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Samir Ahmad, Ana Mestre, Nuno Neng, Conchi Maria Concepcion Ovin Ania, Ana Carvalho, et al.. Carbon-Based Sorbent Coatings for the Determination of Pharmaceutical Compounds by Bar Adsorptive Microextraction. *ACS Applied Bio Materials*, 2020, 3 (4), pp.2078-2091. 10.1021/ac-sabm.9b01206 . hal-02989843

HAL Id: hal-02989843

<https://hal.science/hal-02989843>

Submitted on 6 Nov 2020

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1 **Ahmad S, Mestre AS, Neng N, Ania CO, Carvalho AP, Nogueira**
2 **J. Nanoporous hydrochars as sorbent coating for the**
3 **determination of pharmaceutical compounds by bar adsorptive**
4 **microextraction, ACS Appl. Bio Mater. 3 (2020) 2078-2091.**
5 **<https://doi.org/10.1021/acsabm.9b01206>**

6
7 **Carbon-based sorbent coatings for the determination of**
8 **pharmaceutical compounds by bar adsorptive microextraction**

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19
20 **Abstract**

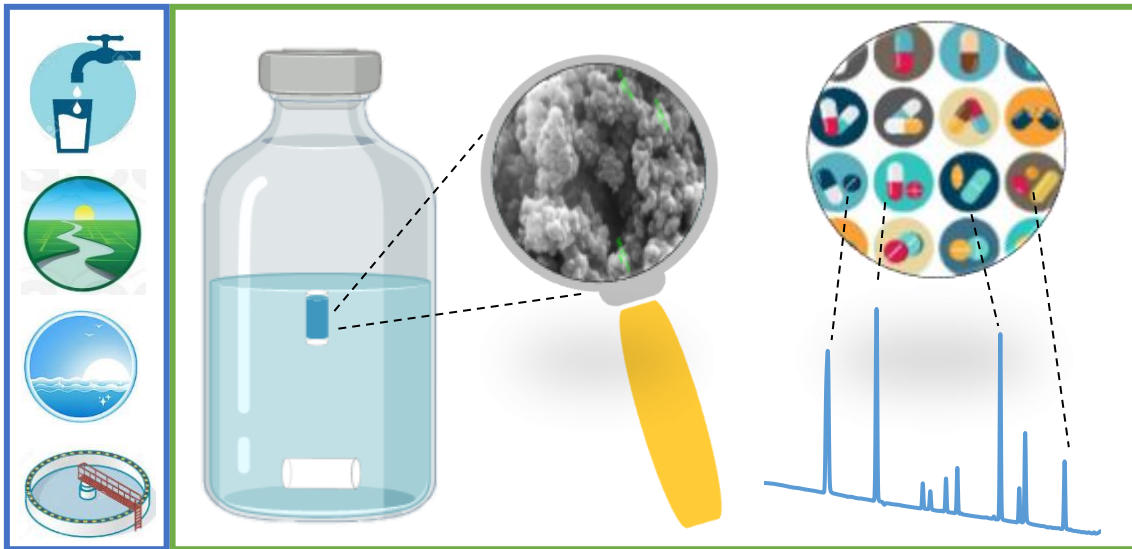
21 Thirteen carbon materials comprising commercial activated carbons and lab-
22 made materials (hydrochars and activated carbons) were assayed as
23 enrichment phase in bar adsorptive microextraction to monitor trace levels of ten
24 common pharmaceutical compounds (PhCs) in environmental water matrices,

25 including surface water, sea water, tap water and wastewater. Polar and non-
26 polar pharmaceuticals were selected – sulfamethoxazole, triclosan,
27 carbamazepine, diclofenac, mefenamic acid, 17 α -ethinylestradiol, 17 β -estradiol,
28 estrone, gemfibrozil and clofibrac acid – as model compounds to cover distinct
29 therapeutic classes. Despite having a less-developed porosity, data showed
30 that “in-house” prepared nanoporous hydrochars obtained from carbohydrates
31 at low temperature (e.g., 180 °C) in the presence of an eutectic salt mixture
32 compete with the best commercial activated carbons for this particular
33 application. The combination of a micro and mesopore network with a rich
34 oxygen-based surface chemistry yielding an acidic nature allowed these
35 hydrochars to present the best overall recoveries (between 20.9 to 82.4 %) for
36 the simultaneous determination of the ten target PhCs with very distinct
37 chemical properties, by high performance liquid chromatography-diode array
38 detection (HPLC-DAD).

39

40

41 **Table to Contents (TOC)**



42

43 **Keywords**

44 Carbon hydrochars; Activated Carbons; Sorbent coating; Bar adsorptive

45 microextraction (BA μ E); HPLC-DAD; Pharmaceutical compounds;

46 Environmental water matrices.

47 **1. Introduction**

48 Pharmaceuticals and personal care products (PPCPs) encompass many
49 different substances, such as drugs used in human and veterinary medicine,
50 fragrances, sunscreen agents, and cosmetics ingredients. More than 3000
51 PPCPs are currently marketed and new molecules enter the market yearly and
52 they are ubiquitously detected in treated wastewater [1]. Moreover,
53 pharmaceuticals compounds (PhCs) are generally biologically active
54 compounds that are often water soluble, therefore can be found in wastewaters
55 and easily end up in natural waters, including ground water, river water, sea
56 water and surface waters [2–5], usually at the trace level, ranging from $\mu\text{g L}^{-1}$ to
57 ng L^{-1} [6]. PhCs include multiple medicines classes, namely lipid regulators,
58 antibacterials/antifungals, β -adrenergic blocking agents, analgesics,
59 tranquilizers, hormones, and antiseptics, among many others [7]. The concern
60 for the possible ecotoxicological effects of these compounds is reflected on
61 decisions of the European Parliament in the field of water policy. In 2013, three
62 widely used PhCs, including the hormonal preparations 17α -ethinylestradiol and
63 17β -estradiol, as well as the painkiller diclofenac, were listed in the watch list of
64 substances to be monitored in the European Union (EU) to support the
65 determination of appropriate measures to address the risk posed by them
66 (Directive 2013/39/EU) [8]. The first revision of this list in 2015 maintained these
67 three pharmaceuticals (Directive 2015/495/EU) [9] but in the most recent
68 revision diclofenac, along with three other substances, was removed from the
69 watch list since the commission concluded that sufficient high-quality monitoring
70 data was already available (Directive 2018/840/EU) [10]. For these reasons,
71 there is a need for innovative analytical approaches that allow for their

72 quantification in environmental water matrices. Furthermore, considering the EU
73 decision on water policy, the development of a simple methodology that allows
74 the simultaneous analysis of the most representative emerging PhCs in water
75 matrices continues to be a hot research topic. As water bodies contain trace
76 amounts of a large range of PhCs with distinct physicochemical properties, the
77 challenge relies on the development of quantification techniques comprising
78 both polar and non-polar compounds.

79 Many analytical approaches have been proposed to analyze trace levels of
80 PhCs in environmental water matrices; these always include a sample
81 enrichment step prior to gas or liquid chromatography [1,8-10]. In the last
82 decades, the development of miniaturized passive sorption-based techniques
83 for sample enrichment has increased, covering *e.g.*, solid phase microextraction
84 (SPME), stir bar sorptive extraction (SBSE) [14–16], and bar adsorptive
85 microextraction (BA μ E) as most representative for trace analysis of polar to
86 nonpolar analytes in aqueous media [11-13]. BA μ E is based on the floating
87 sampling technology enrichment process, allowing for the possibility of selecting
88 the most convenient sorbent coating upon the target PhCs involved [11,18,19].
89 In this regard, and recognizing the relevance of activated carbons as
90 adsorbents of micropollutants, it is interesting to evaluate the potential of
91 different types of carbon materials -*e.g.*, carbohydrate-derived hydrochars and
92 their activated counterparts-, as coating phases for a selective extraction of a
93 wide range of PhCs. Hydrochars can be obtained by the hydrothermal
94 carbonization of a carbohydrate precursor under mild synthesis conditions using
95 water as solvent. As opposed to activated carbons prepared from conventional
96 activation routes, hydrochars are essentially non-porous solids characterized by

97 displaying a surface chemistry rich in oxygen groups. The addition of eutectic
98 salt mixtures during the hydrothermal carbonization allows to obtain nanoporous
99 hydrochars with hierarchical porosity [20] and a rich amphoteric surface
100 chemistry. The combination of these features will prove to play a crucial role in
101 their high performance toward the quantification of PhCs with distinct
102 physicochemical properties.

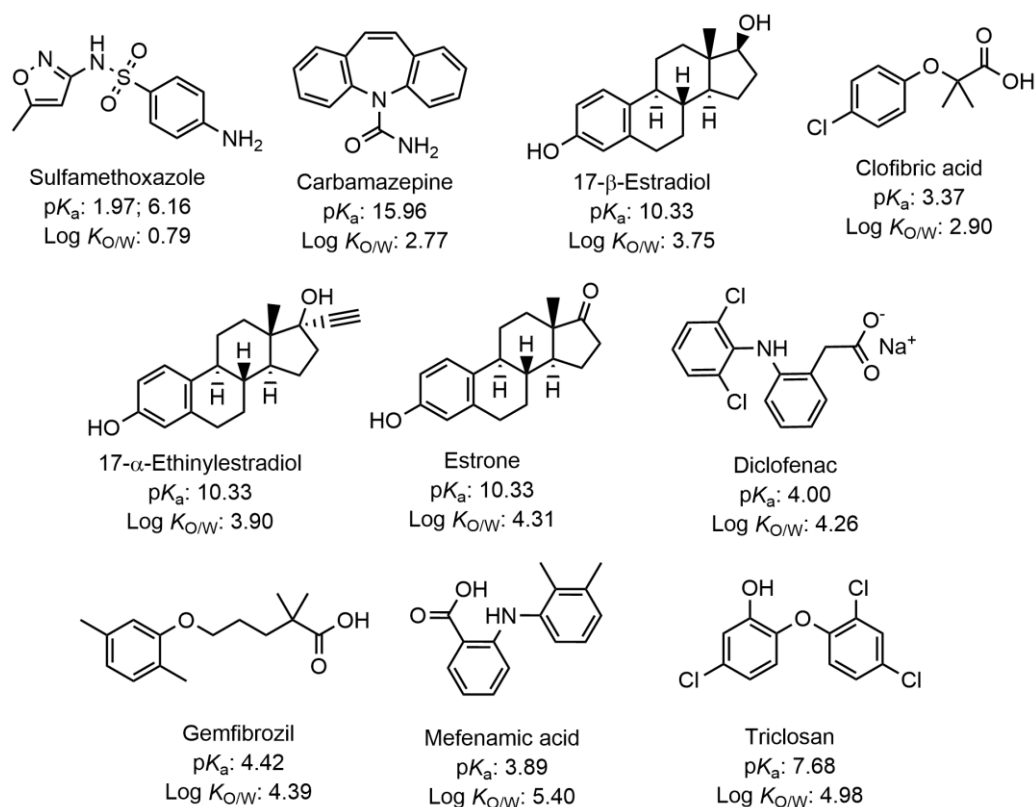
103 This work aims to evaluate the performance of BA μ E devices coated with
104 various carbon materials to simultaneously monitor traces of pharmaceutical
105 compounds (*i.e.* sulfamethoxazole, triclosan, carbamazepine, diclofenac,
106 mefenamic acid, 17 α -ethinylestradiol, 17 β -estradiol, estrone, gemfibrozil and
107 clofibric acid) in deionized water and in environmental water matrices. The
108 BA μ E was used as the first step in the quantification and identification of the
109 PhCs, followed by microliquid desorption (μ LD) and then high performance
110 liquid chromatography with diode array detection (HPLC-DAD). The
111 performance of the distinct carbon materials covering activated carbons,
112 nanoporous carbohydrate-based hydrochars and superactivated hydrochars
113 has been discussed in the light of their porous and chemical features. The
114 validation and application of the optimized methodology (including the influence
115 of polarity, back-extraction time and solvent, stirring rate) for real water matrices
116 is fully discussed, as well as the comparison with other microextraction-based
117 techniques.

118 **2. Experimental**

119 **2.1 Reagents**

120 Glucose, G (> 99 %), fructose, F (> 99 %) and sucrose, S (> 99 %) were
121 obtained from AnalaR NORMAPUR (Leuven, Belgium). Lithium chloride (LiCl,

122 99 %) was acquired from Merck (Darmstadt, Germany), and zinc chloride (ZnCl,
123 98 %) was acquired from Acros Organics (Geel, Belgium). Carbamazepine
124 (99.0 %), triclosan (97.0 %), diclofenac sodium salt (98.0 %) 17- β -estradiol
125 (98.0 %), estrone (99.0 %), gemfibrozil (98.5 %), mefenamic acid (98.5 %),
126 clofibrac acid (98.0 %), sulfamethoxazole (98.0 %) and potassium carbonate
127 (K_2CO_3 , 99 %) were purchased from Sigma-Aldrich (Steinheim, Germany). 17-
128 α -ethinylestradiol (98.0 %) was purchased from Riedel-de-Haën (Seelze,
129 Germany). Figure 1 depicts the chemical structures, as well as the pK_a and log
130 K_{OW} values of the PhCs studied. The solvents used were HPLC-grade
131 methanol (MeOH, 99.8 %), and acetonitrile (ACN, 99.8 %), obtained from Carlo
132 Erba (Arese, Italy). Sodium chloride (NaCl, 99.5 %) was purchased from Merck
133 Millipore (Darmstadt, Germany). Sodium hydroxide (NaOH, 98.0 %) pellets
134 were obtained from AnalaR (BDH chemicals, Lutterworth, U.K.). Hydrochloric
135 acid (HCl, 37 %), acetic acid (99.5 %) and potassium hydroxide (KOH, 85 %)
136 were purchased from Panreac (Barcelona, Spain). The acrylic acid (AA, ≥ 99 %)
137 was purchased from Merck (Hohenbrunn, Germany). All chemicals were used
138 without further purification. Ultra-pure water was obtained from the Milli-Q water
139 purification systems (Merck Millipore, Darmstadt, Germany).



140

141

Figure 1 – Chemical structures, pK_a and log K_{OW} values of the analysed PhCs [21].

142

2.2 Carbon materials synthesis and characterization

143

The hydrochars were prepared by hydrothermal carbonization of

144

carbohydrates: 15 cm³ of 1.5 mol L⁻¹ glucose or sucrose solutions introduced in

145

an autoclave and heated at 190 °C during 5 h [22,23]. These samples are

146

labeled as HG or HS according with the carbohydrate precursor (glucose and

147

sucrose, respectively). Modified sucrose-derived hydrochars were prepared by

148

a similar protocol but adding acrylic acid (e.g., 7, 14 or 27 wt.%) to the starting

149

sucrose aqueous solution [24,25]. The modified hydrochars were labeled as

150

HSAAx, where x stands for the amount of acrylic acid. The sucrose-derived

151

hydrochar was chemically activated as indicated elsewhere [22,23]. Briefly,

152

superactivated carbons HS/H800 and HS/C800 were prepared by activation of

153

1 g of sucrose-derived hydrochar (HS) with 4 g of, respectively, KOH and

154

K₂CO₃ during 1 h at 800 °C.

155 The synthesis of nanoporous hydrochars was inspired on the studies
156 reported by Fechler *et al.* for glucose [20]. Briefly, 11.25 g of eutectic LiCl/ZnCl₂
157 salt mixture (23 molar % LiCl and the remaining corresponds to ZnCl₂) were
158 ground and homogenized in an agate mortar; then 4.5 g of a carbohydrate
159 precursor (G - glucose, F - fructose or S - sucrose) were added, and the
160 resulting mixture was grounded until obtaining a homogeneous sample. The
161 mixture carbohydrate:eutectic salt was introduced in a Teflon-line stainless steel
162 autoclave (35 cm³). After adding 2.3 cm³ of ultra-pure water, the autoclave was
163 closed, shaken vigorously, and placed in an oven (Medline Scientific Limited,
164 model ON-02G) pre-heated to 180 °C. The hydrothermal treatment was
165 performed during 17 h, after what the autoclave was cooled down to room
166 temperature, and the porous hydrochar was washed with distilled water up to no
167 detection of chlorine anions (*i.e.* no precipitation when AgCl is added). After
168 washing, the samples were dried at atmospheric pressure, ground and sieve to
169 store particles with dimensions < 0.297 mm. The porous hydrochars were
170 labelled as npHy, where y stands for the carbohydrate precursor (G, F, or S:
171 npHG, npHF and npHS, respectively).

172 An activated carbon prepared by steam activation of expanded corkboard
173 granules at semi-industrial scale following the procedure reported in ref. [26]
174 was also used (Cork/S800). Commercial powdered activated carbon (PAC)
175 materials CN1 from Cabot-Norit (Com/CN1, supplied by Salmon & Cia. (Lisbon,
176 Portugal)) and R from Riedel-de-Haën (Com/R, Seelze, Germany) were tested
177 for comparison purposes. Further details on the synthesis and characterization
178 of some of these carbons were previously reported (see cited references), and it
179 is presented on table 1 for comparison purposes.

181 Table 1 – Summary of the main textural and surface properties of the carbon materials used as
 182 coatings (apparent surface area – A_{BET} , micropore volume – V_{micro} (pores with widths < 2 nm),
 183 mesopore volume – V_{meso} (pores with widths between 2 and 50 nm), pH at the point of zero
 184 charge – pH_{PZC}).

| Type | Carbon material | Textural properties | Surface properties |
|-----------------------------------|--|---|---|
| Activated carbons | Commercial (Com/CN1 and Com/R) | $A_{\text{BET}} \approx 1000 \text{ m}^2/\text{g}$ Micro+mesopores Similar V_{micro} but V_{meso} of Com/CN1 is the double of Com/R | $\text{pH}_{\text{PZC}}(\text{Com/CN1}) = 5.1$ $\text{pH}_{\text{PZC}}(\text{Com/R}) = 6.5$ |
| | Steam activated cork (Cork/S800) ^a | BET area = $750 \text{ m}^2/\text{g}$ Micro+mesopores | $\text{pH}_{\text{PZC}} \geq 11$ |
| Hydrochar | Glucose and sucrose derived hydrochars (HG and HS) ^c | Non-porous | $\text{pH}_{\text{PZC}} = 2$ |
| | Acrylic acid modified sucrose-derived hydrochar (HSAA7%, HSAA14% and HSAA27%) ^d | Non-porous | $\text{pH}_{\text{PZC}} \approx 2$ Carboxylic, lactonic and phenolic groups in higher percentage than in non-modified HS |
| Activated carbons from hydrochars | Glucose, fructose and sucrose derived nanoporous hydrochars npHG, npHF and npHS) | $A_{\text{BET}}(\text{npHG}) = 529 \text{ m}^2/\text{g}$ $A_{\text{BET}}(\text{npHF}) = 407 \text{ m}^2/\text{g}$ $A_{\text{BET}}(\text{npHS}) = 487 \text{ m}^2/\text{g}$ Micro+mesopore samples with predominance of mesopores | $\text{pH}_{\text{PZC}} = 2.7 - 3.1$ |
| | Chemically activated sucrose-derived hydrochar (HS/C800 and HS/H800) ^b | $A_{\text{BET}}(\text{HS/C800}) = 1350 \text{ m}^2/\text{g}$ $A_{\text{BET}}(\text{HS/H800}) = 2431 \text{ m}^2/\text{g}$ Both microporous but HS/H800 V_{micro} is almost the double of HS/C800 | $\text{pH}_{\text{PZC}} \approx 4$ |

185 ^a Synthesis and characterization reported in [26]

186 ^b Synthesis and characterization reported in [22,23]

187 ^c Synthesis reported in [23,24] and characterization reported in [24]

188 ^d Synthesis and characterization reported in [24]

189

190 **2.3 Characterization of the carbon materials**

191 The textural properties of the porous hydrochars and commercial PACs
 192 were characterized by N_2 adsorption isotherms at $-196 \text{ }^\circ\text{C}$ in an automatic
 193 volumetric apparatus from Micromeritics (ASAP 2010). Before N_2 adsorption-

194 desorption the samples (60 – 100 mg) were outgassed at 120 °C overnight (ca.
195 17 h) under vacuum (pressure < 10⁻² Pa). The apparent surface area, A_{BET} , was
196 estimated from the N₂ adsorption data in the p/p^0 range of the BET plot that
197 assures: positive interception on the ordinate of the BET plot ($C > 0$) and $n_{\text{ads}}(1-$
198 $p/p^0)$ continuously increases with p/p^0 [27,28]. The total pore volume, V_{total} , was
199 quantified with the Gurvich rule [29], the micropore volume, V_{micro} , was
200 calculated with the α_s method taking as reference the isotherm reported by
201 Rodríguez-Reinoso *et al.* [30]. ACRESCENTAR ultra e super... The mesopore
202 volume, V_{meso} , corresponds to the difference $V_{\text{total}} - V_{\text{micro}}$.

203 The surface chemistry properties of the synthesized porous hydrochars and
204 commercial PAC were assessed through the determination of the pH at the
205 point of zero charge, pH_{PZC} , according to the reverse mass titration method [32]
206 using a Symphony SP70P pH meter. Diffuse reflectance infrared Fourier
207 transform (DRIFT) spectra of the porous hydrochars were recorded in a Nicolet
208 Magma-IR560 spectrometer provided with a high sensitivity mercury cadmium
209 telluride detector (MCT-A) that operates at cryogenic temperature. Each
210 spectrum was obtained using the powdered samples with no KBr addition and
211 corresponds to the accumulation of 256 scans, recording with a spectral
212 resolution of 2 cm⁻¹ in the mid-IR (4000 – 650 cm⁻¹) spectral range. The thermal
213 analysis (Setaram Labsys) was carried out on 15 mg of sample under a
214 nitrogen flow rate of 50 cm³ min⁻¹ up to a final temperature of 900 °C (heating
215 rate of 15 °C min⁻¹). The ash content of the glucose-derived porous char was
216 determined in the same equipment after exposure of the sample at 600 °C in air
217 (50 cm³ min⁻¹) for 3 h (constant mass).

218 The morphology of the porous hydrochars was evaluated by Scanning
219 Electron Microscopy (SEM) performed at a Zeiss Supra 55 VP apparatus with 5
220 kV as accelerating voltage and using the powdered samples coated with
221 iridium.

222 ***2.4 Standard preparation and water samples***

223 Stock solutions of individual analytes (1,000.0 mg L⁻¹) used for the working
224 standard mixture were prepared in MeOH and stored at 4 °C and renewed
225 every month. Working standard mixtures of 1.0 mg L⁻¹ were daily prepared in
226 MeOH and used for spiking sample assays. For instrumental calibration,
227 standard mixtures were prepared in MeOH by appropriate dilution from stock
228 solutions.

229 The water samples were obtained in the metropolitan area of Lisbon
230 (Portugal). The sea water samples were collected in the coastal area near
231 Estoril and Costa da Caparica, the lake water from an artificial lake (Campo
232 Grande) and the tap water samples from the public water supply system of
233 Lisbon and Almada. The estuarine water samples were collected at Ponta do
234 Mato, a Tagus river estuary beach. The wastewater treatment plant (WWTP)
235 samples were obtained from Alcântara WWTP after primary decantation and
236 filtration. All samples were collected in clean amber glass bottles and filtered
237 with paper filters (125 mm of diameter, 10-13 µm of pore size, Cat No 1001 125,
238 Whatman; Amersham, U.K.) and kept refrigerated at -20 °C until being used.

239 ***2.5 BAµE-µLD methodology***

240 The BAµE devices (7.5 mm in length and 3 mm in diameter) were in-house
241 prepared as indicated in previous works [17,33]. After being produced, the

242 devices were stored at room temperature in closed glass flasks. The BA μ E
243 devices were cleaned with MeOH and ultra-pure water before use. Considering
244 that microextraction bars are relatively inexpensive and easy to prepare, and
245 aiming to avoid any possible contamination, they were discarded after each
246 use.

247 The BA μ E- μ LD procedure was performed by placing a 25 mL aliquot of the
248 water samples in a 25 mL sampling glass flask, followed by the introduction of a
249 BA μ E device, previously coated with npHS, and a conventional Teflon magnetic
250 stirring bar. The assays were performed in a multipoint agitation plate
251 (Variomag H+P Labortechnik Multipoint 15, Oberschleissheim, Germany) at
252 room temperature using 1,000 rpm for 16 h (pH 2.0). After microextraction, the
253 devices were removed from the samples with clean tweezers, dried for a few
254 seconds using a lint-free tissue and placed into glass vial inserts containing 100
255 μ L of ACN, ensuring their total immersion prior to ultrasonic treatment (Branson
256 3510, Zurich, Switzerland) at room temperature for 60 min. After μ LD, the
257 devices were removed, 100 μ L of ultra-pure water was added, the vials
258 vortexed for 10 s, and closed, followed by HPLC-DAD analysis. The standard
259 addition method (SAM) was applied in real samples assays using four
260 concentration levels ranging from 8.0 μ g L⁻¹ to 104.0 μ g L⁻¹ for all PhCs under
261 study. Blank assays were also performed using the same procedure but without
262 spiking (“zero-point” assays). The assays on real matrices were performed in
263 triplicate.

264 ***2.6 Instrumental set-up***

265 HPLC-DAD analysis were carried out on a benchtop Agilent 1100 series LC
266 chromatographic system (Agilent Technologies, Waldbronn, Germany)

267 equipped with a vacuum degasser (G1322A), autosampler (G1313A),
268 thermostated column compartment (G1316A), quaternary pump (G1311A) and
269 a diode array detector (G1315B). The data acquisition and system control were
270 performed by the software LC3D ChemStation (version Rev.A.10.02[1757],
271 Agilent Technologies). Analyses were performed on a Kinetex hexyl phenyl
272 column, 150.0 × 4.6 mm, 2.6 µm particle size (Phenomenex, Torrance, U.S.A.).
273 The samples were analysed using a gradient mobile phase consisting of 2.5 %
274 acetic acid/ultra-pure water (v/v, solvent A) and ACN (solvent B). The employed
275 elution gradient was as follows: 0 min – 80/20 (solvent A/B); 24 min – 20/80
276 (solvent A/B); 27 min - 20/80 (solvent A/B); 30 min – 80/20 (solvent A/B); 35 min
277 – 80/20 (solvent A/B). All solvents were previously filtered (125 mm in diameter,
278 10-13 µm in pore size, 1001 125, Whatman, U.K.) to remove suspended
279 particles, if any. The detector was set at 280 nm and the column temperature at
280 20 °C. The injection volume was 40 µL with a draw speed of 200 µL min⁻¹ and
281 the flow rate was set at 0.6 mL min⁻¹. For identification purposes, standard
282 addition was used, by spiking the samples with pure standards, as well as by
283 comparing the relative retention time and peak purity with the UV/vis spectral
284 reference data. For quantification purposes, calibration curves using the
285 external standard methodology were performed. Instrument linearity was
286 calculated by injecting ten standard solutions having concentration from 10.0 or
287 30.0 µg L⁻¹ (depending on the compound) to 5,000.0 µg L⁻¹, where it was
288 possible obtain determination coefficients (r^2) higher than 0.99 for the target
289 compounds. For recovery calculations, peak areas obtained from each assay
290 were compared with the peak areas of standard controls used for spiking. Peak
291 areas were obtained by integration of each target compounds corresponding

292 peak using the mentioned software. The sensitivity of the instrumental system
293 was checked through the limits of detection (LODs) and quantification (LOQs)
294 calculated with signal-to-noise (S/N) of 3/1 and 10/1, where it ranged from 1.0
295 $\mu\text{g L}^{-1}$ to 10.0 $\mu\text{g L}^{-1}$ and between 5.0 $\mu\text{g L}^{-1}$ to 27.0 $\mu\text{g L}^{-1}$ for all the PhCs under
296 study, respectively. The instrumental precision was evaluated by consecutively
297 injecting a standard mixture ($n = 6$, 1.0 mg L^{-1}), resulting in relative standard
298 deviations (RSD) lower than 2.9 %.

299

300 **3. Results and discussion**

301 **3.1 Carbon material selectivity as sorbent coating**

302 To maximize the microextraction efficiency by the BA μ E- μ LD process,
303 thirteen carbon materials were tested as enrichment phase for the recovery of
304 PhCs using carbamazepine, 17 α -ethinylestradiol, 17 β -estradiol, diclofenac and
305 triclosan as model compounds. These carbon materials were selected to cover
306 a large range of textural features (from non-porous to highly porous samples
307 with A_{BET} up to 2400 m^2/g) and surface properties (acidic, neutral or basic, with
308 pH_{PZC} ranging from 2 to 11), as it can be observed in tables 1 and 2. Additional
309 information on the physicochemical properties of the studied carbons is
310 summarized in the Supporting Information (topic S1). The evaluation assays
311 were made in triplicate using ultra-pure water samples spiked at the 16.0 $\mu\text{g L}^{-1}$
312 level.

313 As presented in figure 2a, the recovery efficiency of the carbon materials
314 for the five selected PhCs is strongly dependent on both the type of material
315 and the target pharmaceutical compound.

316

317 Table 2 – Textural properties of the porous hydrochars and commercial activated carbons, and
 318 pH_{PZC} .

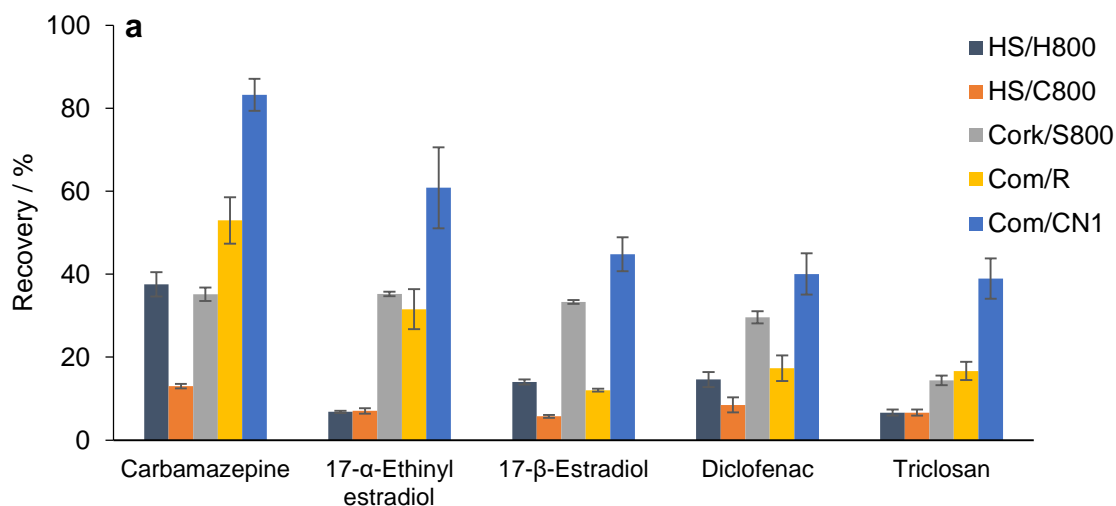
| Sample | A_{BET} ($\text{m}^2 \text{g}^{-1}$) | $V_{\text{total}}^{\text{a}}$ ($\text{cm}^3 \text{g}^{-1}$) | $V_{\text{meso}}^{\text{b}}$ ($\text{cm}^3 \text{g}^{-1}$) | α_s Method | | | pH_{PZC} |
|----------------|--|--|---|---|---|---|--------------------------|
| | | | | $V_{\alpha \text{ total}}$ ($\text{cm}^3 \text{g}^{-1}$) | $V_{\alpha \text{ ultra}}$ ($\text{cm}^3 \text{g}^{-1}$) | $V_{\alpha \text{ super}}$ ($\text{cm}^3 \text{g}^{-1}$) | |
| npHG | 529 | 0.58 | 0.47 | 0.11 | 0.00 | 0.11 | 3.0 |
| npHF | 407 | 0.28 | 0.16 | 0.12 | 0.00 | 0.12 | 2.7 |
| npHS | 487 | 0.47 | 0.35 | 0.12 | 0.00 | 0.12 | 3.1 |
| Com/CN1 | 1179 | 0.98 | 0.68 | 0.30 | 0.00 | 0.30 | 5.1 |
| Com/R | 964 | 0.65 | 0.37 | 0.28 | 0.10 | 0.18 | 6.5 |

319 ^a Evaluated at $p/p^0 = 0.975$ in the N_2 adsorption isotherms at -196 °C

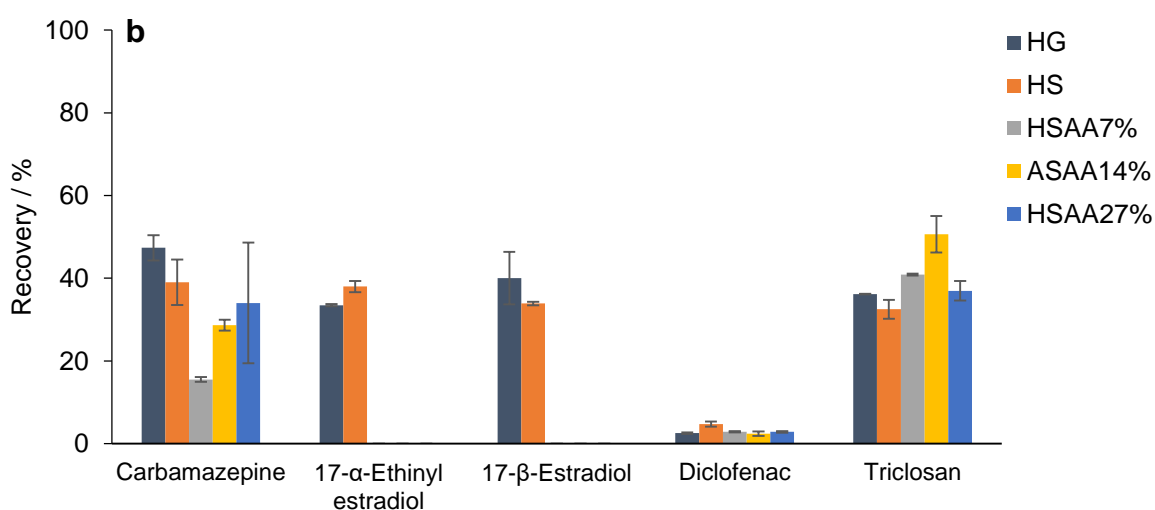
320 ^b Difference between V_{total} and $V_{\alpha \text{ total}}$

321

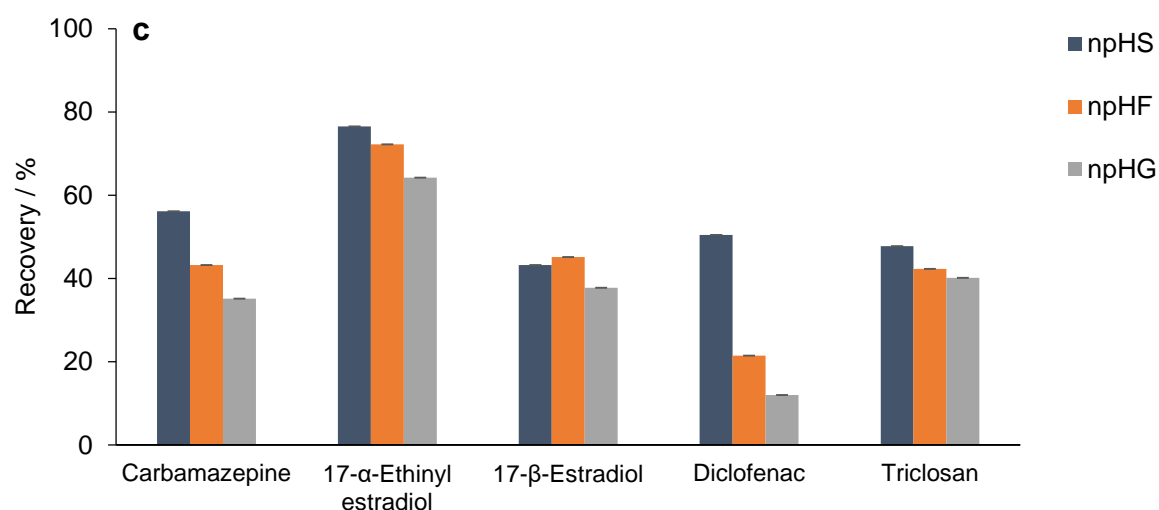
322 From the set of activated carbons tested (samples Com/CN1, Com/R,
 323 Cork/S800, HS/C800 and HS/H800), the commercial sample Com/CN1 with a
 324 BET area higher than $1000 \text{ m}^2/\text{g}$, a micro+mesopore structure and slightly
 325 acidic character (*i.e.*, pH_{PZC} of 5.1) outperformed the steam activated cork
 326 carbon (sample Cork/S800) with lower surface area and basic character, as well
 327 as the activated sucrose-derived hydrochars (samples HS/H800 and HS/C800)
 328 with a better-developed micropore structure and acidic nature. The non-porous
 329 hydrochars (figure 2b) failed to recover diclofenac and, while the samples HG
 330 and HS were able to recover ca. 40 % of the remaining PhCs, the acrylic acid
 331 modified hydrochars (HSAAx%) failed the recovery of 17α -ethinylestradiol and
 332 17β -estradiol. On the contrary, the acidic nanoporous hydrochars (figure 2c)
 333 displaying micro-/mesopore networks and moderate surface areas (Tables 1
 334 and 2) allowed to recover the five target PhCs. Furthermore, the bar prepared
 335 using sample npHS as coating allowed to obtain recoveries comparable to the
 336 best commercial activated carbon for all the PhCs (ranging between 42-78%),
 337 with the exception of carbamazepine.



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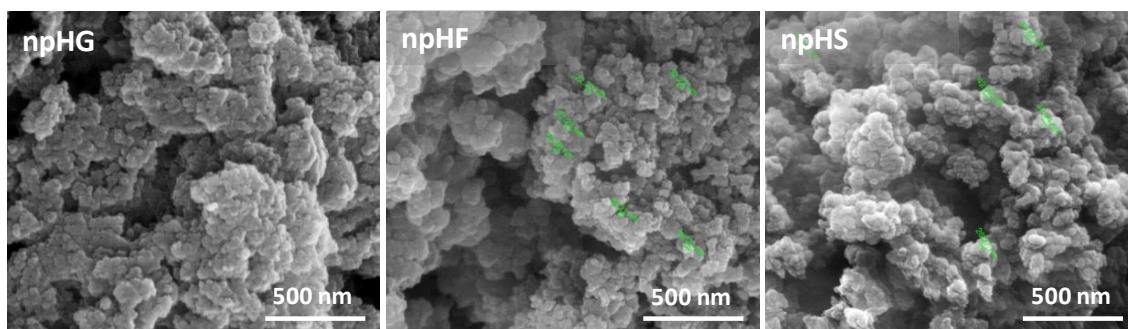
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Figure 2 – Effect of sorbent selectivity on the recovery yields of the five mentioned PhCs using commercial and lab-made activated carbons (a), lab-made hydrochars (b) and lab-made nanoporous hydrochars (c) as sorbent coating obtained by BAμE-μLD/HPLC-DAD. BAμE coating: 1.0-3.0 mg; Spiking level: 16.0 μg L⁻¹; Equilibrium: 16 h (1000 rpm) pH 5.5; μLD: ACN (100 μL) 60 min.

347
348 To gather a deeper understanding of the contribution of the adsorption
349 and desorption processes in the overall recovery of the lowest performing
350 materials, three of them were selected for a complementary assay. Samples
351 HS/H800, HG and HSAA27% were tested for the recovery of the five PhCs
352 using higher initial concentrations, thereby facilitating the quantification after the
353 concentration step (figure S3, SI). In the case of sample HS/H800
354 (superactivated carbon), the low recoveries can be attributed to the irreversible
355 adsorption of the targets inside the well-developed microporous structure; on
356 the contrary, for the non-porous hydrochars, most of the molecules remain in
357 the water matrix, thus the less efficient recovery of polar PhCs seems to be
358 related with their low affinity towards the carbon coating phase. Under these
359 experimental conditions, recoveries of 100% were obtained for triclosan -the
360 most nonpolar target- with these non-porous hydrochars, whereas the recovery
361 of carbamazepine -the most polar compound of the set- would be hindered by
362 the irreversible retention on the acidic surface of such carbon coatings.
363 Interestingly, the relatively high recoveries of herein prepared nanoporous
364 hydrochars characterized by lower surface areas than commercial activated
365 carbons (tables 1 and 2) points out to the paramount importance of combining
366 micro-mesoporosity and appropriate surface chemistry. The porous hydrochars
367 are composed by agglomerates of interconnected units in the nanometric scale
368 (20 – 50 nm) that originate a pore system in the mesoscale (figure 3). This
369 could be important to assure an efficient and fast adsorption and desorption of
370 the target compounds during the enrichment step.



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Figure 3 – SEM images of the nanoporous hydrochars.

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Figure 4 illustrates the influence of the properties of the above mentioned thirteen carbon materials on their performance as enrichment phases. The four graphics present the correlation between selected carbon properties (pH_{PZC} vs A_{BET} , V_{total} , % V_{micro} and % V_{meso}) and the percentage of removal attained for the set of five PhCs (carbamazepine, 17α -ethinylestradiol, 17β -estradiol, diclofenac and triclosan). The number of occurrences corresponding to removals in the first quartile is systematically higher at low pH_{PZC} values associated with percentages of micropores between 15 % and 50 % and consequently to the presence of a micro+mesopore network.

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Summarising, these set of data points out that the selection of an adequate carbon coating for BA μ E- μ LD/HPLC-DAD to assure high recoveries should consider sorbents combining a well-developed pore structure in the full micro to mesopore range, along with acidic surface groups (*i.e.* phenol and carboxylic acid, see DRIFT spectra discussion in Supporting Information).

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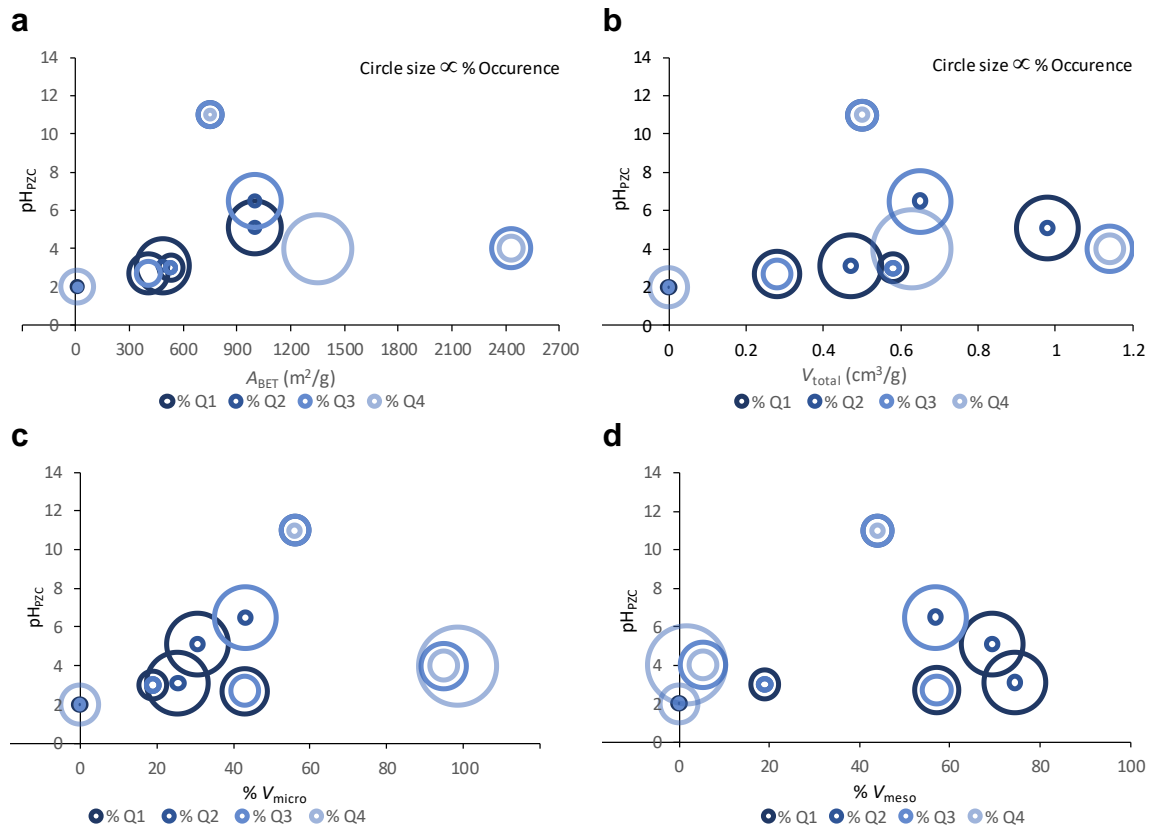
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In light of these preliminary results for the nanoporous hydrochars with the set of five targets, these carbon materials were further tested as enrichment phase for the recovery of the 10 PhCs and benchmarked vs two commercial PACs (figure 5). As seen, under the experimental conditions tested (*ca.* pH 5.5) none of the carbon materials were able to recover clofibric acid, although

392 recoveries up to 50 % were obtained for the other two acidic compounds
 393 (diclofenac and mefenamic acid).



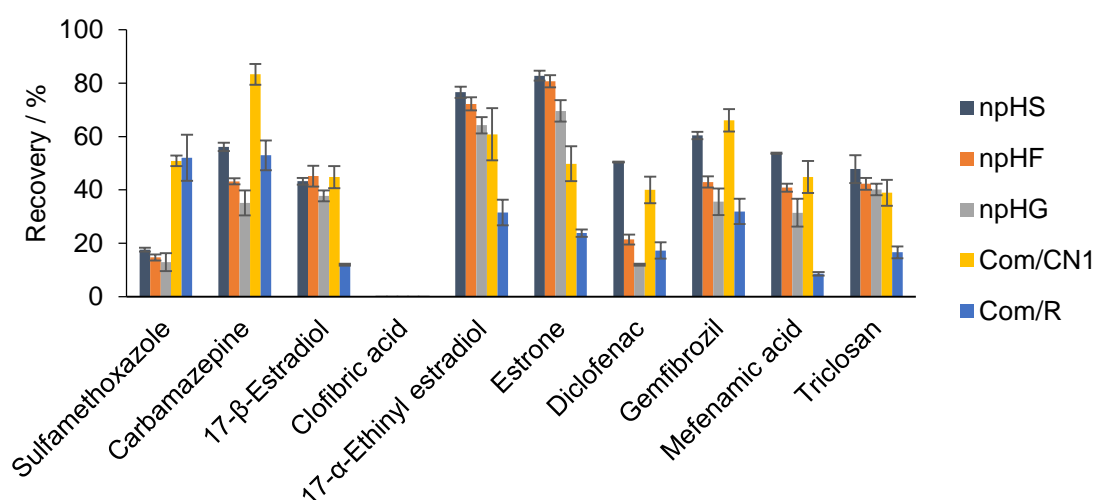
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395 Figure 4 – Influence of carbon materials properties in the removal percentages of five target
 396 PhCs: pH at the point of zero charge (pH_{PZC}) versus BET area (a), total pore volume (b),
 397 percentage of micropore volume (c), and percentage of mesopore volume (d). Circles represent
 398 the percentage of removal (in quartiles) adjusted for the removal range of each PhC, Q1
 399 corresponding to top 25 % removal and Q4 to bottom 25 % removal, and circle sizes are directly
 400 proportional to the percentage of occurrence.

401

402 Com/R presented the lowest performance for the majority of PhCs, with
 403 the exceptions were sulfamethoxazole and carbamazepine. Such low
 404 recoveries may be partially since this carbon was the only material displaying a
 405 slightly positively charged surface under our experimental conditions (i.e., pH
 406 solution < pH_{PZC} 6.5). Despite a less developed pore network, the nanoporous
 407 hydrochars compare favourably with the commercial activated carbons, except
 408 in the case of sulfamethoxazole and carbamazepine. This might be attributed to
 409 their negatively charged surface charge (i.e., pH solution > pH_{PZC} 2.7 – 3.1). For

410 the other pharmaceuticals, the recoveries ranged between 40 % (17- β -estradiol)
 411 and 80 % (17- α -ethinyl estradiol and estrone), with the nanoporous
 412 hydrocarbons prepared from sucrose and fructose competing closely with the
 413 best performing commercial carbon (sample Com/CN1) for the majority of the
 414 target compounds. Considering all this, further optimization assays were carried
 415 out on microextraction bars prepared using samples npHS, npHF and
 416 Com/CN1 as carbon coatings.



417

418 Figure 5 – Effect of sorbent selectivity on the PhCs recovery yields with different carbon based
 419 materials as sorbent coating obtained by BA μ E- μ LD/HPLC-DAD. BA μ E coating: 1.0-3.0 mg;
 420 Spiking level: 16.0 μ g L⁻¹; Equilibrium: 16 h (1000 rpm) pH 5.5; μ LD: ACN (100 μ L) 60 min.
 421

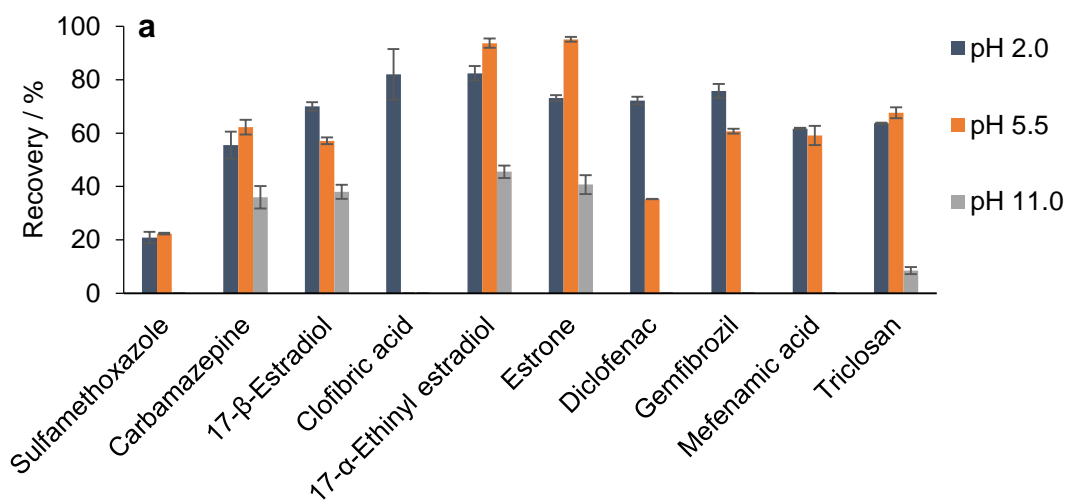
422 After choosing the best performing carbon materials through BA μ E for the
 423 determination of the target PhCs from aqueous media, the μ LD parameters, as
 424 well as the equilibrium time, stirring rate, ionic strength, matrix polarity, and
 425 sample pH were also evaluated. All the results the optimization, with exception
 426 of the latter which will be discussed in the following, can be consulted in SI.

427 The chemical characteristics of the water matrix were also assessed, in
 428 particular pH, ionic strength and polarity. Figure 6 shows the recovery yields

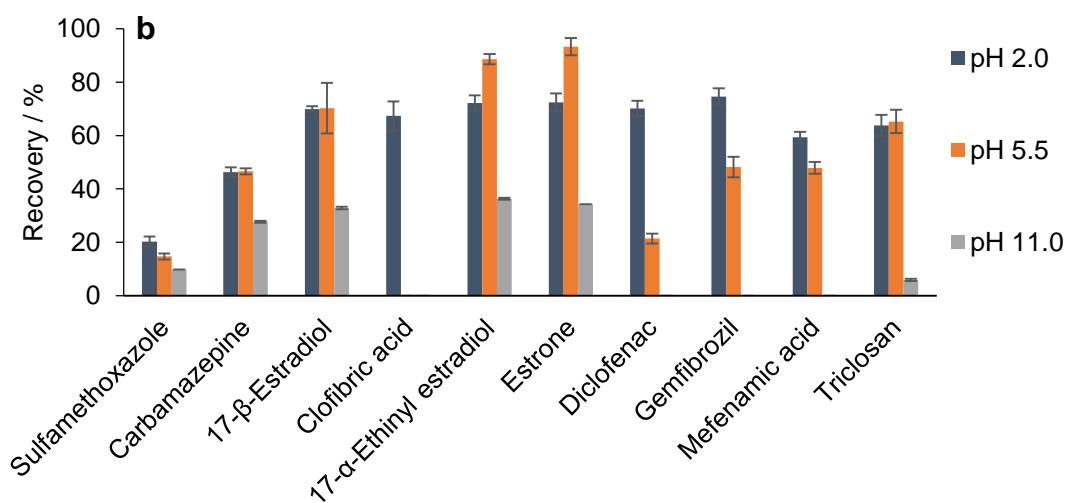
429 obtained for the BA μ E devices at different solution pH between 2 and 10 for the
430 three selected carbon coatings. With the exception of carbamazepine recovery
431 with sample CN1, the solution pH strongly influenced the recovery of all the
432 target analytes. This was somewhat expected since it is well known that this
433 parameter affects the ionic or neutral forms of the PhCs in solution [11], as well
434 as the surface charge of the carbon materials. Under strong acidic pH, clofibric
435 acid -analyte with the lowest pK_a value- was recovered with yields between 70
436 to 90 % for all tested sorbent phases. This points out that the determination of
437 clofibric acid by BA μ E using carbon coatings as enrichment phases, is only
438 possible when this semipolar acidic compound is in the protonated form. Our
439 previous results using cork-derived activated carbons as enrichment materials
440 also identified the critical role of pH in the quantification of clofibric acid, with the
441 best results attained at acidic pH [34].

442 The recovery yields increased at pH 2.0 for all compounds and carbon
443 coatings used, since all the carbon materials display a slightly positively
444 charged surface under these conditions (solution pH < pH_{PZC}). These results
445 can be rationalized considering the log D values (that corrects the log $K_{o/w}$ for
446 the pK_a of each compound by quantifying the amount of both the ionized and
447 non-ionized forms in octanol and water, Scheme S1, SI) of the PhCs at the pH
448 values under study.

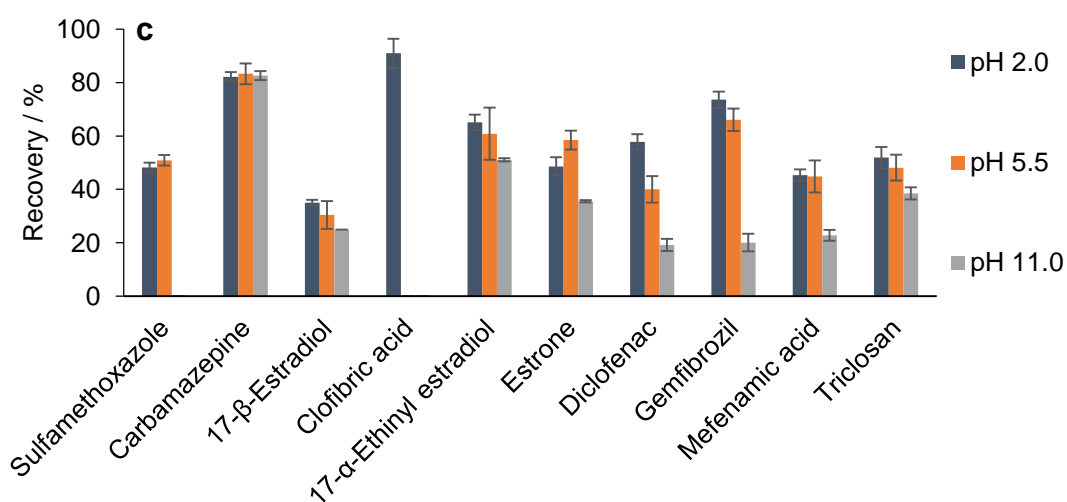
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453 Figure 6 – Effect of matrix pH on the PhCs recovery yields using npHS (a), npHF (b) and
 454 Com/CN1 (c) as sorbent coating obtained by BAμE-μLD/HPLC-DAD. BAμE coating: 1.0 – 3.0
 455 mg; Spiking level: 8.0 μg L⁻¹; Equilibrium: 16 h (1000 rpm); μLD: ACN (100 μL) 60 min.

456 Table S1 (SI) showed that regardless the solution pH there is an overall
457 increase in the recovery yields with the increase in the log D values. In general,
458 at solution pH 2.0, the selected PhCs present higher octanol solubility (favoring
459 both adsorption and desorption), thus contributing to higher recovery yields.
460 When the solution pH is higher than or similar to the pK_a of a given PhCs, its
461 recovery gets close to zero, justifying the greater reduction in the recovery
462 yields in compounds with lower pK_a values. It can so be concluded that the
463 lower recoveries are related with the deprotonation of the target compounds,
464 thus with the higher stability in the water matrix and consequently lower affinity
465 towards the porous solids.

466

467 **3.2 Validation of the BA μ E(HC-S)- μ LD/HPLC-DAD methodology**

468 By using the optimized experimental conditions for each carbon-based
469 sorbents (Com/CN1, npHF and npHS), it was possible to attain average
470 recoveries between 20.3 and 90.9 % for all target compounds in ultra-pure
471 water spiked at the 16.0 $\mu\text{g L}^{-1}$ level. Comparatively, better results were
472 obtained using npHS as carbon coating with most of the PhCs, thus the
473 validation assays of the BA μ E(npHS)- μ LD/HPLC-DAD methodology were
474 carried out using this sorbent phase (table S1, SI).

475 The sensitivity of the methodology was checked through the LODs (0.5 –
476 1.5 $\mu\text{g L}^{-1}$) and LOQs (1.5 – 5.0 $\mu\text{g L}^{-1}$), calculated with signal to noise ratios
477 S/N of 3/1 and 10/1, respectively. The methodology was also evaluated through
478 intraday and interday repeatability assays, calculating the corresponding
479 relative standard deviations (RSD) [35]. Interday repeatability assays were

480 carried out as six replicates a day in three consecutive days and intraday
481 repeatability assays consisted in six replicates performed in the same day
482 (using three spiking levels). Good precisions were achieved for the intraday
483 repeatability assays, with $RSD \leq 8.4 \%$ (diclofenac), and for interday
484 repeatability, was $\leq 12.3 \%$ (mefenamic acid), under optimized experimental
485 conditions. Assays were also performed in ultra-pure water having
486 concentrations ranging from 5.0 to 104.0 $\mu\text{g L}^{-1}$, where convenient linearity was
487 obtained, with r^2 higher than 0.99 for all the target PhCs under study. Table S2
488 (SI) summarizes the LODs, LOQs, as well as intraday and interday precision
489 levels achieved by the proposed methodology, under optimized experimental
490 conditions.

491

492 **3.3 Performance comparison with other microextraction techniques**

493 A comparison of the performance of the BA μ E(npHS)- μ LD/HPLC-DAD
494 methodology and other established static-based microextraction techniques is
495 shown in table 3 [36–44]. As it can be observed, the developed methodology
496 using BA μ E devices coated with sucrose-based hydrochar presents similar or
497 better recovery yields than other miniaturized enrichment techniques, e.g.,
498 SBSE coated with PDMS, PA or EG [38] or SBME coated with C8 polymer [39]
499 for the extraction of carbamazepine; TFME coated with PDMS [44] for the
500 extraction of 17- β -estradiol; SBSE coated with PDMS [42] for the extraction of
501 clofibric acid; SBSE coated with PU [45] for the extraction of diclofenac,
502 gemfibrozil or mefenamic acid. Additionally, the BA μ E(npHS)- μ LD/HPLC-DAD
503 methodology sensitivity is similar when compared to analogue instrumental
504 systems [37,39,45] and/or some mass spectrometry or tandem mass

505 spectrometry instrumental systems [40,44]. On the other hand, instrumental
506 apparatus that employ mass spectrometry or tandem mass spectrometry
507 expectedly presented lower LODs than the proposed technique [38,41,44,46].

508

509 Table 3 – Comparison of the LODs, average recovery yields in this work and other static-based microextraction techniques for the determination of the studied
 510 PhCs in aqueous samples.

| PPCP | Static based microextraction techniques | Instrumental system | Recovery (%) | LOD ($\mu\text{g L}^{-1}$) | Refs. |
|------------------------|---|---------------------|--------------|------------------------------|-----------|
| Sulfamethoxazole | SPME(CW/TPR) | LC-(ESI)MS/MS | 59.2 | 14.0 | [36] |
| | MEPS(C8) | HPLC-DAD | n.a. | LOQ: 5.0 | [37] |
| | BA μ E(npHS) | | 20.9 | 1.5 | This work |
| Carbamazepine | SBSE(PDMS, PA or EG) | LC-(ESI)MS/MS | < 1.0 | n/a | [38] |
| | TFME(PDMS) | GC-MS | 67.1 | 0.72 | [44] |
| | SBME(C8) | HPLC-UV | 35.0-42.0 | 0.7 | [39] |
| | BA μ E(npHS) | HPLC-DAD | 55.5 | 0.5 | This work |
| 17- β -Estradiol | SBSE(PDMS) | LDTD/APCI-MS/MS | ~ 40.0 | 2.8 | [40] |
| | TFME(PDMS) | GC-MS | 85.0 | 0.41 | [44] |
| | SPME(PA) | | 92.0-101.0 | 0.15 | [41] |
| | SBSE(PDMS) | | 7.0 | 0.853 | [46] |
| | BA μ E(npHS) | HPLC-DAD | 70.0 | 2.0 | This work |
| Clofibric acid | SPME(PA) | GC-MS | 95.0-98.0 | 0.75 | [41] |
| | SBSE(PDMS) | | 18.5 | 0.222 | [46] |

| | | | | | |
|------------------------------------|----------------------|-----------------|------------|-----------|-----------|
| | BA μ E(AC) | HPLC-DAD | 79.7-96.1 | 0.21-0.28 | [34] |
| | BA μ E(npHS) | | 82.0 | 2.5 | This work |
| 17- α - Ethinylestradiol | SBSE(PDMS) | LDTD/APCI-MS/MS | ~ 30.0 | 2.6 | [40] |
| | SPME(PA) | GC-MS | 93.0-105.0 | 0.15 | [41] |
| | SBSE(PDMS) | | 9.0 | 0.508 | [46] |
| | BA μ E(npHS) | | HPLC-DAD | 82.4 | 2.0 |
| Estrone | SBSE(PDMS) | LDTD/APCI-MS/MS | ~ 50.0 | 2.2 | [40] |
| | SPME(PA) | GC-MS | 92.0-99.0 | 0.15 | [41] |
| | SBSE(PDMS) | | 12.7 | 0.789 | [46] |
| | BA μ E(npHS) | | HPLC-DAD | 73.1 | 2.0 |
| Diclofenac | SBSE(PDMS, PA or EG) | LC-(ESI)MS/MS | < 1.0 | n/a | [38] |
| | SBSE(PDMS) | GC-MS | 21.0 | 0.037 | [46] |
| | SBSE(PDMS) | HPLC-DAD | 34.6 | 1.6 | [45] |
| | SBSE(PU) | | 77.7 | 0.7 | |
| | SBME(C8) | | 47.0-52.0 | 0.9 | [39] |
| | BA μ E(npHS) | | 72.2 | 0.5 | This work |
| Gemfibrozil | SBSE(PDMS) | GC-MS | 15.5 | 0.013 | [46] |
| | SBSE(PDMS) | HPLC-DAD | 73.4 | 1.7 | [45] |
| | SBSE(PU) | | 84.0 | 0.7 | |

| | | | | | |
|----------------|----------------------|---------------|-------------|---------------|-----------|
| | BA μ E(HC-S) | | 75.8 | 1.0 | This work |
| Mefenamic acid | SBSE(PDMS) | GC-MS) | 29.0 | 0.001 | [46] |
| | SBSE(PDMS) | | 71.3 | 1.5 | [45] |
| | SBSE(PU) | HPLC-DAD | 48.4 | 1.3 | |
| | BA μ E(npHS) | | 61.7 | 0.5 | This work |
| Triclosan | SBSE(PDMS, PA or EG) | LC-(ESI)MS/MS | 40.0 - 80.0 | 0.005 – 0.010 | [38] |
| | SPME(PA) | | 76.0-88.0 | 0.15 | [41] |
| | SBSE(PDMS) | GC-MS | 23.8 | 0.0002 | [46] |
| | BA μ E(npHS) | HPLC-DAD | 63.7 | 1.0 | This work |

511 CW/TPR: Carbowax-templated resin; LC-(ESI)MS/MS: Liquid chromatography coupled to tandem mass spectrometry with electrospray ionization;
512 LDTD/APCI-MS/MS: Laser diode thermal desorption atmospheric pressure chemical ionization tandem mass spectrometry; MEPS: Microextraction by packed
513 sorbent; PA: Polyacrylate; PDMS: Polydimethylsiloxane; PEG: Polyethylene glycol; PU: Polyurethane; SBME: Solid bar microextraction; TFME: Thin-film
514 microextraction;

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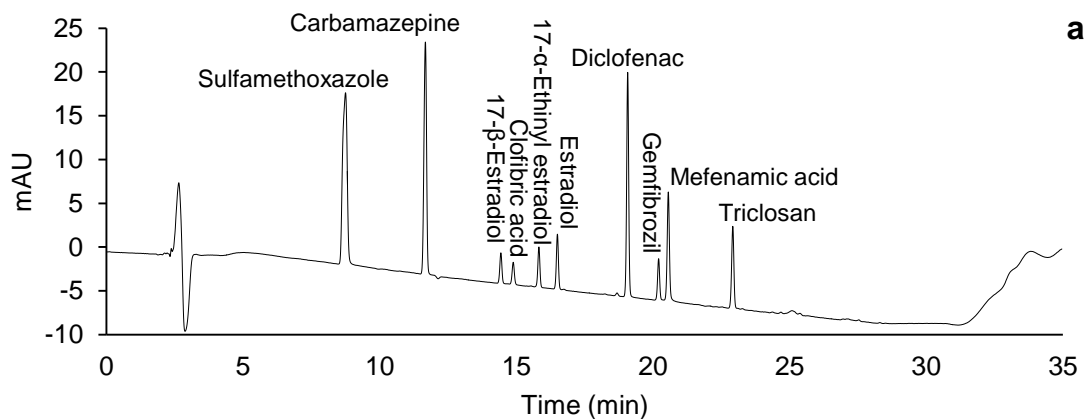
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517 **3.4 Application to environmental water matrices**

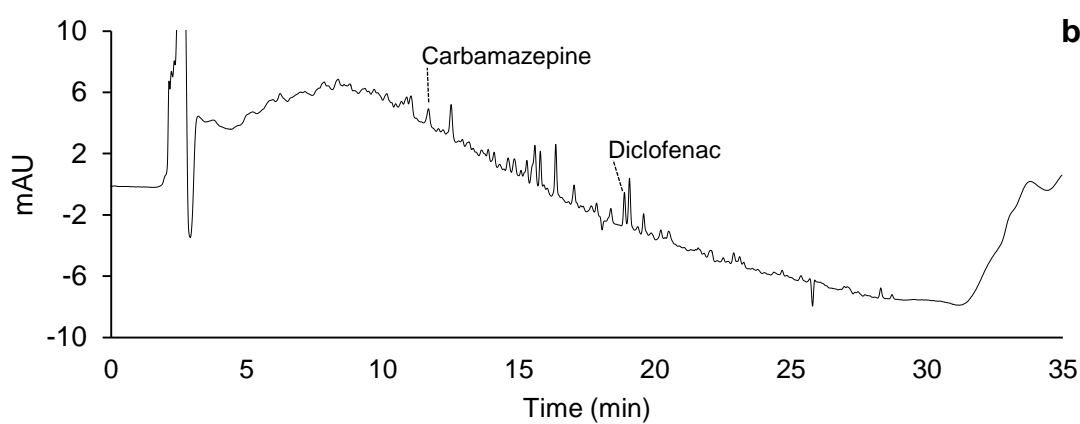
518 To evaluate the applicability of BA μ E(npHS)- μ LD/HPLC-DAD methodology
519 to real matrices, assays were performed in sea, lake, estuarine, tap and WWTP
520 water samples, through the SAM. This approach is usually the best strategy for
521 quantification purposes to determine the levels of analytes under study and to
522 reduce possible matrix interferences in real samples [11,12,47]. In a first step,
523 the water matrices were spiked with four working standards to produce the
524 corresponding spiking levels (8.0 $\mu\text{g L}^{-1}$ to 104.0 $\mu\text{g L}^{-1}$) for the ten PhCs under
525 study. "Zero-point" assays were also performed without spiking to ensure
526 maximum control of the analytical methodology. Good linear correlations were
527 achieved, with r^2 higher than 0.99. The chromatograms of neat standard mix at
528 the 8.0 $\mu\text{g L}^{-1}$ level for the ten PhCs (figure 7a) and WWTP sample without
529 spiking obtained by BA μ E(npHS)- μ LD/HPLC-DAD, under optimized
530 experimental conditions (figure 7b), exemplify the results obtained proving high
531 sensitivity at the trace level. The proposed methodology allowed to quantify two
532 of the analytes under study in the WWTP sample (carbamazepine: 4.01 ± 0.46
533 $\mu\text{g L}^{-1}$; diclofenac: $1.99 \pm 0.21 \mu\text{g L}^{-1}$).

534

535



536



537

538 Figure 7 – Chromatograms obtained from assays performed on an ultrapure water sample
 539 spiked at the $16.0 \mu\text{g L}^{-1}$ level (a) and a non-spiked WWTP sample (b), performed and by
 540 BA μ E(npHS)- μ LD/HPLC-DAD, under optimized experimental conditions.

541

542 4. Concluding remarks

543 Thirteen carbon sorbents prepared from different precursors and
 544 methodologies – commercial activated carbons, hydrochars and nanoporous
 545 hydrochars, and superactivated carbons – were tested as sorbent coatings for
 546 bar adsorptive microextraction followed by microliquid desorption and high
 547 performance liquid chromatography-diode array detection (BA μ E(npHS)-
 548 μ LD/HPLC-DAD methodology) for the simultaneous determination of traces of

549 ten PhCs from distinct therapeutic classes in synthetic and environmental water
550 matrices.

551 The lab-made nanoporous hydrochars proved to compete with commercial
552 activated carbon adsorbents for the enrichment of the PhCs, due to a
553 hierarchical pore structure in the full micro-mesopore range combined with a
554 rich surface chemistry composed of acid O-groups that favour both the
555 adsorption and desorption of the target compounds, thus contributing to a high
556 performance at the trace level. The method also demonstrated to be an
557 environmentally friendly approach, easy to implement, sensitive, robust and
558 requiring low sample volume. In short, the proposed analytical methodology
559 seems to be a very effective microextraction-based alternative to fulfill the EU
560 Decision 2015/495, as well as the USEPA guidelines for PhCs monitoring,
561 particularly if combined with tandem mass spectrometry systems, which may
562 provide even better detection limits.

563

564 **Conflicts of Interest**

565 The authors declare no conflict of interest.

566

567 **Acknowledgments**

568 The authors wish to thank Fundação para a Ciência e a Tecnologia (FCT,
569 Portugal) for funding Centro de Química e Bioquímica (UID/MULTI/00612/2019)
570 and Centro de Química Estrutural (Pluriannual funding 2020-2023). SMA thanks
571 FCT for the PhD grant (SFRH/BD/107892/2015), ASM acknowledges FCT for

572 the financial support to the EMBRACE project (CEECIND/01371/2017) and
573 NRN acknowledges FCT for the financial support through the contract
574 established from DL 57/2016. The authors also wish to thank Salmon & Cia
575 (Portugal) for offering the commercial Norit carbon material.

576

577 **References**

- 578 [1] L. Arpin-Pont, M.J. Martínez-Bueno, E. Gomez, H. Fenet, Occurrence of
579 PPCPs in the marine environment: a review, *Environ. Sci. Pollut. Res.* 23
580 (2016) 4978–4991. doi:10.1007/s11356-014-3617-x.
- 581 [2] A.B. Caracciolo, E. Topp, P. Grenni, Pharmaceuticals in the environment:
582 Biodegradation and effects on natural microbial communities. A review, *J*
583 *Pharm Biomed Anal.* 106 (2015) 25–36. doi: 10.1016/j.jpba.2014.11.040.
- 584 [3] W. Mnif, A.I. Hassine, A. Bouaziz, A. Bartegi, O. Thomas, B. Roig, Effect
585 of endocrine disruptor pesticides: a review, *Int J Env. Res Public Heal.* 8
586 (2011) 2265–2303. doi:10.3390/ijerph8062265.
- 587 [4] W.C. Li, Occurrence, sources, and fate of pharmaceuticals in aquatic
588 environment and soil, *Env. Pollut.* 187 (2014) 193–201. doi:
589 10.1016/j.envpol.2014.01.015.
- 590 [5] R. Zhao, T. Ma, S. Li, Y. Tian, G. Zhu, Porous Aromatic Framework
591 Modified Electrospun Fiber Membrane as a Highly Efficient and Reusable
592 Adsorbent for Pharmaceuticals and Personal Care Products Removal,
593 *ACS Appl. Mater. Interfaces.* 11 (2019) 16662–16673.
594 doi:10.1021/acsami.9b04326.

- 595 [6] S.D. Richardson, T.A. Ternes, Water Analysis: Emerging Contaminants
596 and Current Issues, *Anal. Chem.* 86 (2014) 2813–2848.
597 doi:10.1021/Ac500508t.
- 598 [7] J.Q. Jiang, Z. Zhou, V.K. Sharma, Occurrence, transportation, monitoring
599 and treatment of emerging micro-pollutants in waste water - A review from
600 global views, *Microchem. J.* 110 (2013) 292–300.
601 doi:10.1016/j.microc.2013.04.014.
- 602 [8] Directive 2013/39/EU of the European Parliament and of the Council of 12
603 August 2013 amending Directives 2000/60/EC and 2008/105/EC as
604 regards priority substances in the field of water policy, *Off. J. Eur. Union.*
605 L226 (2013) 1–17.
- 606 [9] Commission Implementing Decision (EU) 2015/495 of 20 March 2015
607 establishing a watch list of substances for Union-wide monitoring in the
608 field of water policy pursuant to Directive 2008/105/EC of the European
609 Parliament and of the Council, *Off. J. Eur. Union.* L78 (2015) 40-42.
- 610 [10] Commission Implementing Decision (EU) 2018/840 of 5 June 2018
611 establishing a watch list of substances for Union-wide monitoring in the
612 field of water policy pursuant to Directive 2008/105/EC of the European
613 Parliament and of the Council and repealing Commission Implementing
614 Decision (EU) 2015/495, *Off. J. Eur. Union.* L141 (2018) 9-12.
- 615 [11] N.R. Neng, J.M.F. Nogueira, Development of a bar adsorptive micro-
616 extraction-large-volume injection-gas chromatography-mass
617 spectrometric method for pharmaceuticals and personal care products in
618 environmental water matrices, *Anal Bioanal Chem.* 402 (2012) 1355–

- 619 1364. doi:10.1007/s00216-011-5515-0.
- 620 [12] C. Almeida, J.M. Nogueira, Determination of trace levels of parabens in
621 real matrices by bar adsorptive microextraction using selective sorbent
622 phases, *J Chromatogr A*. 1348 (2014) 17–26.
623 doi:10.1016/j.chroma.2014.04.057.
- 624 [13] T.S. Oliveira, M. Murphy, N. Mendola, V. Wong, D. Carlson, L. Waring,
625 Characterization of Pharmaceuticals and Personal Care products in
626 hospital effluent and waste water influent/effluent by direct-injection LC-
627 MS-MS, *Sci. Total Environ.* 518 (2015) 459–478. doi:
628 10.1016/j.scitotenv.2015.02.104.
- 629 [14] J.M.F. Nogueira, Stir-bar sorptive extraction – 15 years making sample
630 preparation more environment friendly, *TrAC Trends Anal. Chem.* 71
631 (2015) 214-223. doi:http://dx.doi.org/10.1016/j.trac.2015.05.002.
- 632 [15] J.M. Nogueira, Novel sorption-based methodologies for static
633 microextraction analysis: A review on SBSE and related techniques, *Anal*
634 *Chim Acta.* 757 (2012) 1–10. doi:10.1016/j.aca.2012.10.033.
- 635 [16] F. Wang, J. Zheng, J. Qiu, S. Liu, G. Chen, Y. Tong, et al., In situ
636 hydrothermally grown TiO₂@C core-shell nanowire coating for highly
637 sensitive solid phase microextraction of polycyclic aromatic hydrocarbons,
638 *ACS Appl. Mater. Interfaces.* 9 (2017) 1840–1846.
639 doi:10.1021/acsami.6b14748.
- 640 [17] N.R. Neng, A.R. Silva, J.M. Nogueira, Adsorptive micro-extraction
641 techniques--novel analytical tools for trace levels of polar solutes in
642 aqueous media, *J Chromatogr A*. 1217 (2010) 7303–7310.

- 643 doi:10.1016/j.chroma.2010.09.048.
- 644 [18] S.M. Ahmad, C. Almeida, N.R. Neng, J.M.F. Nogueira, Bar adsorptive
645 microextraction (BA μ E) coated with mixed sorbent phases-Enhanced
646 selectivity for the determination of non-steroidal anti-inflammatory drugs in
647 real matrices in combination with capillary electrophoresis., J.
648 Chromatogr. B. Analyt. Technol. Biomed. Life Sci. 1008 (2016) 115–24.
649 doi:10.1016/j.jchromb.2015.11.018.
- 650 [19] C. Almeida, J.M.F. Nogueira, Determination of steroid sex hormones in
651 real matrices by bar adsorptive microextraction (BA μ E)., Talanta. 136
652 (2015) 145–54. doi:10.1016/j.talanta.2014.11.013.
- 653 [20] N. Fechner, S.A. Wohlgemuth, P. Jäker, M. Antonietti, Salt and sugar:
654 Direct synthesis of high surface area carbon materials at low
655 temperatures via hydrothermal carbonization of glucose under
656 hypersaline conditions, J. Mater. Chem. A. 1 (2013) 9418–9421.
657 doi:10.1039/c3ta10674h.
- 658 [21] ChemAxon, Marvin 6.2.2, (2014). <http://www.chemaxon.com>.
- 659 [22] A.S. Mestre, C. Freire, J. Pires, A.P. Carvalho, M.L. Pinto, High
660 performance microspherical activated carbons for methane storage and
661 landfill gas or biogas upgrade, J. Mater. Chem. A. 2 (2014) 15337–15344.
662 doi:10.1039/c4ta03242j.
- 663 [23] A.S. Mestre, E. Tyszko, M.A. Andrade, M. Galhetas, C. Freire, A.P.
664 Carvalho, Sustainable activated carbons prepared from a sucrose-derived
665 hydrochar: Remarkable adsorbents for pharmaceutical compounds, RSC
666 Adv. 5 (2015) 19696–19707. doi:10.1039/c4ra14495c.

- 667 [24] T.A.G. Duarte, A.P. Carvalho, L.M.D.R.S. Martins, Styrene oxidation
668 catalyzed by copper(II) C-scorpionates in homogenous medium and
669 immobilized on sucrose derived hydrochars, Catal. Today. (2019) in
670 press. doi:10.1016/j.cattod.2019.04.044.
- 671 [25] R. Demir-Cakan, N. Baccile, M. Antonietti, M.M. Titirici, Carboxylate-rich
672 carbonaceous materials via one-step hydrothermal carbonization of
673 glucose in the presence of acrylic acid, Chem. Mater. 21 (2009) 484–490.
674 doi:10.1021/cm802141h.
- 675 [26] A.S. Mestre, R.A. Pires, I. Aroso, E.M. Fernandes, M.L. Pinto, R.L. Reis,
676 et al., Activated carbons prepared from industrial pre-treated cork:
677 Sustainable adsorbents for pharmaceutical compounds removal, Chem.
678 Eng. J. 253 (2014) 408–417. doi:10.1016/j.cej.2014.05.051.
- 679 [27] J. Rouquerol, P. Llewellyn, F. Rouquerol, Is the bet equation applicable to
680 microporous adsorbents?, 2991 (2007) 49–56. doi:10.1016/S0167-
681 2991(07)80008-5.
- 682 [28] M. Thommes, K. Kaneko, A. V. Neimark, J.P. Olivier, F. Rodriguez-
683 Reinoso, J. Rouquerol, et al., Physisorption of gases, with special
684 reference to the evaluation of surface area and pore size distribution
685 (IUPAC Technical Report), Pure Appl. Chem. 87 (2015) 1051–1069.
686 doi:10.1515/pac-2014-1117.
- 687 [29] F. Rouquerol, J. Rouquerol, K.S.W.S.W.K. Sing, P. Llewellyn, G. Maurin,
688 J. Rouquerol, et al., Adsorption by Powders and Porous Solids, 2014.
689 doi:10.1016/B978-0-08-097035-6.00012-7.
- 690 [30] F. Rodriguez-Reinoso, J.M. Martin-Martinez, C. Prado-Burguete, B.

- 691 McEnaney, A standard adsorption isotherm for the characterization of
692 activated carbons, *J. Phys. Chem.* 91 (1987) 515–516.
693 doi:10.1021/j100287a006.
- 694 [31] J. Jagiello, J.P. Olivier, 2D-NLDFT adsorption models for carbon slit-
695 shaped pores with surface energetical heterogeneity and geometrical
696 corrugation, *Carbon* 55 (2013) 70–80. doi:10.1016/j.carbon.2012.12.011.
- 697 [32] J.S. Noh, J.A. Schwarz, Estimation of the point of zero charge of simple
698 oxides by mass titration, *J. Colloid Interface Sci.* 130 (1989) 157–164.
699 doi:10.1016/0021-9797(89)90086-6.
- 700 [33] C. Almeida, R. Strzelczyk, J.M. Nogueira, Improvements on bar
701 adsorptive microextraction (BA_{mu}E) technique--application for the
702 determination of insecticide repellents in environmental water matrices,
703 *Talanta*. 120 (2014) 126–134. doi:10.1016/j.talanta.2013.11.031.
- 704 [34] N.R. Neng, A.S. Mestre, A.P. Carvalho, J.M. Nogueira, Cork-based
705 activated carbons as supported adsorbent materials for trace level
706 analysis of ibuprofen and clofibrac acid in environmental and biological
707 matrices, *J Chromatogr A*. 1218 (2011) 6263–6270.
708 doi:10.1016/j.chroma.2011.07.025.
- 709 [35] S. Comtois-Marotte, T. Chappuis, S. Vo Duy, N. Gilbert, A. Lajeunesse,
710 S. Taktek, et al., Analysis of emerging contaminants in water and solid
711 samples using high resolution mass spectrometry with a Q Exactive
712 orbital ion trap and estrogenic activity with YES-assay, *Chemosphere*.
713 166 (2017) 400–411. doi:10.1016/j.chemosphere.2016.09.077.
- 714 [36] V.K. Balakrishnan, K.A. Terry, J. Toito, Determination of sulfonamide

- 715 antibiotics in wastewater: A comparison of solid phase microextraction
716 and solid phase extraction methods, *J. Chromatogr. A.* 1131 (2006) 1–10.
717 doi:10.1016/j.chroma.2006.07.011.
- 718 [37] F.H. Salami, M.E.C. Queiroz, Microextraction in packed sorbent for
719 analysis of sulfonamides in poultry litter wastewater samples by liquid
720 chromatography and spectrophotometric detection, *J. Liq. Chromatogr.*
721 *Relat. Technol.* 37 (2014) 2377–2388.
722 doi:10.1080/10826076.2013.836710.
- 723 [38] N. Gilart, N. Miralles, R.M. Marce, F. Borrull, N. Fontanals, Novel coatings
724 for stir bar sorptive extraction to determine pharmaceuticals and personal
725 care products in environmental waters by liquid chromatography and
726 tandem mass spectrometry, *Anal Chim Acta.* 774 (2013) 51–60.
727 doi:10.1016/j.aca.2013.03.010.
- 728 [39] N. AL-Hadithi, B. Saad, M. Grote, A solid bar microextraction method for
729 the liquid chromatographic determination of trace diclofenac, ibuprofen
730 and carbamazepine in river water, *Microchim. Acta.* 172 (2011) 31–37.
731 doi:10.1007/s00604-010-0463-5.
- 732 [40] S. V Duy, P.B. Fayad, B. Barbeau, M. Prevost, S. Sauve, Using a novel
733 sol-gel stir bar sorptive extraction method for the analysis of steroid
734 hormones in water by laser diode thermal desorption/atmospheric
735 chemical ionization tandem mass spectrometry, *Talanta.* 101 (2012) 337–
736 345. doi:10.1016/j.talanta.2012.09.036.
- 737 [41] C. V Antoniou, E.E. Koukouraki, E. Diamadopoulos, Analysis of Selected
738 Pharmaceutical Compounds and Endocrine Disruptors in Municipal

739 Wastewater Using Solid-Phase Microextraction and Gas
740 Chromatography, *Water Environ. Res.* 81 (2009) 664–669.
741 doi:10.2175/106143008X390834.

742 [42] M.G. Pintado-Herrera, E. González-Mazo, P.A. Lara-Martín,
743 Environmentally friendly analysis of emerging contaminants by
744 pressurized hot water extraction-stir bar sorptive extraction-derivatization
745 and gas chromatography-mass spectrometry, *Anal. Bioanal. Chem.* 405
746 (2013) 401–411. doi:10.1007/s00216-012-6453-1.

747 [43] A.R.M. Silva, F.C.M. Portugal, J.M.F. Nogueira, Advances in stir bar
748 sorptive extraction for the determination of acidic pharmaceuticals in
749 environmental water matrices Comparison between polyurethane and
750 polydimethylsiloxane polymeric phases., *J. Chromatogr. A.* 1209 (2008)
751 10–6. doi:10.1016/j.chroma.2008.08.103.

752 [44] A. Giordano, J. Vásquez, M. Retamal, L. Ascar, Ibuprofen,
753 carbamazepine and β -estradiol determination using thin-film
754 microextraction and gas chromatography-mass spectrometry, *J. Braz.*
755 *Chem. Soc.* 27 (2016) 1744–1749. doi:10.5935/0103-5053.20160055.

756 [45] A.R.M. Silva, F.C.M. Portugal, J.M.F. Nogueira, Advances in stir bar
757 sorptive extraction for the determination of acidic pharmaceuticals in
758 environmental water matrices Comparison between polyurethane and
759 polydimethylsiloxane polymeric phases, *J. Chromatogr. A.* 1209 (2008)
760 10–16. doi:10.1016/j.chroma.2008.08.103.

761 [46] M.G. Pintado-Herrera, E. González-Mazo, P.A. Lara-Martín,
762 Environmentally friendly analysis of emerging contaminants by

763 pressurized hot water extraction-stir bar sorptive extraction-derivatization
764 and gas chromatography-mass spectrometry, *Anal. Bioanal. Chem.* 405
765 (2013) 401–411. doi:10.1007/s00216-012-6453-1.

766 [47] S.M. Ahmad, C. Almeida, N.R. Neng, J.M.F. Nogueira, Application of bar
767 adsorptive microextraction (BA μ E) for anti-doping control screening of
768 anabolic steroids in urine matrices, *J Chromatogr B Anal. Technol Biomed*
769 *Life Sci.* 969C (2014) 35–41. doi:10.1016/j.jchromb.2014.07.040.

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772