Carbon-Based Sorbent Coatings for the Determination of Pharmaceutical Compounds by Bar Adsorptive Microextraction

Samir Ahmad, Ana Mestre, Nuno Neng, Conchi Maria Concepcion Ovin Ania, Ana Carvalho, José Nogueira

► To cite this version:

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

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

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

Carbon-based sorbent coatings for the determination of pharmaceutical compounds by bar adsorptive microextraction

Samir M. Ahmad¹, Ana S. Mestre^{1*}, Nuno R. Neng¹, Conchi O. Ania², Ana P. Carvalho¹, José M.F. Nogueira^{1*}

¹*Centro de Química e Bioquímica and Centro de Química Estrutural, Faculdade de Ciências, Universidade de Lisboa, 1749-016 Lisboa, Portugal*

²*CNRS, CEMHTI UPR3079, University of Orléans, F-45071 Orléans, France*

*Corresponding authors

E-mail address: asmestre@fc.ul.pt (Ana S. Mestre) and nogueira@fc.ul.pt (José M.F. Nogueira), Centro de Química e Bioquímica and Centro de Química Estrutural, Faculdade de Ciências, Universidade de Lisboa, Campo Grande Ed. C8, 1749-016, Lisboa, Portugal. Tel.: +351 217500899; Fax: +351 217500088.

Abstract

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

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

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.

1. Introduction

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

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

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

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

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

2. Experimental

2.1 Reagents

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

99 %) was acquired from Merck (Darmstadt, Germany), and zinc chloride (ZnCl,
98 %) was acquired from Acros Organics (Geel, Belgium). Carbamazepine
(99.0 %), triclosan (97.0 %), diclofenac sodium salt (98.0 %) 17- β -estradiol
(98.0 %), estrone (99.0 %), gemfibrozil (98.5 %), mefenamic acid (98.5 %),
clofibric acid (98.0 %), sulfamethoxazole (98.0 %) and potassium carbonate
(K₂CO₃, 99 %) were purchased from Sigma-Aldrich (Steinheim, Germany). 17-
 α -ethinyloestradiol (98.0 %) was purchased from Riedel-de-Haën (Seelze,
Germany). Figure 1 depicts the chemical structures, as well as the pK_a and log
 K_{OW} values of the PhCs studied. The solvents used were HPLC-grade
methanol (MeOH, 99.8 %), and acetonitrile (ACN, 99.8 %), obtained from Carlo
Erba (Arese, Italy). Sodium chloride (NaCl, 99.5 %) was purchased from Merck
Millipore (Darmstadt, Germany). Sodium hydroxide (NaOH, 98.0 %) pellets
were obtained from AnalaR (BDH chemicals, Lutterworth, U.K.). Hydrochloric
acid (HCl, 37 %), acetic acid (99.5 %) and potassium hydroxide (KOH, 85 %)
were purchased from Panreac (Barcelona, Spain). The acrylic acid (AA, $\geq$ 99 %) was
purchased from Merck (Hohenbrunn, Germany). All chemicals were used
without further purification. Ultra-pure water was obtained from the Milli-Q water
purification systems (Merck Millipore, Darmstadt, Germany).

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

2.2 Carbon materials synthesis and characterization

The hydrochars were prepared by hydrothermal carbonization of carbohydrates: 15 cm³ of 1.5 mol L⁻¹ glucose or sucrose solutions introduced in an autoclave and heated at 190 °C during 5 h [22,23]. These samples are labeled as HG or HS according with the carbohydrate precursor (glucose and sucrose, respectively). Modified sucrose-derived hydrochars were prepared by a similar protocol but adding acrylic acid (e.g., 7, 14 or 27 wt.%) to the starting sucrose aqueous solution [24,25]. The modified hydrochars were labeled as HSAAx, where x stands for the amount of acrylic acid. The sucrose-derived hydrochar was chemically activated as indicated elsewhere [22,23]. Briefly, superactivated carbons HS/H800 and HS/C800 were prepared by activation of 1 g of sucrose-derived hydrochar (HS) with 4 g of, respectively, KOH and K₂CO₃ during 1 h at 800 °C.

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

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

Table 1 – Summary of the main textural and surface properties of the carbon materials used as coatings (apparent surface area – A_{BET} , micropore volume – V_{micro} (pores with widths < 2 nm), mesopore volume – V_{meso} (pores with widths between 2 and 50 nm), pH at the point of zero 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	$\text{pH}_{\text{PZC}} \approx 4$

^a Synthesis and characterization reported in [26]

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

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

^d Synthesis and characterization reported in [24]

2.3 Characterization of the carbon materials

The textural properties of the porous hydrochars and commercial PACs were characterized by N_2 adsorption isotherms at -196°C in an automatic volumetric apparatus from Micromeritics (ASAP 2010). Before N_2 adsorption-

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

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

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

2.4 Standard preparation and water samples

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

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

2.5 BAµE-µLD methodology

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

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

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

2.6 Instrumental set-up

HPLC-DAD analysis were carried out on a benchtop Agilent 1100 series LC 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

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

3. Results and discussion

3.1 Carbon material selectivity as sorbent coating

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

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

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.

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.

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

Figure 3 – SEM images of the nanoporous hydrochars.

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.

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).

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

3.3 Performance comparison with other microextraction techniques

A comparison of the performance of the BA μ E(npHS)- μ LD/HPLC-DAD methodology and other established static-based microextraction techniques is shown in table 3 [36–44]. As it can be observed, the developed methodology using BA μ E devices coated with sucrose-based hydrochar presents similar or better recovery yields than other miniaturized enrichment techniques, e.g., SBSE coated with PDMS, PA or EG [38] or SBME coated with C8 polymer [39] for the extraction of carbamazepine; TFME coated with PDMS [44] for the extraction of 17- β -estradiol; SBSE coated with PDMS [42] for the extraction of clofibric acid; SBSE coated with PU [45] for the extraction of diclofenac, gemfibrozil or mefenamic acid. Additionally, the BA μ E(npHS)- μ LD/HPLC-DAD methodology sensitivity is similar when compared to analogue instrumental 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)		82.4	2.0	This work
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)		73.1	2.0	This work
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
	SBSE(PDMS)	GC-MS)	29.0	0.001	[46]
	SBSE(PDMS)		71.3	1.5	
Mefenamic acid	SBSE(PU)	HPLC-DAD	48.4	1.3	[45]
	BA μ E(npHS)		61.7	0.5	This work
	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]
Triclosan	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;

515

516

3.4 Application to environmental water matrices

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

Figure 7 – Chromatograms obtained from assays performed on an ultrapure water sample spiked at the 16.0 µg L⁻¹ level (a) and a non-spiked WWTP sample (b), performed and by BAµE(npHS)-µLD/HPLC-DAD, under optimized experimental conditions.

4. Concluding remarks

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

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

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

Conflicts of Interest

The authors declare no conflict of interest.

Acknowledgments

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

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

References

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

1364. doi:10.1007/s00216-011-5515-0.

[12] C. Almeida, J.M. Nogueira, Determination of trace levels of parabens in real matrices by bar adsorptive microextraction using selective sorbent phases, *J Chromatogr A*. 1348 (2014) 17–26. doi:10.1016/j.chroma.2014.04.057.

[13] T.S. Oliveira, M. Murphy, N. Mendola, V. Wong, D. Carlson, L. Waring, Characterization of Pharmaceuticals and Personal Care products in hospital effluent and waste water influent/effluent by direct-injection LC-MS-MS, *Sci. Total Environ.* 518 (2015) 459–478. doi:10.1016/j.scitotenv.2015.02.104.

[14] J.M.F. Nogueira, Stir-bar sorptive extraction – 15 years making sample preparation more environment friendly, *TrAC Trends Anal. Chem.* 71 (2015) 214–223. doi:http://dx.doi.org/10.1016/j.trac.2015.05.002.

[15] J.M. Nogueira, Novel sorption-based methodologies for static microextraction analysis: A review on SBSE and related techniques, *Anal Chim Acta*. 757 (2012) 1–10. doi:10.1016/j.aca.2012.10.033.

[16] F. Wang, J. Zheng, J. Qiu, S. Liu, G. Chen, Y. Tong, et al., In situ hydrothermally grown TiO₂@C core-shell nanowire coating for highly sensitive solid phase microextraction of polycyclic aromatic hydrocarbons, *ACS Appl. Mater. Interfaces*. 9 (2017) 1840–1846. doi:10.1021/acsami.6b14748.

[17] N.R. Neng, A.R. Silva, J.M. Nogueira, Adsorptive micro-extraction techniques--novel analytical tools for trace levels of polar solutes in aqueous media, *J Chromatogr A*. 1217 (2010) 7303–7310.

doi:10.1016/j.chroma.2010.09.048.

[18] S.M. Ahmad, C. Almeida, N.R. Neng, J.M.F. Nogueira, Bar adsorptive microextraction (BA μ E) coated with mixed sorbent phases-Enhanced selectivity for the determination of non-steroidal anti-inflammatory drugs in real matrices in combination with capillary electrophoresis., J. Chromatogr. B. Analyt. Technol. Biomed. Life Sci. 1008 (2016) 115–24. doi:10.1016/j.jchromb.2015.11.018.

[19] C. Almeida, J.M.F. Nogueira, Determination of steroid sex hormones in real matrices by bar adsorptive microextraction (BA μ E)., Talanta. 136 (2015) 145–54. doi:10.1016/j.talanta.2014.11.013.

[20] N. Fechner, S.A. Wohlgemuth, P. Jäker, M. Antonietti, Salt and sugar: Direct synthesis of high surface area carbon materials at low temperatures via hydrothermal carbonization of glucose under hypersaline conditions, J. Mater. Chem. A. 1 (2013) 9418–9421. doi:10.1039/c3ta10674h.

[21] ChemAxon, Marvin 6.2.2, (2014). <http://www.chemaxon.com>.

[22] A.S. Mestre, C. Freire, J. Pires, A.P. Carvalho, M.L. Pinto, High performance microspherical activated carbons for methane storage and landfill gas or biogas upgrade, J. Mater. Chem. A. 2 (2014) 15337–15344. doi:10.1039/c4ta03242j.

[23] A.S. Mestre, E. Tyszkowski, M.A. Andrade, M. Galheta, C. Freire, A.P. Carvalho, Sustainable activated carbons prepared from a sucrose-derived hydrochar: Remarkable adsorbents for pharmaceutical compounds, RSC 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.

McEnaney, A standard adsorption isotherm for the characterization of activated carbons, *J. Phys. Chem.* 91 (1987) 515–516. doi:10.1021/j100287a006.

[31] J. Jagiello, J.P. Olivier, 2D-NLDFT adsorption models for carbon slit-shaped pores with surface energetical heterogeneity and geometrical corrugation, *Carbon* 55 (2013) 70–80. doi:10.1016/j.carbon.2012.12.011.

[32] J.S. Noh, J.A. Schwarz, Estimation of the point of zero charge of simple oxides by mass titration, *J. Colloid Interface Sci.* 130 (1989) 157–164. doi:10.1016/0021-9797(89)90086-6.

[33] C. Almeida, R. Strzelczyk, J.M. Nogueira, Improvements on bar adsorptive microextraction (BA_{mu}E) technique--application for the determination of insecticide repellents in environmental water matrices, *Talanta*. 120 (2014) 126–134. doi:10.1016/j.talanta.2013.11.031.

[34] N.R. Neng, A.S. Mestre, A.P. Carvalho, J.M. Nogueira, Cork-based activated carbons as supported adsorbent materials for trace level analysis of ibuprofen and clofibric acid in environmental and biological matrices, *J Chromatogr A*. 1218 (2011) 6263–6270. doi:10.1016/j.chroma.2011.07.025.

[35] S. Comtois-Marotte, T. Chappuis, S. Vo Duy, N. Gilbert, A. Lajeunesse, S. Taktek, et al., Analysis of emerging contaminants in water and solid samples using high resolution mass spectrometry with a Q Exactive orbital ion trap and estrogenic activity with YES-assay, *Chemosphere*. 166 (2017) 400–411. doi:10.1016/j.chemosphere.2016.09.077.

[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. Vázquez, 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

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

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