tested. Regarding the reproducibility of the retention times, RSD values were always lower than 1.2% (n = 30, inter-day evaluation).

The determination of five (out of the six) pollutants studied in this work was also achieved using LC-TOF (fluorene excluded for not being adequate for TOF detection), with conditions described in Section 2.3. The overall separation is shown in Figure ESM-2 of the ESM, with separation achieved in less than 10 min.

Table ESM-2 of the ESM shows several quality analytical parameters of the calibrations obtained by LC-TOF. LODs and LOQs were estimated by the LC-TOF software, and verified by injection of standards in ACN prepared at those levels. LOQs ranged from 3.82 $\mu g \cdot L^{-1}$ for atrazine to 6.65 $\mu g \cdot L^{-1}$ for triclosan, being on average ~6 times lower than those obtained by HPLC-DAD. Calibration curves present adequate linearity, with R values higher than 0.9996. The precision of the chromatographic method was calculated using two standards at concentration levels not prepared when constructing the calibration curve, but included within the calibration range (50 and 500 $\mu g \cdot L^{-1}$). In all cases the RSD values were lower than 6.3% for the peak areas, and below 2.0% for the retention times (n = 30, inter-day evaluation).

295

296 *3.2. Characterization of the as synthetized MOFs*

297

298 The as synthetized HKUST-1, UiO-64, MOF-5(Zn), MOF-74(Zn) and MIL-
299 53(Al), were characterized by XRD, SEM, and TG/DTA analysis. Gas adsorption
300 isotherms to determine the porous properties of the MOFs through BET analyses were
301 also carried out.

302 A summary of the characterization data of each MOF is included in Table 1. The
303 crystal size was determined from SEM images, the porous volume and surface area were
304 obtained by BET analysis, and the activation and degradation temperature were obtained
305 from TG/TDA analysis. Proper comparison between experimental PRXD patterns and
306 theoretical ones was also performed (Figure ESM-3 of the ESM). Pore apertures widths
307 were obtained from the analysis of the crystal structures using the Cambridge Structural
308 Database (CSD) [31]. The CSD codes are listed also in Table 1.

309 The obtained surface areas of the MOFs tested in this study range from 505 $m^2 \cdot g^{-1}$
310 for MOF-74(Zn) to 1068 $m^2 \cdot g^{-1}$ for HKUST-1. Some of the BET surface areas
311 encountered are below the reported values, being MOF-5(Zn) one of the critical cases
312 where the synthesis route, the handling of the material, the activation and the storage
313 produce the largest variations in the surface area [32]. In all cases, they are quite adequate
314 surface area values for a material intended as sorbent. It must be considered that typical
315 values of zeolites (as example of common high efficient sorbents) normally range
316 between being ~300 and ~600 $m^2 \cdot g^{-1}$ [8,9]. Regarding pore volumes, they varied from
317 0.28 $cm^3 \cdot g^{-1}$ for MOF-5(Zn) to 0.48 $cm^3 \cdot g^{-1}$ for UiO-64 and HKUST-1, with pore aperture
318 widths ranging from 0.6 nm for UiO-64 to 1.1 nm for MOF-74(Zn). All MOFs are

thermally stable up to 400 ºC, and present degradation temperatures ranging from 450 ºC to 600 ºC.

The MOFs selected for this study represent a small but diverse representation of the MOF library. MOF-5(Zn) as a model of the primitive cubic system of isoreticular MOF, it has homogeneous pores and a large pore aperture width with the terephthalate aromatic rings covering the walls of the pores, leading to a hydrophobic environment. HKUST-1 represents one of the MOFs with more unsaturated metal sites per unit cell. It has different cavity sizes and a large pore aperture, it combines the reactivity of the unsaturated metal sites with the hydrophobicity of the trimesate aromatic rings in the pores. MOF-74(Zn) has a very large pore aperture (1.1 nm) and a hydrophilic environment produced by the unsaturated Zn metal sites. UiO-64 is a water stable Zr(IV) MOF, that besides the small pore aperture width, it has an intricate channel network with multiple H-bond anchoring positions. Finally, MIL-53(Al) has been selected to represent the flexible MOF family with variable pore aperture and a pore environment with the aromatic groups of the terephthalate, but also with unsaturated aluminum sites.

3.3. Evaluating the suitability of tested MOFs as sorbents in D-µSPE

A screening study was carried out firstly to select the best MOF as generic sorbent for the determination of a group of pollutants of different nature, using D-µSPE-HPLC-DAD as analytical method. Selected pollutants include one polycyclic aromatic hydrocarbon, two hormones, two drugs, and one disinfectant. Their structures and properties are quite different, as it can be observed in Table 2. The purpose was to evaluate the influence of the MOF nature in the extraction efficiency of analytes with different structures and polarities, intending to select a generic sorbent.

For the D-μSPE method, these preliminary studies were carried out using 20 mg of MOF in 10 mL of ultrapure water solution containing 20 $\mu g \cdot L^{-1}$ of analytes of interest. Given the fact that the method has not been optimized yet; relatively strong conditions were used (high MOF amounts for being a microextraction method, high stirring times and velocities, relatively high elution volume, relatively high spiked amount of compounds…). Thus, for each MOF the solution was vortexed during 5 min to ensure high contact material-analyte. Then, all studied MOF could be easily separated from the remaining aqueous solutions by centrifugation (5 min at 3500 rpm), with further decantation of the supernatant. To perform elution of analytes (expectedly trapped by the MOFs), 500 μL of ACN were added to the MOF, ensuring a good contact by vortexing for another 5 min. The MOF is separated again from the eluate by centrifugation (5 min at 3500 rpm). The ACN eluate is then sampled with a pipette, filtered through 0.2 μm, and directly injected into de HPLC-DAD system. This screening study was carried out by triplicate with each MOF.

Figure 1 shows the results (in terms of extraction efficiency, E_R in %, for each analyte with each MOF) of this preliminary study. Clearly, MIL-53(Al) was the best sorbent for the selected group of analytes, because this MOF was able to extract and subsequently elute all analytes studied. This MOF presents a flexible structure with variable pore sizes, which would justify its versatility for this group of analytes [33].

Despite the clear success of MIL-53(Al) in this screening study, it is also interesting to point out there are negligible extraction efficiency for a variety of the tested MOFs and analytes. The straightforward conclusion is that not every MOF adsorbs every analyte, and the extraction efficiency should be evaluated in a case by case basis. The D-μSPE method for these analytes comprises a complex methodology with several variables involved, but we can simplify them to just two: *i*) the MOF should be able to extract

368 efficiently the analyte from the water environment, and *ii*) The solvent, in this case, ACN,
369 should be able to elute the analytes from the MOF. Problems in the elution from MOFs
370 have been pointed out [8,22]. The efficiency in the elution process depends on the
371 magnitude of the host-guest *versus* the solvent-guest interaction. Optimization of the
372 elution solvent nature for each MOF and each analyte should enhance the extraction
373 performance, but it seems unpractical fairly. ACN is a relatively polar solvent, and should
374 be able to elute properly the trapped analytes in the MOF.

375 Regarding the first variable, the adsorption of the analytes into the MOF material,
376 the pore aperture of the MOF seems to play a central role. They are listed in Table 1, but
377 those are not restrictive values, since some flexibility is always allowed [33]. Considering
378 the geometry of the molecules in the solid state as a model for their appearance in solution,
379 all the tested analytes can enter in the pores of all the MOFs tested, except for atrazine in
380 UiO-64. However, carbamazepine dimerize in the solid state through amide-to-amide
381 hydrogen bonds [34], a situation that it has been also observed in solution [35]. In a polar
382 solvent, the dimerization is weak and occurs through π-type interactions exposing the
383 amide groups towards the environment [35]. Then, those MOFs with enough pore
384 aperture to accommodate a dimer and containing unsaturated metal sites, able to anchor
385 the carboxamide group, will show better performance.

386 MIL-53(Al), HKUST-1 and MOF-74(Zn) exhibit unsaturated metal sites, not only
387 inside the pores but also on the surface of the crystallites. Additionally, the pores of MIL-
388 53(Al) are large enough to accommodate the dimerized molecule so we observe
389 extraction in Figure 1. HKUST-1 probably can retain the carbamazepine on the surface
390 although it cannot enter inside the pores (a situation that cannot be discarded) and thus,
391 we observe certain extraction in the screening study. MOF-74(Zn), however, does not
392 exhibit the unsaturated metal sites in a water environment, since they are readily occupied

393 by the water molecules [36] and, even having large pores in the structure, the E_R is
394 negligible for carbamazepine.
395 The case of the atrazine is similar to the carbamazepine, being a good hydrogen
396 bond donor, in the solid state forms a catemer, an hydrogen bonded tape persistent in
397 other *s*-triazines [37]. It seems that the presence of unsaturated metal sites in the structure
398 is key for the extraction of these hydrogen bond donor molecules since only MIL-53(Al)
399 and HKUST-1 are able to adsorb them.
400 Interestingly, only MIL-53(Al) seems to be able to extract estrone from the water
401 media. It has been reported that a composite polydimethylsiloxane (PDMS)/MOF-5 is
402 able to extract estrone and other estrogens from water [38], thus maybe the role of the
403 polymer is important for such extraction, and in our case MOF-5 is perhaps able to extract
404 estrone but not significantly. Estrone can also form H-bonds through the terminal –OH
405 group, and in the solid state it forms supramolecular chains via O–H···O bonds with the
406 carbonyl group [39].
407 The progesterone molecule is quite similar to estrone, but it cannot act as an H-
408 bond donor, and has a lower solubility in water (see Table 2). However, all the tested
409 MOFs can extract it from water. The packing in the solid state of progesterone is driven
410 by hydrophobic interactions and weak C–H···O interactions with the carbonyl groups
411 [40]. Therefore, we expect some hydrophobic interactions with the organic linkers of the
412 MOFs, but weak enough so the elution with ACN be very efficient. In this way, the E_R
413 for progesterone is significant but small for all the MOFs tested.
414 Hydrophobicity has been pointed out as the main force driving the extraction of
415 triclosan from water by MIL-53(Al), which is able to extract up to 400 $mg \cdot g^{-1}$ [41]. In the
416 solid state, the triclosan molecules are held together by hydrogen bonds involving the
417 hydroxo groups and aromatic π-π interactions. [42] The high E_R for MIL-53(Al) supports

418 the previous study, and the low values for MOF-74, UiO-64 and HKUST-1 follow the
419 trend observed for progesterone, being triclosan also a hydrophobic molecule able to
420 establish some H-bonds. It is remarkable the efficiency observed for MOF-5. The
421 efficient extraction of polychlorinated biphenyls by MOF-5(Zn) has been reported
422 already, being the proposed absorption mechanism: host-guest π-π stacking and
423 hydrophobic interactions [43].

424 Fluorene is a polycyclic aromatic hydrocarbon, highly hydrophobic, able to
425 establish π-type interactions, but not strong H-bonds as either donor or acceptor.
426 Therefore, those MOFs with relatively hydrophilic environments show negligible
427 extraction: UiO-64 and MOF-74(Zn). The extraction efficiency of the HKUST-1 for
428 PAHs has been already demonstrated [15]. However, HKUST-1 did not show a good
429 performance in a previous report for the extraction of fluorene, although it was in
430 combination with PDMS in a solid-phase microextraction fiber (SPME) [44]. In our
431 experiments, HKUST-1 shows a good performance, being the better sorbent for fluorene.
432 MIL-53(Al) and MOF-5(Zn) with the relatively hydrophobic pores show extraction
433 efficiencies poorer than that of the HKUST-1.

434 In summary, the more versatile sorbent material is the MIL-53(Al) MOF for the
435 selected group of analytes of variety nature and thus, it was further used in the
436 optimization of the methodology.

437

438 *3.4. Optimization of the D-μSPE-HPLC-DAD method using MIL-53(Al) as sorbent*

439 The main variables exerting an effect in the D-μSPE method are the amount of
440 sorbent material (directly related with the sample volume), the dispersion strength and
441 the contact time between the sorbent material and the aqueous solution containing the

442 analytes, and the nature of the elution solvent (together with the elution volume and even
443 the number of elution steps).

444 The amount of MIL-53(Al) in the D-μSPE method was optimized intending to
445 obtain the highest extraction efficiencies with the lowest amount of sorbent. Figure 2
446 shows the extraction efficiencies obtained using varying amounts of MOF (from 5 to 40
447 mg). Higher amounts were not tested to ensure the utilization of a microextraction
448 approach. Amounts lower than 5 mg were not considered given the further difficulties in
449 its manipulation during elution. In all cases, 10 mL of an aqueous standard containing all
450 contaminants at 20 $\mu g \cdot L^{-1}$ and the specific amount of MIL-53(Al) were strongly mixed
451 by vortex (5 min), followed by centrifugation (3500 rpm, 5 min). Elution was
452 accomplished using 500 μL of ACN, followed by direct HPLC injection of eluate. From
453 Figure 2, it can be observed clearly that best results were obtained with the lowest amount
454 of MIL-53(Al), which is quite advantageous in terms of costs and environmental-
455 friendliness. It must be considered that the fixed amount of elution solvent is perhaps
456 insufficient to ensure proper elution of analytes when higher amounts of MIL-53(Al) are
457 used. However, if higher elution volumes of ACN are used with higher MOF amounts,
458 the final preconcentration achieved is also lower. Therefore, we chose 5 mg of MIL-
459 53(Al) as proper sorbent amount.

460 The strength of MIL-53(Al) dispersion was evaluated by application of different
461 vortex times. Thus, we observed that 5 min were enough to ensure proper dispersion and
462 adequate extraction efficiency. Longer times did not increase extraction efficiency or
463 precision, and they are not even convenient considering a manual vortexing.

464 The elution step was optimized, considering first the suitability of including an
465 evaporating step right after elution. If evaporation is successful (in terms of efficiency)
466 for the group of pollutants studied, it is possible to test afterwards a higher number of

elution solvents, even those non-compatible with HPLC mobile phases, because evaporation and reconstitution can be accomplished. However, a set of studies demonstrated that this evaporation step to dryness is accompanied by losses of analytes together with certain irreproducibility. Thus, evaporation to dryness was discarded and only elution solvents compatible with HPLC mobile phases (specifically methanol and ACN) were tested in this study. ACN clearly demonstrated better efficiency, and so the number of elution steps using ACN was also evaluated. In each elution step vortex was applied for 5 min to ensure adequate interaction MOF containing analytes with the elution solvent (ACN). Figure ESM-4 of the ESM shows the results when subjecting 10 mL of an aqueous standard containing pollutants at 20 $\mu g \cdot L^{-1}$ to the optimized method (5 mg of MIL-53(Al) and 5 min of vortex), and then eluting pollutants using: A) two elution steps with 500 µL of ACN each (2×500); B) three elution steps using 250 µL of ACN each (3×250); and C) three elution steps using 200 µL of ACN each (3×200). In any case, the total elution volume was never higher than 1 mL. Best results were obtained when eluting three consecutive times with 200 µL of ACN. Once selected three consecutive elution steps (entire volume 600 µL), volume was reduced down to 100 µL (not to dryness given the problems above mentioned) to avoid losses of preconcentration during elution.

The optimum procedure of the D-µSPE-HPLC-DAD method for the determination of the studied group of pollutants is summarized in Figure 3.

3.5. Quality analytical parameters of the D-µSPE-HPLC-DAD method

Calibrations were obtained using aqueous standards of analytes (in ultrapure water) subjected to the already optimized D-µSPE-HPLC-DAD method. Several quality analytical parameters are shown in Table 3. Correlation coefficients (R) higher than 0.996 were obtained in all cases. LODs were calculated as the initial concentration in the

aqueous sample able to generate a signal to noise ratio of three after the overall procedure (S/N = 3) and LOQs were obtained as ten times signal noise ratio (S/N = 10). All calculated LODs and LOQs were verified by preparation of aqueous standards at those levels, being subjected to the entire method. LOQs ranged from 0.14 $\mu g \cdot L^{-1}$ for triclosan to 0.73 $\mu g \cdot L^{-1}$ for estrone, thus obtaining LOQs which are on average ~72 times lower than those obtained without the preconcentration step. It is important to highlight the low detection limits for the group of analytes considered obtained using DAD, being comparable to others studies from literature (see Table ESM-3 of the ESM).

The inter-day precision (as RSD, in %) of the overall D-μSPE-HPLC-DAD procedure was assessed at two spiked levels, by quadruplicate, as shown in Table 4. RSD values ranged from 3.5% for carbamazepine to 8.7% for fluorene at the lowest spiked level, and from 2.4% for triclosan to 11% for estrone at the highest spiked level.

Average relative recoveries of 109% and 112% were obtained at the low and high spiked level, respectively. Regarding real extraction efficiencies (E_R, in %) considering the entire method, they range from 31.0% for atrazine to 61.3% for carbamazepine at the low spiked level, which is quite acceptable considering that extraction efficiencies around 100% are not always achieved when developing microextraction approaches [45]. In general, most reports on microextraction methods, particularly those involving MOFs, include only relative recoveries (RR), rather than real extraction efficiency values of the procedure.

3.6. Quality analytical parameters of the D-μSPE-LC-TOF method

The D-μSPE-LC-TOF method was also validated, as shown in Table 5. The calibration curves in this case present R values higher 0.996. LOQs range from 43 $ng \cdot L^{-1}$ for atrazine to 70 $ng \cdot L^{-1}$ for carbamazepine, thus being on average ~82 times lower than

517 those obtained by LC-TOF without preconcentration (Table ESM-2 of the ESM), and ~7
518 times lower than those obtained by D-μSPE-HPLC-DAD. It is important to highlight the
519 sensitivity achieved for the group of analytes considered, being comparable to other
520 studies from literature using conventional approaches (Table ESM-3 of the ESM).
521 Regarding relative recoveries, extraction efficiencies, and precision, similar
522 values to those of D-μSPE-HPLC-DAD were obtained (see Table 4), being on average
523 ~105%, ~50.4%, and ~4.0%, respectively, for the lowest spiked level.
524
525 *3.7. Analysis of tap water and wastewaters using the optimized D-μSPE method*
526
527 Tap water and wastewater samples of high complexity were analyzed as described
528 in section 2.4., using the optimized D-μSPE–HPLC-DAD and D-μSPE–LC-TOF. The
529 obtained results are shown in Table 6. Both methods were adequate for determining the
530 analytes. Estrone and triclosan were quantified in wastewater-1 and estrone in
531 wastewater-3. A Student's t-test ($\alpha = 0.05$) revealed the absence of significant differences
532 among results found with both methods.
533 Furthermore, tap water sample-1 and wastewater-2 were used as blank matrixes
534 to perform recovery and precision studies, thus evaluating the influence of the matrix
535 effect. Results obtained with both methods as shown in Table ESM-4 (of the ESM). In
536 tap water, a good agreement with the analytical performance of the methods in deionized
537 waters is observed, except for triclosan, being this analyte affected by matrix effect. In
538 any case, average extraction efficiencies of 44% using DAD and 54% using TOF, average
539 relative recoveries of 110% using DAD and 109% using TOF, and RSD values (in %)
540 ranging from 3.1% to 18% were obtained. Regarding wastewaters, a higher matrix effect
541 is observed with the majority of compounds, obtaining average extraction efficiencies of

34.5% and 34.9% and relative recoveries of 98.6% and 76.0%, using DAD or TOF, respectively, and being the exceptions atrazine and estrone. Precision values were adequate, with RSD values lower than 18%. In this type of samples, the use of matrix-matched calibrations is highly recommended.

Conclusions

Five MOFs (HKUST-1, MOF-5(Zn), MIL-53(Al), UiO-64 and MOF-74(Zn)), constituting a small but diverse representation of the MOF library, were adequately synthesized, characterized and tested in a miniaturized solid-phase extraction method under dispersive mode.

Six analytes (carbamazepine, atrazine, progesterone, estrone, triclosan and fluorene) were properly selected as monitoring pollutants, including characteristics of hydrophobicity, polarity, and/or aromaticity, to find a generic MOF able to extract these pollutants of diverse structure from environmental waters using D-μSPE.

The study of the partitioning of target analytes to MOFs had revealed how difficult is to make a prediction for the adsorption of a target analyte in a specific MOF material. The MOF's pore environment, pore size and pore aperture widths, the presence of unsaturated metal sites, and the nature of the metal have a major influence in their efficiency in D-μSPE. MIL-53(Al) demonstrated to be the most successful MOF as generic sorbent given its versatility and flexibility.

The D-μSPE method was optimized adequately with MIL-53(Al), and the entire methods using HPLC-DAD and LC-TOF were successfully validated. The methods are characterized for requiring low amounts of MIL-53(Al) (5 mg); low sample volume requirements (10 mL); short sample preparation times (10 min for extraction and 30 min for proper elution); simplicity in the sample preparation step (vortex and centrifugation);

and minimization of the organic solvent requirements in the sample preparation (only 600 μL of acetonitrile for elution). Furthermore, the developed methods present adequate analytical performance and detection limits down to 0.040 $\mu g \cdot L^{-1}$ for triclosan when using HPLC-DAD and down to 0.013 $\mu g \cdot L^{-1}$ for atrazine when using LC-TOF.

Ongoing work is aimed to improve the compliance of the Green Analytical Chemistry (GAC) principles, of sample preparation methods based on MOFs by utilizing MOFs with environmental-friendlier preparation routes, while including the knowledge on partitioning of analytes obtained from this study to design better MOFs for target monitoring.

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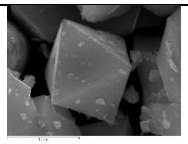
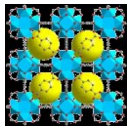
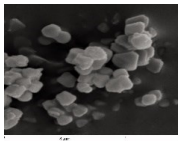
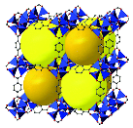
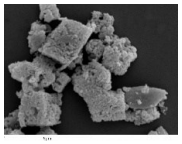
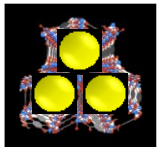
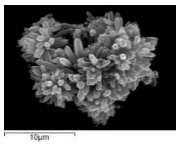
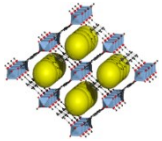
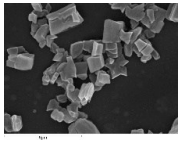
Figure Captions

Figure 1. Screening study to evaluate the performance of different MOFs in a D-μSPE-HPLC-DAD approach for a group of contaminants of quite different nature. Fixed conditions as described in the text.

Figure 2. Influence of the MIL-53(Al) amount on the extraction efficiency of the D-μSPE-HPLC-DAD method. Fixed conditions as described in the text.

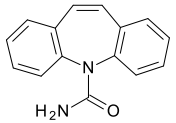
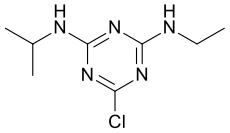
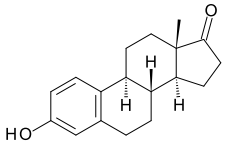
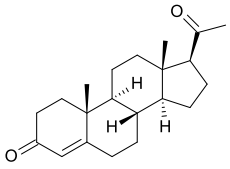
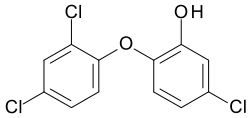
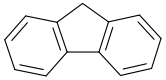
Figure 3. Scheme of entire D-μSPE-HPLC-DAD or -LC-TOF method using MIL-53(Al) under optimum conditions.

Table 1. Characterization parameters of each as synthetized MOF.

MOF	Structure[a]	Metal	Organic ligand	SEM[b] image	Crystal size[c] (µm)	Pore volume[d] ($cm^3 \cdot g^{-1}$)	Surface area[d] ($m^2 \cdot g^{-1}$)	T_{activ}[e] / T_{degrad}[e] (°C)	Pore aperture[f]	CDS code[g]
HKUST-1		Cu	trimesic acid		15 – 50	0.48	1068	120 / 600	7.5 Å	FIQCEN
UiO-64		Zr	fumaric acid		0.3 – 1.4	0.48	762	150 / 600	6 Å	BOHKAM
MOF-5(Zn)		Zn	terephthalic acid		2 – 10	0.28	579	150 / 500	8 Å	MIBQAR
MOF-74(Zn)		Zn	2,5-dihydroxyterephthalic acid		5 – 12	0.29	505	150 / 450	11 Å	ORIVOK
MIL-53(Al)		Al	terephthalic acid		0.5 – 3	0.47	978	400 / 600	10-12 Å (flexible)	SABVOH

[a]structure simulations
[b]scan electron microscopy images
[c]estimated from SEM images
[d]results obtained by BET surface area analysis. The nitrogen isotherms were carried out at 77 K and $P/P_0 = 0.07 – 0.30$
[e]estimated by TG/DTA
[f]stimated from their crystal structure
[g][31]

Table 2. Several characteristics of the group of analytes studied.

Analyte	Structure	Molecular weight (g·mol^{-1})	Volume[a] (Å^3)	Water solubility[a] at 25 ºC (mg·L^{-1})	LogK$_{OW}$[a,b]	pK$_a$[a]	Vapor pressure[a] at 25 ºC (atm)
Carbamazepine		236.27	210.32	17.7	2.45	13.9	7.6×10^{-10}
Atrazine		215.68	190.90	34.7 (26 °C)	2.61	2.27	1.7×10^{-8}
Estrone		270.37	263.17	30	3.13	10.3	2.0×10^{-11}
Progesterone		314.46	321.10	8.81	3.87	-	4.5×10^{-11}
Triclosan		289.54	212.05	10 (20 ºC)	4.76	7.80	4.3×10^{-8}
Fluorene		166.22	157.31	1.98	4.18	-	3.00×10^{-3}

[a]obtained from SciFinder® 2017 database
[b]*n*-octanol/water partition coefficient

Table 3. Several quality analytical parameters of entire D-μSPE-HPLC-DAD method.

Analyte	**Working range ($\mu g \cdot L^{-1}$)**	**R**	**($S_{y/x}$)×10^{-3}**	**(Slope ± SD[b])×10^{-4}**	**LOD ($\mu g \cdot L^{-1}$)**	**LOQ ($\mu g \cdot L^{-1}$)**
Carbamazepine	0.30 – 10	0.996	18	5.3 ± 0.2	0.09	0.27
Atrazine	0.30 – 10	0.999	7.4	3.8 ± 0.1	0.07	0.23
Estrone	0.80 – 10	0.998	3.4	1.21 ± 0.04	0.22	0.73
Progesterone	0.60 – 7.5	0.998	1.9	0.86 ± 0.03	0.15	0.50
Triclosan	0.25 – 10	0.996	9.4	2.2 ± 0.1	0.04	0.14
Fluorene	0.30 – 10	0.997	1.4	0.38 ± 0.01	0.07	0.22

[a]standard deviation of the regression (or error of the estimate)
[b]standard deviation of slopes and intercepts (respectively) associated to the n = 6 calibration levels
[c]inter-day precision for the peak-areas (n = 6, using 3 non-consecutive days)
[d]spiked level 1, corresponding to 2 $\mu g \cdot L^{-1}$
[e]spiked level 2, corresponding to 8 $\mu g \cdot L^{-1}$

Table 4. Analytical performance of the entire D-μSPE in combination with HPLC-DAD and LC-TOF method in terms of relative recovery, extraction efficiency, and inter-day precision, using standards in ultrapure water.

Analyte	**HPLC-DAD**						**LC-TOF**					
	Spiked level 1 (2 μg·L^{-1})			**Spiked level 2 (8 μg·L^{-1})**			**Spiked level 1 (0.7 μg·L^{-1})**			**Spiked level 2 (7 μg·L^{-1})**		
	E_R[a] (%)	**RR[b] (%)**	**RSD[c] (%)**	**E_R[a] (%)**	**RR[b] (%)**	**RSD[c] (%)**	**E_R[a] (%)**	**RR[b] (%)**	**RSD[c] (%)**	**E_R[a] (%)**	**RR[b] (%)**	**RSD[c] (%)**
Carbamazepine	61.3	102	3.5	61.7	105	6.4	57.1	103.7	1.3	62.6	113.1	2.8
Atrazine	31.0	97	7.2	30.2	111	9.3	32.6	93.3	2.6	35.2	101.6	2.3
Estrone	44.1	106	4.5	37.8	98	11	40.0	114.6	7.5	39.2	124.0	10.1
Progesterone	41.7	101	7.5	32.7	126	8.3	52.9	101.1	3.9	57.7	104.4	6.3
Triclosan	37.7	123	4.5	59.5	120	2.4	62.7	112.0	7.1	71.3	118.2	8.6
Fluorene	31.5	124	8.7	40.5	112	2.7	-	-	-	-	-	-

[a]extraction efficiency, taking into account the entire preconcentration achieved with the method
[b]relative recovery
[c]relative standard deviation (n = 4)

Table 5. Several quality analytical parameters of entire D-μSPE-LC-TOF method.

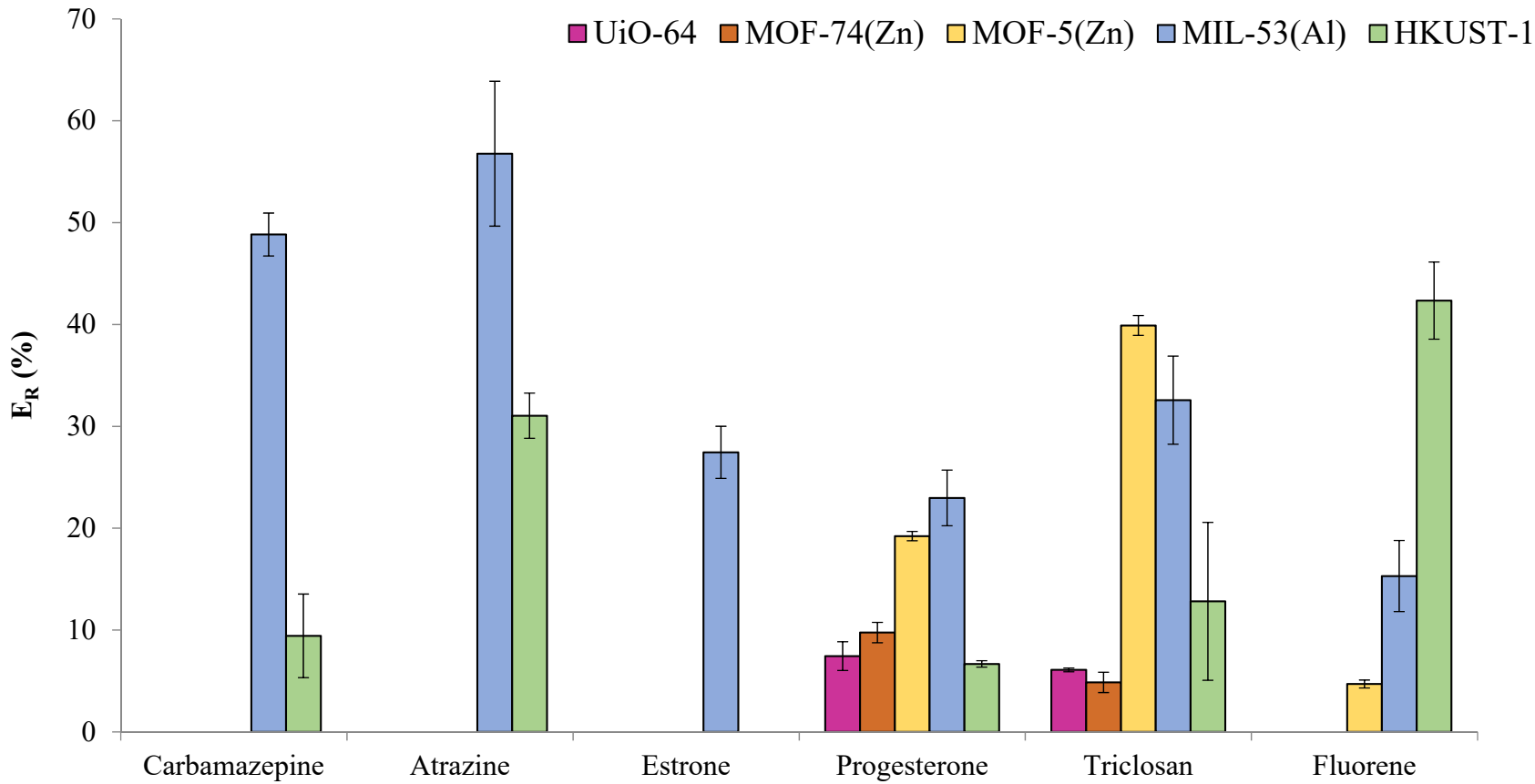
Analyte	**Working range ($\mu g \cdot L^{-1}$)**	**R**	**($S_{y/x}$)×10^{-4}**	**(Slope ± SD[b])×10^{-4}**	**LOD ($ng \cdot L^{-1}$)**	**LOQ ($ng \cdot L^{-1}$)**
Carbamazepine	0.10 – 10	0.9996	3.0	25.5 ± 0.3	21	70
Atrazine	0.07 – 10	0.9992	8.0	45 ± 1	13	43
Estrone	0.25 – 10	0.9984	10.9	66 ± 4	17	58
Progesterone	0.07 – 10	0.9962	12.3	4 ± 1	17	55
Triclosan	0.25 – 10	0.9995	9.0	14 ± 1	18	61

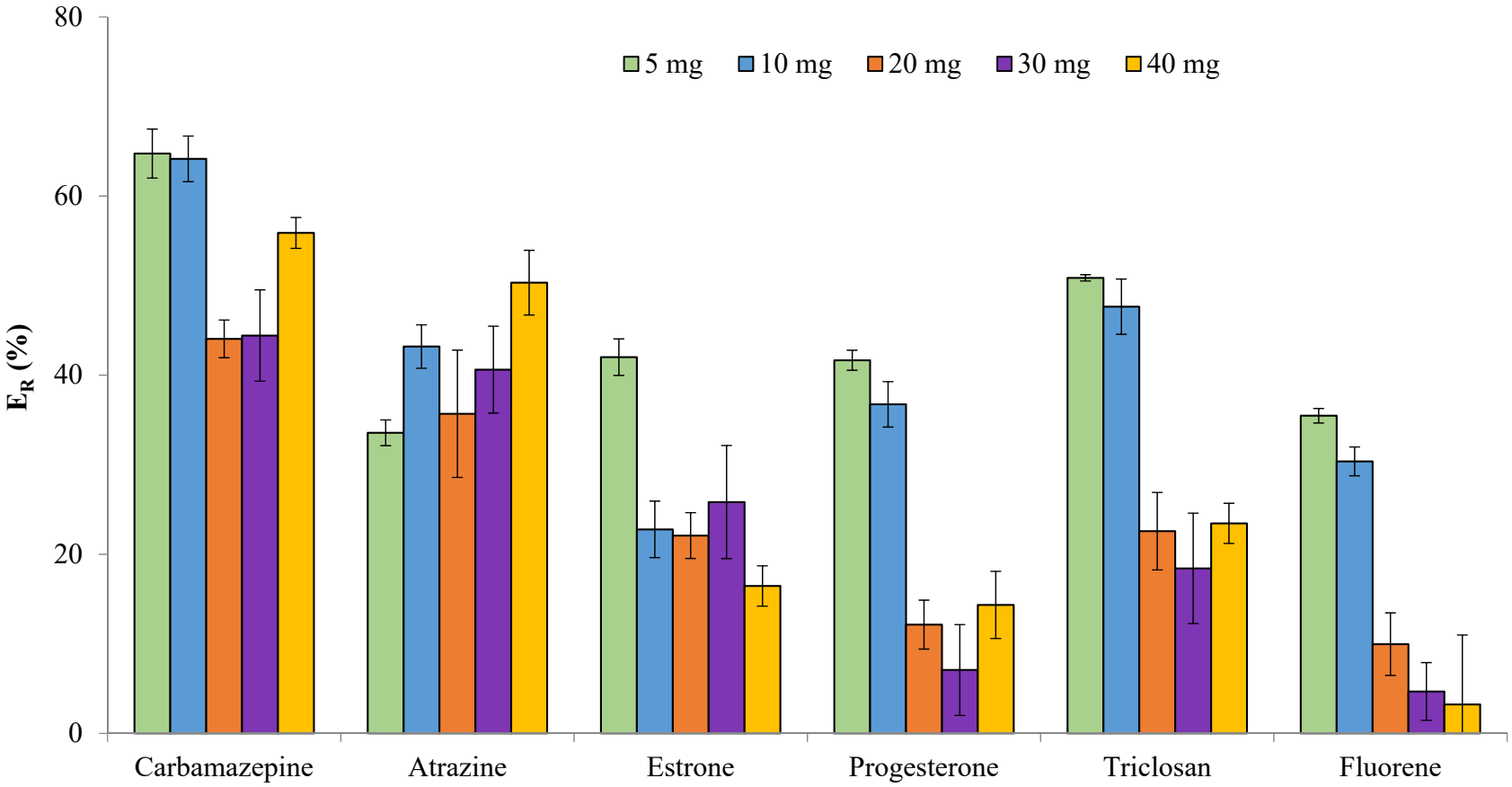
[a]standard deviation of the regression (or error of the estimate)
[b]standard deviation of slopes and intercepts (respectively) associated to the n = 6 calibration levels
[c]inter-day precision for the peak-areas (n = 6, using 3 non-consecutive days)
[d]spiked level 1, corresponding to 0.7 $\mu g \cdot L^{-1}$
[e]spiked level 2, corresponding to 7 $\mu g \cdot L^{-1}$

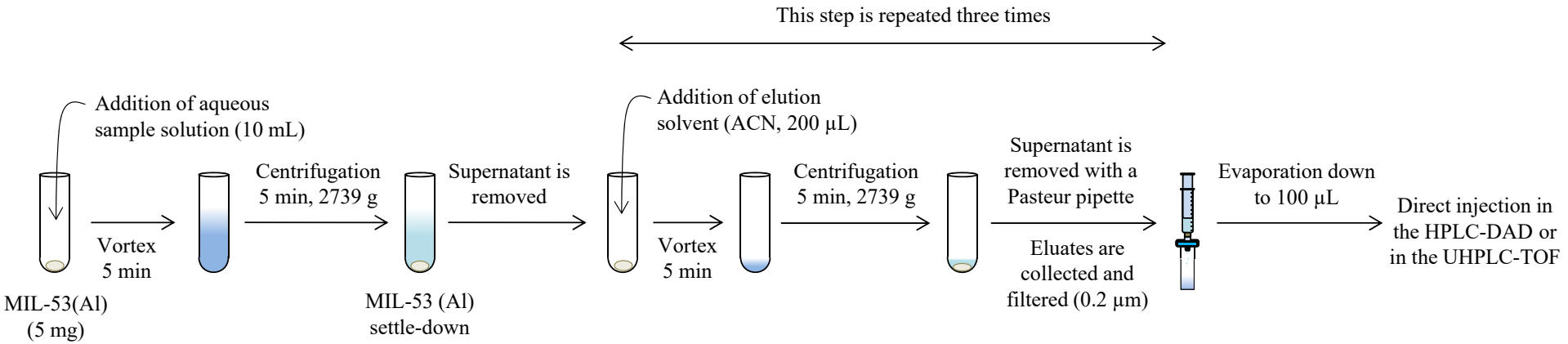
Table 6. Analysis of wastewaters by the optimized D-μSPE method.

Analyte	**HPLC-DAD**				**LC-TOF**			
	Tap water-1	Wastewater-1	Wastewater-2	Wastewater-3	Tap water-1	Wastewater-1	Wastewater-2	Wastewater-3
Carbamazepine	nd	nd	nd	nd	nd	nd	nd	nd
Atrazine	nd	nd	nd	nd	nd	nd	nd	nd
Estrone	nd	$2.9^{a} \pm 1.4^{b}$	nd	$1.5^{a} \pm 0.9^{b}$	nd	$2.8^{a} \pm 1.0^{b}$	nd	$1.3^{a} \pm 0.4^{b}$
Progesterone	nd	nd	nd	nd	nd	nd	nd	nq
Triclosan	nd	$2.2^{a} \pm 0.8^{b}$	nd	nd	nd	$3.9^{a} \pm 1.3^{b}$	nd	nd
Fluorene	nd	nd	nd	$0.6^{a} \pm 0.1^{b}$	nd	-	-	-

nd: non-detected
nq: non-quantified
[a]sample content in $\mu g \cdot L^{-1}$
[b]standard deviation (n = 3)


UiO-64
MOF-74(Zn)
MOF-5(Zn)
MIL-53(Al)
HKUST-1
E_R (%)
70
60
50
40
30
20
10
0
Carbamazepine
Atrazine
Estrone
Progesterone
Triclosan
Fluorene


80
60
40
20
0
E_R (%)
5 mg
10 mg
20 mg
30 mg
40 mg
Carbamazepine
Atrazine
Estrone
Progesterone
Triclosan
Fluorene


This step is repeated three times
Addition of aqueous sample solution (10 mL)
Vortex 5 min
Centrifugation 5 min, 2739 g
Supernatant is removed
Addition of elution solvent (ACN, 200 µL)
Vortex 5 min
Centrifugation 5 min, 2739 g
Supernatant is removed with a Pasteur pipette
Eluates are collected and filtered (0.2 µm)
Evaporation down to 100 µL
Direct injection in the HPLC-DAD or in the UHPLC-TOF
MIL-53(Al) (5 mg)
MIL-53 (Al) settle-down

Supplementary Material

Insights in the analytical performance of neat metal-organic frameworks in the determination of pollutants of different nature from treated wastewaters using dispersive miniaturized solid-phase extraction and liquid chromatography

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Table of contents

Table ESM-1. Several quality analytical parameters of the HPLC-DAD method, without performing any preconcentration step.

Analyte	Retention time[a] ± SD[b]	Working range ($\mu g \cdot L^{-1}$)	$(S_{y/x})^{c} \cdot 10^{-3}$	R	(Slope ± SD[d])·10^{-3}	LOD ($\mu g \cdot L^{-1}$)	LOQ ($\mu g \cdot L^{-1}$)	RSD[e] (%)	
								Level 1[f]	Level 2[g]
Carbamazepine	2.6 ± 0.1	25 – 800	9.3	0.9994	0.91 ± 0.01	4.03	13	5.7	0.8
Atrazine	4.3 ± 0.1	25 – 1000	11	0.9998	1.49 ± 0.01	6.13	20	3.0	2.0
Estrone	6.1 ± 0.1	75 – 1500	4.0	0.9997	0.272 ± 0.003	14.6	49	5.4	2.9
Progesterone	7.8 ± 0.1	50 – 1500	9.2	0.9998	0.767 ± 0.006	11.9	40	3.6	2.1
Triclosan	9.70 ± 0.04	25 – 1250	2.7	0.9999	0.569 ± 0.002	4.46	15	6.2	3.4
Fluorene	10.00 ± 0.04	25 – 600	2.8	0.9999	0.807 ± 0.005	2.78	9.3	6.8	4.9

[a]average retention time n = 30 (inter-day)
[b]standard deviation of the retention times (n = 30)
[c]standard deviation of the regression (or error of the estimate)
[d]standard deviation of slopes and intercepts (respectively) associated to the n = 6 calibration levels
[e]inter-day precision for the peak-areas (n = 12, using 3 non-consecutive days)
[f]40 $\mu g \cdot L^{-1}$ for carbamazepine, atrazine, triclosan and fluorene, and 90 $\mu g \cdot L^{-1}$ for estrone and progesterone
[g]500 $\mu g \cdot L^{-1}$ for fluorene, 700 $\mu g \cdot L^{-1}$ for carbamazepine and atrazine, and 1100 $\mu g \cdot L^{-1}$ for estrone and progesterone

Table ESM-2. Several quality analytical parameters of the LC-TOF method, without performing any preconcentration step.

Analyte	Retention time[a] ± SD[b]	Working range ($\mu g \cdot L^{-1}$)	($S_{y/x}$)[c]·10^{-4}	R	(Slope ± SD[d])·10^{-3}	LOD ($\mu g \cdot L^{-1}$)	LOQ ($\mu g \cdot L^{-1}$)	RSD[e] (%)	
								Level 1[f]	Level 2[g]
Carbamazepine	1.76 ± 0.05	5 – 1000	4.3	0.9997	3.88 ± 0.04	1.19	3.98	1.4	0.7
Atrazine	2.40 ± 0.03	5 – 1000	5.2	0.9999	9.1 ± 0.1	1.15	3.82	0.9	0.5
Estrone	4.44 ± 0.01	10 – 1000	3.6	0.9996	3.5 ± 0.1	1.22	4.05	5.1	3.2
Progesterone	7.18 ± 0.08	10 – 1000	2.0	0.9996	1.42 ± 0.02	1.40	4.65	3.0	2.1
Triclosan	9.74 ± 0.05	10 – 800	3.2	0.9999	2.4 ± 0.1	2.00	6.65	6.3	4.6

[a]average retention time n = 30 (inter-day)
[b]standard deviation of the retention times (n = 30)
[c]standard deviation of the regression (or error of the estimate)
[d]standard deviation of slopes and intercepts (respectively) associated to the n = 6 calibration levels
[e]inter-day precision for the peak-areas (n = 12, using 3 non-consecutive days)
[f]spiked level: 50 $\mu g \cdot L^{-1}$
[g]spiked level: 500 $\mu g \cdot L^{-1}$

Table ESM-3. Performance of other methods from literature for the determination of similar group of analytes from waters.

Analyte	Water vol. (in mL)	Sample preparation	LOD ($ng \cdot L^{-1}$)	Chromatographic method	Reference
carbamazepine & 12 derivatives	100	SPE	3	LC-MS/MS	Environ Sci Pollut Res 24 (2017) 16893
carbamazepine	25	BAμE[a]	5	HPLC-DAD	Int. J. Environ. Anal. Chem. 97 (2017) 484
carbamazepine	1.8	Online SPE	0.3	LC-MS/MS	Environ Sci Pollut Res 24 (2017) 8692
carbamazepine	1000	SPE	0.09	UHPLC-MS/MS	J. Chromatogr. B, 1047 (2017) 160
carbamazepine	500	SPE	0.28 $\mu g \cdot L^{-1}$	HPLC-MS/MS	Chemosphere 175 (2017) 505
carbamazepine	10	QuEChERS[d]	10	LC-MS/MS	J. AOAC Int. 100 (2017) 592
atrazine	500	SPE	2.7 $\mu g \cdot L^{-1}$	HPLC-MS/MS	Chemosphere 175 (2017) 505
atrazine	10	SPE nanofibers	90	HPLC-DAD	J. Chromatogr. A, 1491 (2017) 16
atrazine	100	SPE nanofibers	10	HPLC-MS	Chin. J. Anal. Chem. 127 (2004) 1273
estrone related hormones	25	BAμE[a]	100	HPLC-DAD	Int. J. Environ. Anal. Chem. 97 (2017) 484
estrone and derivates	10	HF-LPME[b]	0.07	HPLC-MS/MS	J. Chromatogr. A, 1488 (2017) 26
progesterone	30	FPSE[c]	60	HPLC-MS/MS	J. Chromatogr. A, 1437 (2016) 116
triclosan	10	QuEChERS[d]	33	LC-MS/MS	J. AOAC Int. 100 (2017) 592
triclosan	25	BAμE[a]	10	HPLC-DAD	Int. J. Environ. Anal. Chem. 97 (2017) 484

[a]bar adsorptive microextraction
[b]hollow fiber liquid-phase extraction
[c]fabric phase sorptive extraction
[d]dispersive solid-phase extraction: Quick, Easy, Cheap, Effective, Rugged, and Safe

Table ESM-4. Analytical performance of the entire D-μSPE in combination with HPLC-DAD or LC-TOF method in terms of extraction efficiency, relative recovery, and intra-day precision with tap water and wastewater samples.

Analyte	Chromatographic determination	Tap water-1			Wastewater-2		
		E_R[a] (%)	RR[b] (%)	RSD[c] (%)	E_R[a] (%)	RR[b] (%)	RSD[c] (%)
Carbamazepine	HPLC-DAD[d]	62.5	107	8.2	23.4	39.5	11
	LC-TOF[e]	58.2	109	9.2	38.9	71.8	21
Atrazine	HPLC-DAD[d]	35.2	99.8	3.3	40.4	121	7.7
	LC-TOF[e]	37.0	96.0	6.5	42.0	115	14
Estrone	HPLC-DAD[d]	44.5	107	3.1	46.5	112	6.4
	LC-TOF[e]	40.4	116	5.7	29.0	83.2	18
Progesterone	HPLC-DAD[d]	44.5	105	18	12.5	29.9	5.3
	LC-TOF[e]	56.5	105	7.2	13.8	26.0	9.9
Triclosan	HPLC-DAD[d]	48.0	130	7.2	39.8	119	5.0
	LC-TOF[e]	79.8	121	8.7	50.8	83.9	16
Fluorene	HPLC-DAD[d]	29.8	110	11	44.6	170	3.7

[a]extraction efficiency, taking into account the preconcentration achieved with the method
[b]relative recovery (evaluated with calibrations in deionized water)
[c]relative standard deviation (n = 3, intra-day)
[d]spiked level of 2 $\mu g \cdot L^{-1}$ (n = 3)
[e]spiked level of 0.7 $\mu g \cdot L^{-1}$ (n = 3)

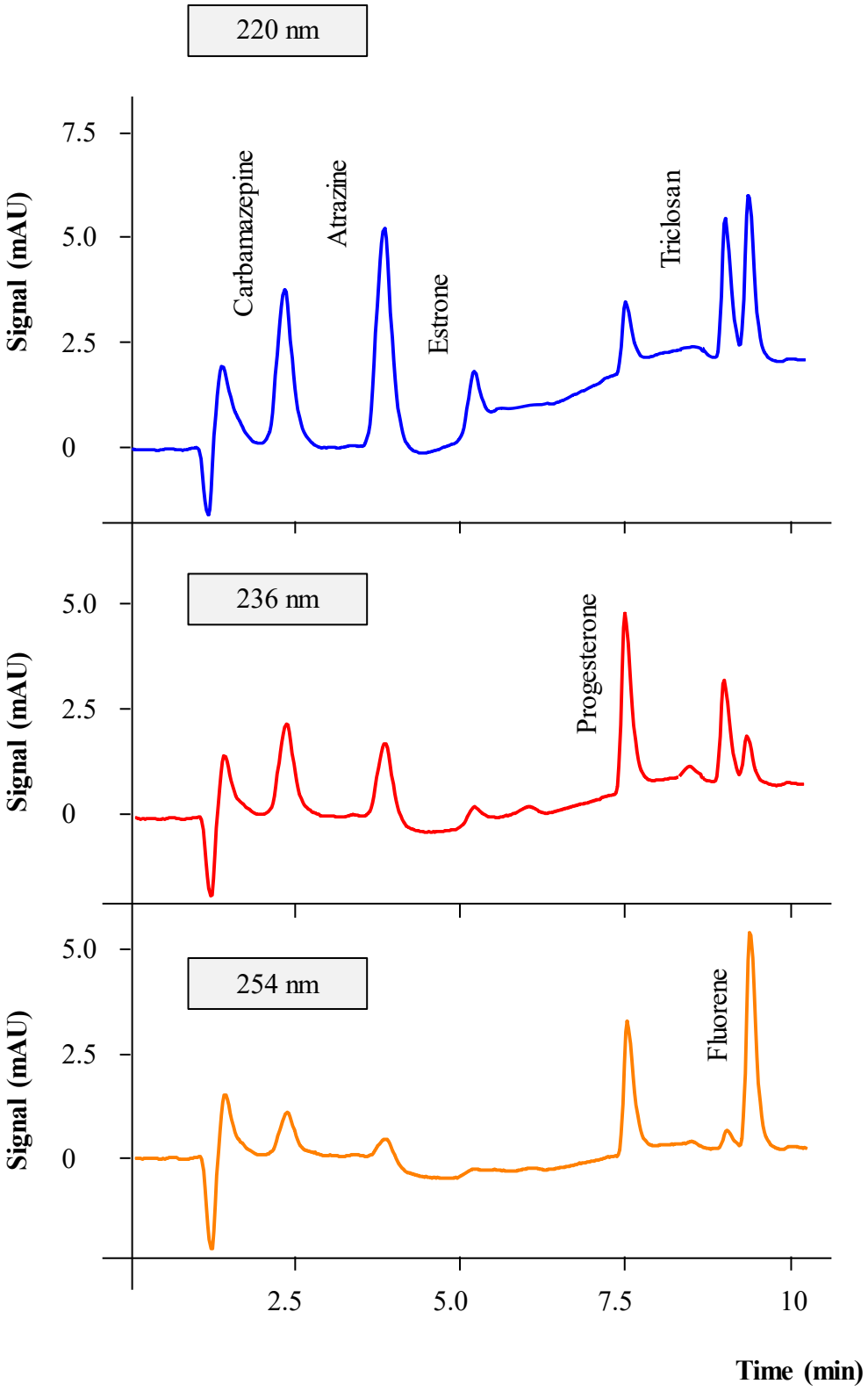

Figure ESM-1. Chromatogram obtained after subjecting an aqueous standard containing all analytes (10 µg·L^{-1}) to the entire D-µSPE-HPLC-DAD method under optimum conditions.

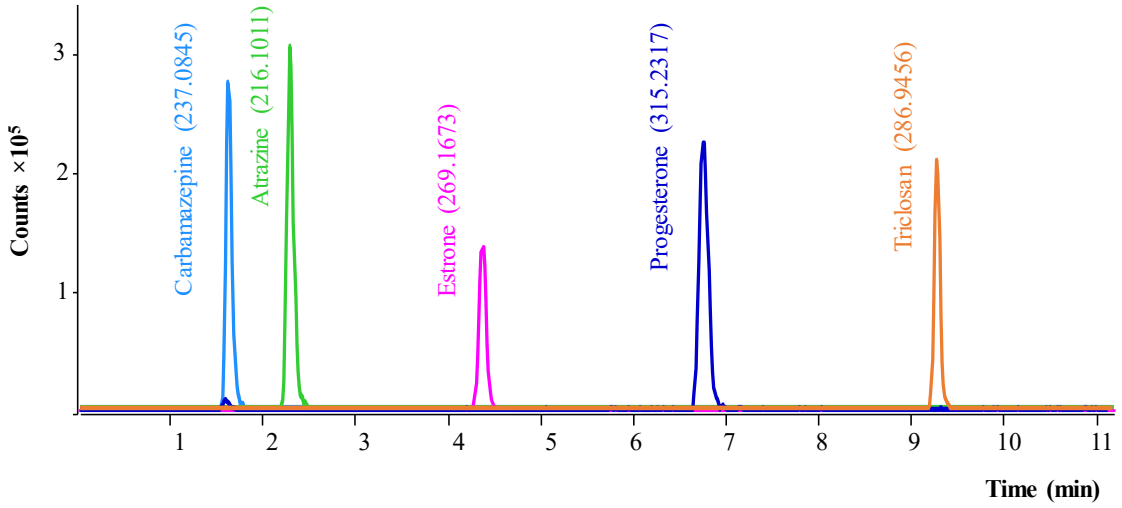

Figure ESM-2. Extracted ion chromatogram obtained after subjecting an aqueous standard containing all analytes (5 $\mu g \cdot L^{-1}$) to the entire D-µSPE-LC-TOF method under optimum conditions. Number in parenthesis corresponds to the accurate masses for each target compound. Carbamazepine, atrazine and progesterone monitored in positive mode and estrone and triclosan in negative mode.

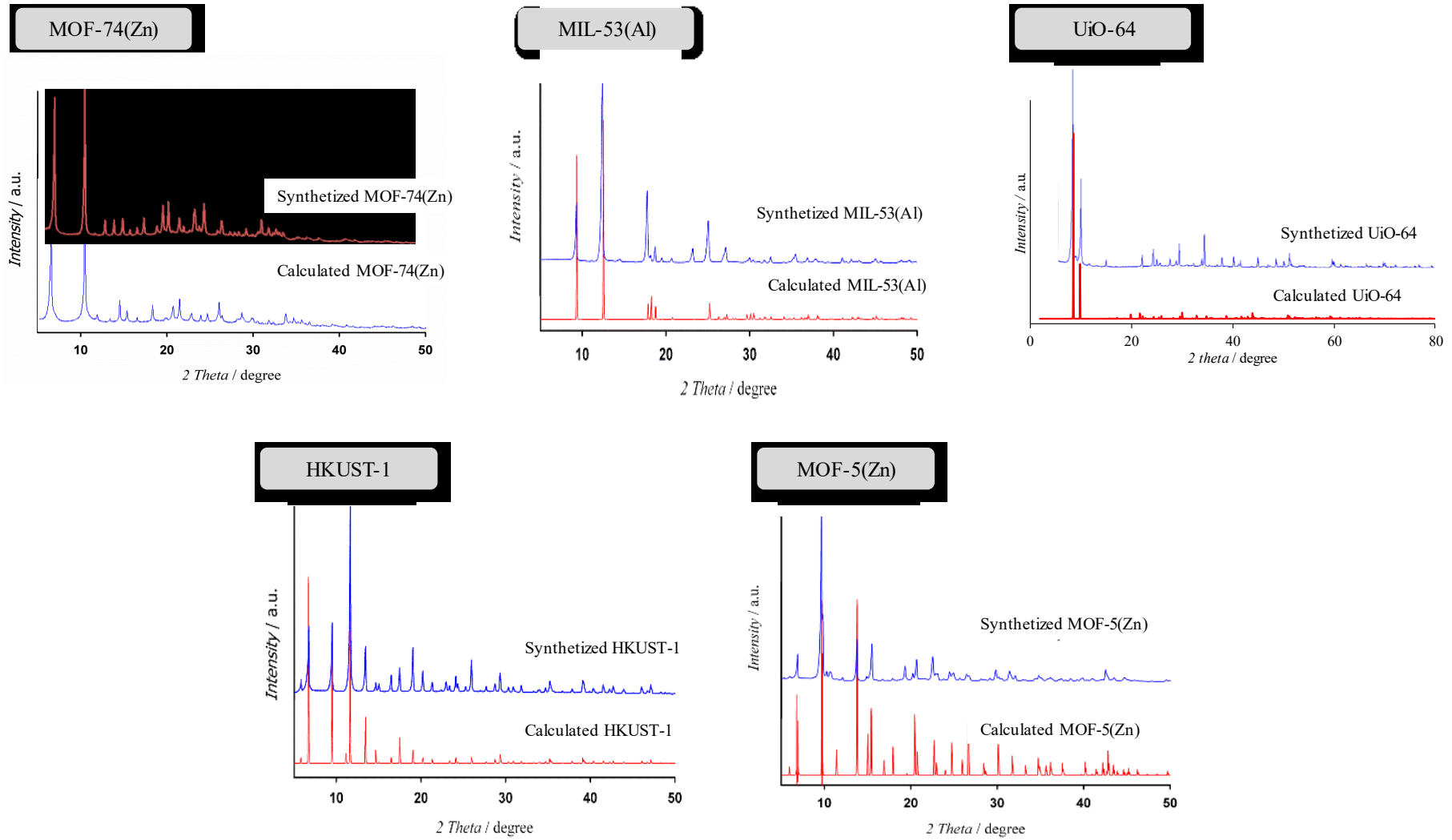

Figure ESM-3. Powder diffraction patterns of the each synthetized metal-organic framework, compared with the simulated ones.

Figure ESM-4. Extraction efficiencies of each analyte after performing the entire D-μSPE-HPLC-DAD method to an aqueous standard (20 $\mu g \cdot L^{-1}$) using 5 mg of MIL-53(Al), and employing different elution steps: A) two elution steps with 500 μL; B) three elution steps with 250 μL; and C) three elution steps with 200 μL. In all cases, acetonitrile is the elution solvent. Remaining conditions as described in the text.