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Abstract

The electrochemical behavior of some of the most relevant endocrine-disrupting phenols using unmodified carbon screen-printed electrodes (SPEs) is described for the first time. Experiments were made to assess the electrochemical behavior of phenol (PHOH), pentachlorophenol (PCP), 4-*tert* octylphenol (OP) and bisphenol A (BPA) and their determination in the most favorable conditions, using voltammetric methods such as cyclic voltammetry (CV), linear sweep voltammetry (LSV) and square wave voltammetry (SWV) in Britton Robinson (BR) buffer. Further, the usefulness of the electrochemical approach was validated with real samples from a local river and was compared to commercial Phenols Test Kit, which is commonly used for on-site screening in industrial streams and wastewaters. Finally, the approach was compared with a lab-bench standard method using real samples, i.e., high-performance liquid chromatography with a photodiode array detector (HPLC-DAD).

Keywords: endocrine-disrupting phenolic compounds, simultaneous voltammetric detection, anodic pretreatment, spiked river samples, HPLC-DAD accuracy evaluation.

1. Introduction

Phenols are organic compounds classified as priority pollutants due to their impact on the ecosystem, e.g. chlorophenols, alkylphenols and bisphenols [1,2]. Phenolic compounds are commonly found in the environment from either natural [3–5] or synthetic sources [6,7]. Most hazardous synthetic phenols penetrate the ecosystem due to their wide use in disinfectants, dyes, polymers, drugs, explosives, pesticides, and other organic substances [8]. For instance, the European production of phenol (PHOH) reached 1.8M tons in 2020, almost half of which was converted into phenolic resin and quart of which was converted into plastic precursor bisphenol A (BPA), accounting for over a quarter of the global phenol market [9]. Moreover, the continuous release of these chemicals can lead to a prominent accumulation in the environment (such as in live organisms, i.e. fat tissue) [10]. Hence, drainage of municipal and industrial sewage to surface water has become a serious environmental issue [11,12]. Phenol concentration levels fluctuate from one place and/or country to another. The highest concentrations of phenols are observed near the outlets of industrial streams and wastewaters. As an example, the concentration of BPA [13], pentachlorophenol (PCP) [14] and octylphenol (OP) [15] detected in European rivers is between 4 – 92 nM, 0 – 4 nM and 0.02 – 63.01 nM, respectively. The cytotoxicity of phenols is determined by their hydrophobicity and the formation of phenoxyl radicals [16], with higher values upon the increasing degree of chlorination [17]. Some phenols are categorized as endocrine-disrupting chemicals (EDCs) exhibiting estrogenic properties such as BPA, OP, or nonylphenol [18–20]. Several studies have verified how the phenolic EDCs affect and damage the endocrine, developmental, reproductive, neurological, cardiovascular, metabolic and/or immune systems [21,22]. Hence, exposure to these chemicals in an early life stage leads to an increased prevalence of numerous diseases including asthma, learning and behavior problems, early puberty, infertility, cancer, and obesity [23–25]. Surprisingly, to date, no strict agreements neither legal concentration limits exist for the control and executive regulation of EDCs [12,26,27]. Therefore, there is an undoubted need to assess the concentration levels of phenolic EDCs in wastewaters in order to control, better understand and minimize the impact of EDCs on ecosystems and human health [28].

Traditionally, phenols have been quantified with high-performance liquid chromatography (HPLC) and gas chromatography (GC) coupled with detection

techniques such as ultraviolet-visible spectroscopy (UV/VIS), photodiode array detector (DAD) or mass spectrometry (MS) among others [29–31]. These techniques have important disadvantages being expensive, time-consuming (hours) and requiring derivatization steps (e.g., GC), preconcentration steps (e.g. solid-phase or liquid-liquid extraction) and trained personnel, being not suitable for on-site testing. On the other hand, commercially available tests (e.g. phenols test kit of Hanna Instruments®, HACH® or CHEMetrics™) can quantify phenols in water based on colorimetric or spectrophotometric readout [32–34]. Albeit the kits are easy to use, fast, inexpensive, and portable, they still exhibit some drawbacks in terms of selectivity (determining only the total phenol amount) and sensitivity (i.e., 0.02 mg L^{-1} Hanna Instruments® https://www.hannainstruments.be/nl/).

In the last years, electrochemical detection methods have been used to identify harmful phenols in aqueous solutions (see **Table 1**) mainly because of their outstanding advantages such as multiplex and miniaturization options, selectivity, sensitivity, cost-effectiveness, rapid response, and portability [35]. The specific electrochemical fingerprint (EF) of the electroactive phenolic compounds allows their selective detection [36]. Thus, the feasibility of the voltammetric identification has been demonstrated by using modified glassy carbon electrodes (GCE), which results in nanomolar range limits of detection (LOD) for BPA, catechol, p-cresol and p-nitrophenol [37,38]. However, this type of GCE cannot be integrated into a portable configuration. Notably, in the last decade, several modified screen-printed electrodes (SPEs) have been reported for BPA detection (one of the most common phenolic EDCs) exhibiting higher sensitivity, reproducibility and stability. Nevertheless, these approaches have a common drawback caused by the electro-polymerization of phenols into the electrode surface, whereby polymeric non-soluble substances are formed due to the coupling of phenoxyl radicals [39,40]. This causes electrode fouling or passivation by adsorption of these substances, which blocks and deactivates the electrode surface of the SPE. This issue could be avoided by single-use of SPEs as the example recently reported by Wang *et al.* for BPA detection based on an electrochemical miniaturized device [41], or modifying the SPEs with carbonaceous nanomaterials [42–45]. At the same time, several enzymatic biosensors have also been proposed to detect phenolic compounds at lower LOD (nM range) [46–49]. Nonetheless, in the case of enzymes different factors must be considered such as their

chemical and thermal instability, reproducibility and the immobilization process, especially when dealing with industrial wastewater samples. To overcome these drawbacks, a novel bio-inspired photoelectrochemical sensor for phenol detection was recently developed by this group [50]. The detection mechanism is based on a robust, perfluorinated molecular photosensitizer, that mimics the enzymatic reaction providing outstanding sensitivity and limit of detections in the nM to pM level [51]. Despite the last advances, the literature lacks an in-depth understanding of the EFs of a broad range of phenolic compounds.

The electrochemical behavior of PHOH and three different hazardous derivatives (i.e., pentachlorophenol (PCP), OP and BPA) using carbon SPEs is presented. The chemical structure and main features of the selected phenols are specified in **Table S1** in the Supplementary Material (SM). Firstly, the electrochemical reversibility and mass-transport mechanism were investigated by CV and LSV, respectively, and the EFs of four phenols were studied in Britton Robinson buffer by SWV in the entire pH range (2 – 12). Secondly, the stability of the phenols at pH 12 over time (up to 5 hours) was measured under different storage conditions of the samples: *i)* in ice and dark, *ii)* at room temperature and in dark, and *iii)* at room temperature and daylight. Subsequently, calibration curves of all phenols were carried out (pH 12 BR buffer) in the concentration range from 1 to 50 µM, N=3. Afterward, the electrochemical oxidation of binary and complex mixtures of the four phenols was studied. Furthermore, the electrochemical approach is compared to commercial phenols tests which are difficult to interpret (i.e., colorimetric) and lack selectivity (without being able to distinguish different phenols). Finally, the accuracy of the optimized approach was successfully evaluated for the PHOH, OP, PCP and BPA identification in real samples from a local river (Scheldt, Belgium) against a lab-bench standard method (HPLC-DAD). Altogether, the insights gained from this study will be of assistance towards the development of a fast accurate, selective and sensitive electrochemical sensing approach for the detection of phenolic EDCs in industrial wastewaters and process streams.

Table 1. Summary of the electrochemical sensors for hazardous phenols present in aqueous solutions over the past five years.

Detection method	Phenol type	Working electrode	Linear range (µM)	Sensitivity (µA µM^{-1})	LOD (nM)	Real sample	Ref

CV, LSV, DPV	2,4,6-trichlorophenol PCP	PRhB/GO/MWCNTs/GCE	0.004 – 0.1 & 0.1 – 100 0.002 – 0.1 & 0.1 – 90	26.26 & 0.22 36.25 & 0.23	0.8 0.5	–	[52]
CV	PCP, 2,3,7,8-tetrachlorodibenzo-p-dioxin	Pt/ZnO/AChE/chitosan bioelectrode	0.001 – 0.02	–	0.5 0.8	guar gum samples	[53]
CV	BPA	Lac/Ag–ZnONPs/MWCNTs/C-SPE	0.5 – 2.99	–	6.0	disposal water	[54]
DPV	OP	NiO-Ni-GCN nanocomposites modified electrode	0.01 – 1 & 1 – 50	0.20 & 0.03	3.3	lake water	[55]
CV, DPV	catechol, p-cresol, p-nitrophenol	SWCN-GCE	0.1 – 2	135.08 94.90 110.38	2.3 3.7 7.7	tap water	[37]
CV, AMP	BPA	MWCNT-GCE	0.004 – 0.1	3.5	3.5	water contained in plastic and baby bottles	[38]
CV, SWV	BPA	CoF-MWCNTs-SPE	0.5 – 50 & 0.02 – 1.5	0.005	200.0 10.0	tap water, drinking water, mineral water	[44]
CV, LSV	BPA	Disposable Au-film electrode	50 – 1000	–	131.4	lake and plastic water	[41]
AMP	catechol, dopamine, octopamine, pyrogallol, 3,4-dihydroxy-L-phenylalanine	HRP-SPCE, HRP-MWCNT-SPCE, HRP-SWCNT-SPCE	0.5–500 0.5–250 1–250	5.1* 4.5* 1.6*	110.2 640.2 3341 50.10 980.7	–	[46]
CV, SWV	PHOH, PCP, OP, BPA	Unmodified SPE	5 – 50	0.034 0.052 0.036 0.053	930 915 331 176	Scheldt river	This work

* Sensitivity in $\mu A\ \mu M^{-1}\ cm^{-2}$.

AMP: Amperometry CV: cyclic voltammetry, LSV: linear sweep voltammetry, DPV: differential pulse voltammetry, PCP: pentachlorophenol, PRhB: poly(Rhodamine B), GO: graphene oxide, MWCNTs: Multiwall carbon nanotubes, GCE: glassy carbon electrode, Pt: platinum, ZnO: zinc oxide, AChE: acetylcholinesterase, BPA: bisphenol A, Lac: Laccase, Ag– ZnONPs: silver doped zinc oxide nanoparticles, C-SPE: carbon-screen-printed electrodes, OP: octylphenol, NiO-Ni-GCN: Nickel Oxide and Nickel Co-doped Graphitic Carbon Nitride, SWCN-GCE: single-wall carbon nanotube-glassy carbon electrode, CoF: cobalt ferrites, Au-film: gold-film, HRP-SPCE: horseradish peroxidase screen-printed carbon electrode, PHOH: phenol.

2. Experimental

2.1. Reagents

Phenol and 4-*tert* octylphenol both with purity 99% were obtained from J&K Scientific GmbH (Germany). Pentachlorophenol and bisphenol A with purity 97% and 99% respectively, were acquired from Sigma-Aldrich-Chemie GmbH & Co KG (Germany).

Ethanol with a purity of 99.8% was purchased from Acros Organics™ (Geel, Belgium). All analytical grade salts of potassium chloride, sodium phosphate, sodium acetate, sodium borate and potassium hydroxide were obtained from Sigma-Aldrich (Overijse, Belgium). All phenols stocks were prepared in ethanol, in a concentration of 1 mM (for the electrochemical analysis) and 10 mM (for the Scheldt spiked analysis). Electrochemical measurements were performed in Britton Robinson buffer at 20 mM ionic strength with supporting electrolyte 100 mM KCl, by applying 80 µL of the buffer onto the SPE. All aqueous solutions were prepared in ultrapure water obtained from 18.2 MΩ cm^{-1} doubly deionized water (Sartorius, Arium® Ultrapure Water Systems). Adjustment of the pH was performed using a 100 mM KOH solution.

2.2. Instrumentation and apparatus

All CV, LSV and SWV measurements were performed using a MultiPalmSens4 or EmStat Blue potentiostats (PalmSens, The Netherlands) with PSTrace/MultiTrace or PStouch software, respectively. Disposable ItalSens IS-C graphite screen-printed electrodes (SPE) (provided by PalmSens, Utrecht, the Netherlands), containing a graphite working electrode (Ø = 3 mm), a carbon counter electrode, and a silver reference electrode were used for all measurements. The CV parameters used were a potential range of -0.5 V to 1.1 V (3 scans), 5 mV step potential and 50 mV s^{-1} scan-rate. The LSV parameters used were potential range of 0 V to 1 V, 5 mV step potential and scan-rate range from 5 to 500 mV s^{-1}. The optimal SWV parameters used were a potential range of -0.3 V to 1.1 V, frequency 10 Hz, 25 mV amplitude and 5 mV step potential. All the voltammograms are background corrected using the “moving average iterative background correction” (peak width = 1) tool in the PSTrace software. During the anodic pretreatment (for the degradation of phenol over time) the applied potential was 0.9 V. The LOD of the phenols was determined by the ratio of 3 times the standard deviation of the blank over the slope of the calibration curve. Whereas the limit of quantification (LOQ) was calculated by the ratio of 10 times the standard deviation over the slope of the calibration curve.

The pH was measured using a Metrohm 913 pH-meter from Metrohm AG (Herisau, Switzerland) connected to a HI-1131 glass bodied pH electrode from Hanna Instruments™ (Bedfordshire, United Kingdom). HI3864 Phenols Test Kit was purchased from Hanna Instruments™ (Temse, Belgium).

The HPLC-DAD experiments were performed with a Shimadzu HPLC system ('s-Hertogenbosch, The Netherlands) equipped with a Prominence LC-20AT connected to a DGU-20A5R degassing unit with a CBM-20A integrator, a SIL-20AC HT cooled autosampler (with a 0.1 - 100 µL injection volume range and up to 35 MPa operating pressure) and a SPD-M20A photodiode array detector with temperature-controlled flow cell, wavelength range 190-800 nm, W-halogen- and D2-lamp, 4 channel analogue outlet, includes standard cell, 10 mm path, 10 µL. Phenol samples (25 µL injection volume and 1 mL min^{-1} flow rate) were separated by reversed phase HPLC-DAD on a 100 x 4.6 mm id, 2.6 µm particle size, 100 Å, Kinetex C-18 LC column from Phenomenex (Utrecht, The Netherlands) and eluted with mobile phase A consisted of 0.1% phosphoric acid in ultrapure water (v/v) and mobile phase B consisted of 0.1% phosphoric acid in acetonitrile/ultrapure water (95/5, v/v). The gradient started at 0 min at 20% B, from 0 to 3 min: 20% B to 100% B, from 3 to 5 min: 100% B, from 5 to 5.1 min: 20% B and from 5.1 until 12 min 20% B to re-equilibrate the column for the next analysis. The phenols were detected at selected wavelength of 220 nm. All measurements were done in triplicate. All data analysis were done mathematically with the software LabSolutions.

3. Results and Discussion

3.1. Exploring the electrochemical behavior of phenols: reversibility study and mass-transfer mechanism

The electrochemical reversibility of redox processes of PHOH, PCP, OP and BPA was explored using CV. The cyclic voltammograms (three scans) at 100 µM concentration of all phenols in pH 12 BR buffer on SPEs are shown in **Fig. 1**. Blank results are displayed in the SM (**Fig. S1**). A sharp single anodic peak was noted for all phenols after the first CV scan, which is consistent with the oxidation peak of the corresponding phenol. The oxidation peak potentials (E_p) observed (PHOH at 0.44 V, PCP at 0.60 V, OP at 0.18 V and BPA at 0.26 V) are characteristic of the analyte at the specific pH 12. None of the phenols displayed a cathodic/reduction peak in the reverse potential scan, which reveals the irreversible nature of the ongoing processes at the bare SPE. Moreover, fouling of the generated phenoxyl radicals in the first oxidation step influences the electrochemical signal of the next cycle scans as expected [39,40]. Therefore, the oxidation peak decreases in subsequent scans since less electrode surface area is available due to the adsorption of phenoxyl radicals and/or oxidation

products on the electrode surface, as can be seen in **Fig. 1**. To reveal the irreversibility of the adsorption process, the same experiment was performed rinsing the SPE and drop-casting a fresh phenol before each scan, results shown in **Fig. S2A-D**. A small decrease in current intensity of the second and third scans are displayed for PHOH (**Fig. S2A**) and PCP (**Fig. S2B**), this indicates the irreversibility of the phenoxyl radicals and/or oxidation products after rinsing the SPE. Besides, a clear decrease in the second and third scans is observed for BPA (**Fig. S2D**), probably due to the fouling, as previously described in **section 1**. On the other hand, an increase of the signal during the second and third scans is shown for OP (**Fig. S2C**), being in concordance with the adsorption mechanism observed during the mass-transfer study (see below).

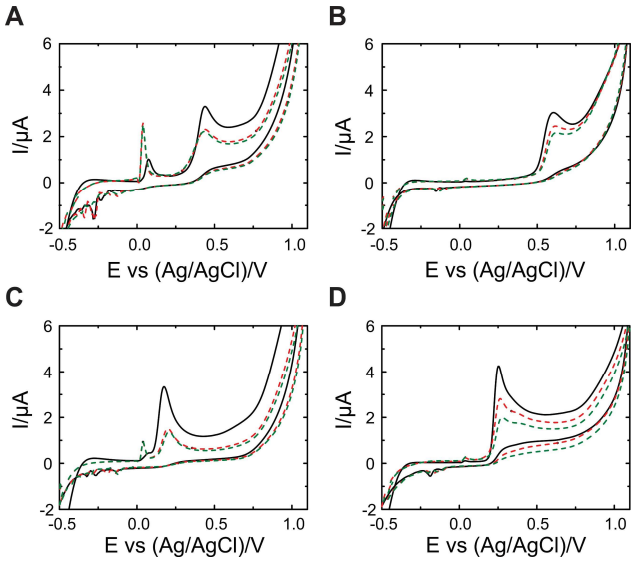

Fig. 1. Cyclic voltammograms of **A)** PHOH, **B)** PCP, **C)** OP and **D)** BPA using 100 μM concentration in pH 12 Britton Robinson buffer at Italsens SPE. First scan (black line), second scan (red dotted line) and third scan (green dotted line). Three consecutive scans were performed within the same phenol droplet.

Besides the electrochemical irreversibility of all phenols, the nature of the mass-transport mechanisms at the electrode surface was revealed from the scan-rate experiments. Therefore, solutions containing PHOH, PCP, OP or BPA at 500 μM concentration in pH 12 BR buffer were evaluated by LSV on bare SPEs varying the scan-rate (5, 10, 25, 50, 75, 100, 200, 300 and 500 mV s^{-1}), results shown in **Fig. S3A-D**. According to the LSV results, a non-linear relationship was obtained between the I_p and the scan-rate (v), suggesting that the electrochemical reaction is governed by a diffusion-controlled process in PHOH, PCP and BPA (**Fig. S3E** for PHOH, I_p (μA) = 2.26 v (mV s^{-1}) + 0.58, R^2 = 0.99; **Fig. S3F** for PCP, I_p (μA) = 1.44 v (mV s^{-1}) + 1.05, R^2 = 0.99; **Fig. S3H** for BPA, I_p (μA) = 2.09 v (mV s^{-1}) + 2.25, R^2 = 0.99). On the

other hand, a linear relationship was observed in OP, which means an adsorption-controlled process (**Fig. S3G** for OP, I_p (μA) = 0.25 v (mV s^{-1}) + 1.03, R^2 = 0.99), in harmony with the aforementioned **Fig. S2C**. To confirm these findings, the I_p was plotted against the square root of the scan-rate (**Fig. S3I-L**). In this case, a linear relationship should be presented for a diffusion-controlled process, which was the case for PHOH, PCP and BPA as it was previously confirmed. Besides, the logarithm of I_p and the logarithm of the scan-rate were plotted. Herein, a slope close to the theoretical value of charge transfer coefficient (α = 0.50, corresponding to diffusion-controlled process) is expected for PHOH, PCP and BPA meanwhile a slope higher to the theoretical value (α > 0.50, corresponding to an adsorption-controlled process) is expected for OP. Thus, the theoretical values were consistent for most of the phenols where **Fig. S3M-P** shows a slope of 0.49 for PHOH, 0.46 for PCP, 0.83 for OP and 0.62 for BPA, respectively.

3.2. Influence of the pH in the electrochemical behavior of the different phenols

The EF of each phenol was analyzed on SPE in the entire pH range (2 – 12) using SWV (**Fig. 2**). An improved resolution of the irreversible oxidation process provided by SWV, making the identification of the four phenols easier. A single oxidation peak was observed for PHOH, PCP and OP since all of them contain one phenolic substituent. On the other hand, a major peak with a shoulder at lower pHs (2 – 4) is shown for BPA, **Fig. 2D**, previously reported by Kuramitz *et al.* [56]. In general, at lower pH values (from pH 2 to pH 5) the oxidation peaks for all phenols were in the same potential range (0.7 V – 0.9 V). Notably, these values shift to less positive potentials when increasing the pH, facilitating the identification of the four different phenols at higher pHs. Given the existing similarity between E_p at acidic pHs, the broader peak separation was reached at pH 12 (**Fig. 2**), where the four phenols have different oxidation potentials (0.42 V for PHOH, 0.59 V for PCP, 0.19 V for OP and 0.25 V for BPA). Therefore, pH 12 was chosen as optimal pH, which simplifies the simultaneous determination of the different phenols without any overlap between peaks.

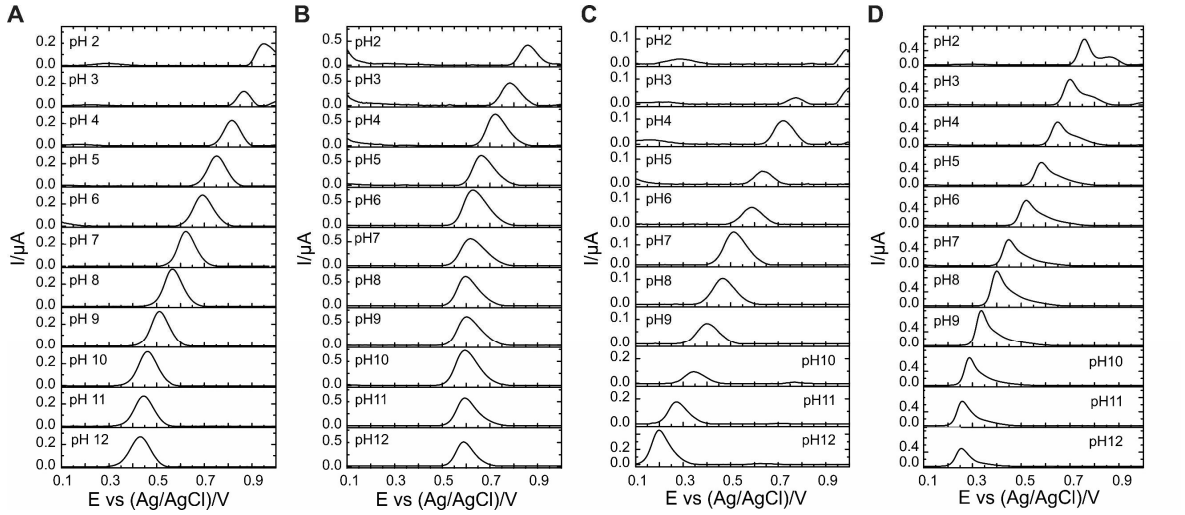

Fig. 2. Baseline corrected square wave voltammograms of 10 µM concentration of phenols: **A)** PHOH, **B)** PCP, **C)** OP and **D)** BPA; obtained during pH screening in Britton Robinson buffer (20mM and 0.1 mM KCl, in the pH range 2 to 12) on Italsens SPE.

The linear relationship between the oxidation E_p of the four phenols in function of the pH is displayed in **Fig. S4**. Thus, a linear behavior is shown for PHOH, PCP, OP and BPA until pH 11, pH 7, pH 12 and pH 11, respectively, with Nernstian slopes (60 ± 2 mV decade^{-1}, average of four phenols) indicating that the number of protons is equal to the number of electrons transferred during the electrochemical oxidation process at the bare SPE. These results are supported by the literature which reports that one electron and one proton are transferred in the process of PHOH [57] and two electrons and two protons are exchanged in the processes of PCP, OP and BPA [42,58,59]. At these pHs, far above the pK_a value (9.99, 4.98, 10.23 and 9.6, respectively), the phenols are all deprotonated and can be found in their phenolate anions form, where proton exchange cannot take place during the electrochemical process.

3.3. Stability and degradation studies of phenols over time

Many published studies have prepared and stored the stock solutions of phenols in different ways such as in absolute ethanol[38,60,61] or ultrapure water[57], at low[38,57,61] or room temperatures[53], in daylight or darkness[34], and freshly prepared. Therefore, the next step to take into consideration was the stability of the phenol's stocks. Hence, the possible degradation of the four phenols over time (0, 30, 120 and 300 min) was evaluated by performing a stability study at pH 12 in BR buffer using different types of storage conditions: *i)* ice and dark; *ii)* room temperature (RT) and dark; and *iii)* room temperature and daylight. A remarkable stability of BPA, PHOH

and PCP solutions overtime under the different storage conditions (10 µM concentration) is shown in **Fig. 3**. On the other hand, OP appears to be the most unstable compound throughout time, showing fluctuations in the peak oxidation intensity (**Fig. 3C**) probably due to the adsorption-controlled mechanism involved in this specific case. The relative standard deviation (RSD) of the I_p and E_p of the four phenols is summarized in **Table 2**. Excellent RSDs of E_p (< 3%) over time at pH 12 for all storage conditions is shown for all four phenols.

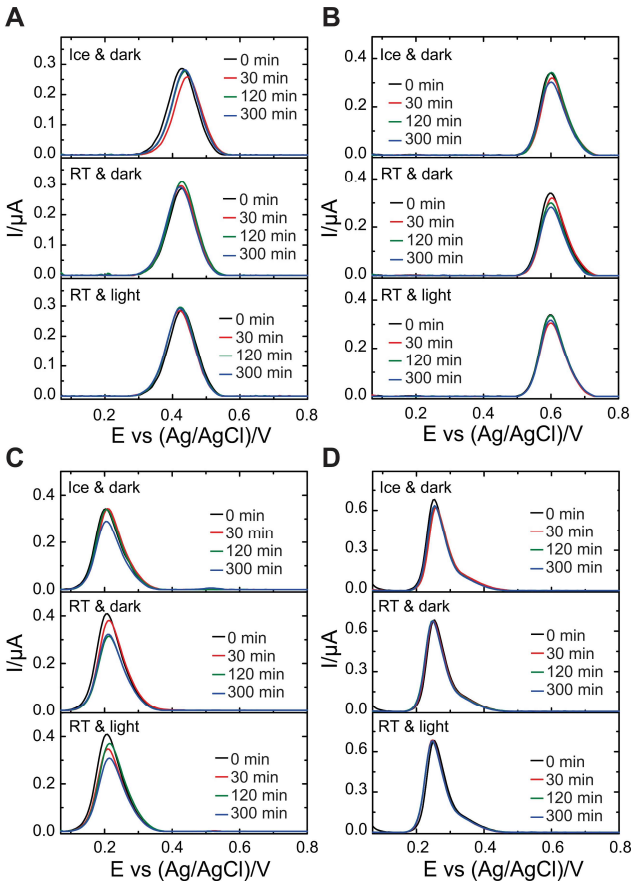

Fig. 3. Baseline corrected square wave voltammograms of 10 µM phenols in pH 12 BR, **A)** PHOH, **B)** PCP, **C)** OP and **D)** BPA. Stability of different stocks over the time (from 0 to 5 hours) stored in ice and dark; at room temperature and dark; and at room temperature and daylight.

Table 2. Relative Standard Deviation (RSD) of peak current (I_p) and peak potential (E_p) obtained from the stability study over time (0, 30, 120 and 300 min) of all phenols (PHOH, PCP, OP and BPA) at 10 µM concentration in pH 12 BR using three different storage conditions (N=4).

	Storage	PHOH	PCP	OP	BPA
RSD (%) of I_p over time	ice & dark	9.80	5.94	7.66	4.59
	RT & dark	3.36	8.34	12.86	1.82
	RT & light	2.01	5.06	12.06	1.97
RSD (%) of E_p over time	ice & dark	2.59	0.42	1.47	0.98
	RT & dark	1.64	0.48	1.39	1.00

RT & light	1.48	0.42	1.39	1.00

Due to the high toxicity that these hazardous phenolic compounds promote into the environment, a simple way for their elimination from (industrial) wastewaters is highly needed. The voltammetric curves obtained after an anodic pretreatment of the samples are summarized in **Fig. 4a**. The anodic pretreatment was selected as the easiest way of degradation of phenol within the sample drop. As it can be seen in **Fig. 4b,** after 180 minutes of anodic pretreatment, 64% of the phenol is oxidized. Moreover, to eliminate not only the phenol but also the hazardous byproducts[57] such as catechol and/or hydroquinone, the selected applied potential was 0.9 V, which is far above the peak potentials observed during the entire electrochemical study. It is important to highlight herein the evaporation that takes place within the drop of the sample throughout time. To control this issue, the setup of this specific experiment was designed to close and preserve humidity inside a reduced space. However, the total evaporation rate cannot be avoided and considering this fact, the final degradation could be likely lower than the represented in **Fig.4**. Hence, with this straightforward anodic pretreatment, the phenol concentration present in the sample can be decreased up to two-thirds promoting two major advantages for future applications: *i)* on-site detection and *ii)* environmental removal.

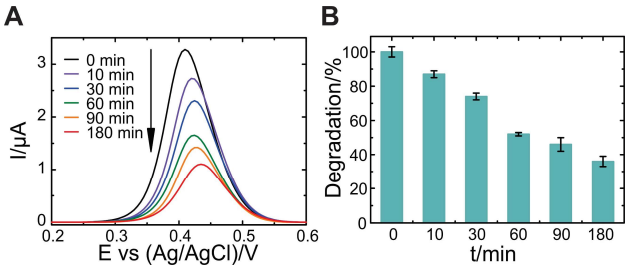

Fig. 4. Baseline corrected square wave voltammograms of **A)** 100 μM PHOH in pH 12 BR after anodic pretreatment at 0.9 V over time (from 0 to 3 hours). Corresponding degradation plot of **B)** PHOH over time (N=3).

3.4. Analytical performance of the SPE during calibration curves

Under the optimized parameters and conditions, the analytical performance of the bare SPE was evaluated to determine different concentrations of phenols (N=3). Square wave voltammograms upon increasing concentrations of PHOH, PCP, OP and BPA (1 – 50 μM) are exhibited in **Fig. 5A-D** with the corresponding linear relationships for the oxidation peaks (**Fig. 5E-H**). The analytical parameters have been collected in **Table**

3 and show outstanding reproducibility among the triplicates for each phenol (with RSD of I_p < 10% and RSD of E_p < 2%), sensitivity and limit of detection.

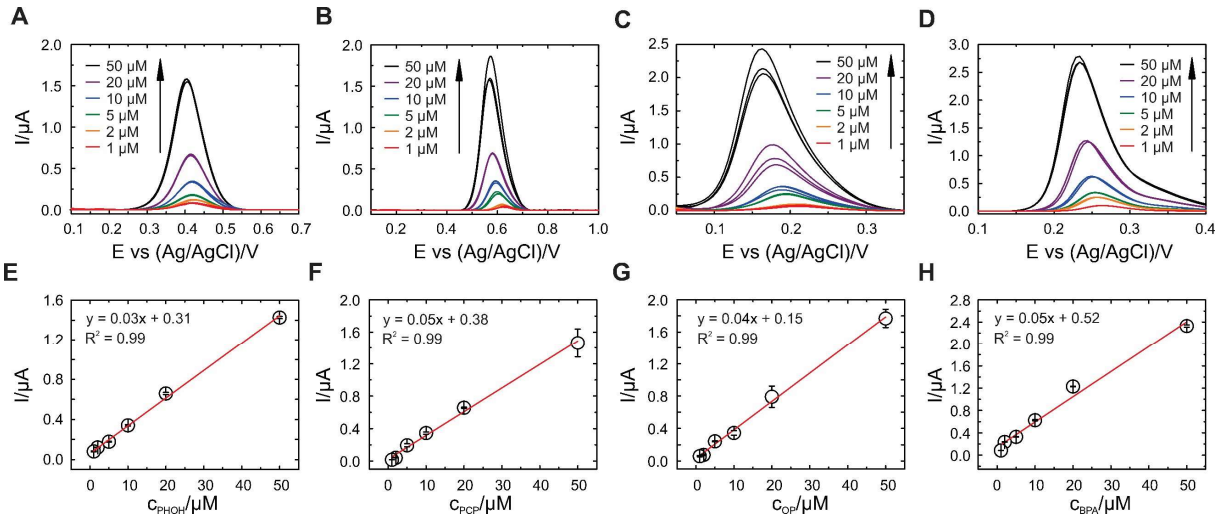

Fig. 5. Baseline corrected square wave voltammograms for **A)** PHOH, **B)** PCP, **C)** OP and **D)** BPA in pH 12 Britton Robinson buffer in a concentration range from 1 to 50 µM using Italsens SPE (N=3). Corresponding calibration curves of all phenols **E)** PHOH, **F)** PCP, **G)** OP and **H)** BPA showing the average of the peak current upon increasing concentrations of each phenol (N=3).

Table 3. Analytical parameters for the electrochemical approach, obtained from calibrations curves of all phenols (PHOH, PCP, OP and BPA) in a range from 1 to 50 µM concentration and RSDs obtained from the reproducibility study (N=3).

	PHOH	PCP	OP	BPA
Peak potential (V)	0.420 ± 0.003	0.593 ± 0.003	0.188 ± 0.003	0.251 ± 0.003
Sensitivity (µA µM^{-1})	0.033 ± 0.001	0.047 ± 0.005	0.038 ± 0.003	0.054 ± 0.002
R-squared	0.998	0.998	0.997	0.994
Linear range (µM)	5 – 50	5 – 50	5 – 50	5 – 50
Limit of detection (µM)	0.930 ± 0.015	0.915 ± 0.086	0.331 ± 0.031	0.176 ± 0.007
Limit of quantification (µM)	3.099 ± 0.003	3.049 ± 0.015	1.104 ± 0.003	0.586 ± 0.004
RSD of I_p (%) at 10 µM, N=3	2.36	4.14	8.38	0.31
RSD of E_p (%) at 10 µM, N=3	0.69	0.49	1.55	1.15

3.5. Selective identification of all phenols in complex mixtures and validation with the commercial Phenols Test Kit.

To achieve the main goal of this work and present an accurate, rapid and user-friendly method to distinguish and identify these four hazardous phenols in real (industrial) wastewaters, a pH screening (2 – 12) of the complex mixture containing all phenols in an equimolar concentration of 10 µM was performed. Thus, the possible interference

caused by the different phenols present in the complex mixture on each other's EF was investigated. The entire pH screening where the optimal peak separation was achieved at pH 12 is shown in **Fig. 6A**, proving that the four phenols can be easily and simultaneously distinguished at this pH (E_{pPHOH} = 0.39 V, E_{pPCP} = 0.61 V, E_{pOP} = 0.21 V and E_{pBPA} = 0.25 V). A negligible overlapping of the electrochemical response of OP and BPA was witnessed although it does not interfere with the final identification of the four different phenols present in the sample. Besides, suppression of the PCP peak was observed in all the complex mixtures (**Fig. 6A**). To thoroughly evaluate possible shifts in the peak potential as well as suppression effects, the electrochemical performance of binary mixtures was subsequently carried out (**Fig. 6B**). The results exhibited suppression of the PCP peak only when PHOH is present, and total suppression of PCP was observed at higher PHOH ratios (i.e. 70:30 and 90:10 PHOH:PCP) as displayed in **Fig. S5**. Moreover, this suppression could be likely due to the reaction rate of oxidation of each phenol where probably the by-products generated after oxidation of PHOH (faster reaction) would attach to the surface of the electrode preventing the oxidation peak of PCP to be seen [51,57]. Another possible explanation lies in the formation of a complex between PCP and PHOH [62]. Further exploration and clarification of the suppression mechanism involved need to be achieved, however, it is not the main focus of the present work. Besides, despite the suppression observed and based on the acquired results, the simultaneous differentiation of all the phenols (in binary and complex mixtures) is successfully allowed by the proposed electrochemical approach. Remarkably, and considered for future steps, a tailor-made Matlab script, previously developed by this group [63,64], could be used to enhance peak separation and identification of the SWV-data of phenol mixtures samples.

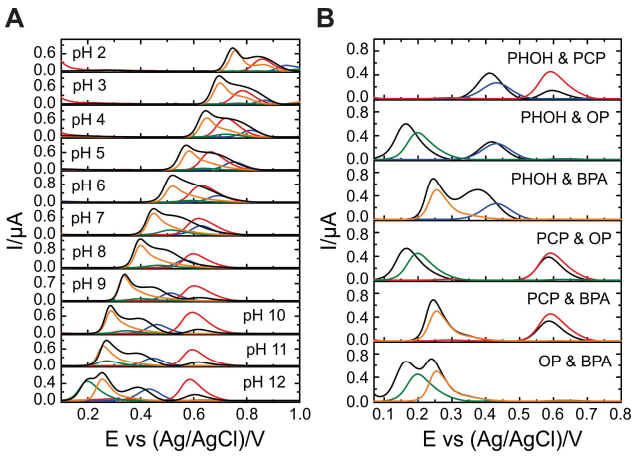

Fig. 6. Baseline corrected square wave voltammograms obtained after **A)** pH screening (pH 2 to 12) in Britton Robinson buffer of the complex mixture (black line) using 10 μM concentration of each phenol (1:1:1:1 ratio) and **B)** binary mixture of phenols (black line) of 10 μM concentration of each phenol (1:1 ratio) in pH 12. Single phenol solutions of PHOH (blue line), PCP (red line), OP (green line) and BPA (orange line) were also provided.

Nowadays, on-site analysis in industrial streams and wastewaters is performed employing test kits allowing quantification of total phenol amount although lacking selectivity. Therefore, a comparison of the current approach based on SWV detection and the Phenol Test Kit (**Fig. S6**) analysis was performed whereby Scheldt river water was spiked with all phenols (PHOH, PCP, OP and BPA) at three different equimolar concentrations (50, 100 and 200 μM). Subsequently, these samples were diluted 50 times for the Phenols Test Kit analysis and 10 times in pH 12 BR buffer for the electrochemical measurements. **Table 4** summarizes the analytical parameters of the electrochemical approach and Phenols Test Kit validation results. However, the Phenols Test Kit analysis allows to determine the total phenol amount in samples sensitively but lacks selectivity. An underestimation of the total phenol amount in all the mixtures is shown by the Phenols Test Kit analysis. In fact, most *para*-substituted phenols do not produce color with the 4-aminoantipyrine reagent.[65] The reaction with 4-aminoantipyrine occurs in the para position to the phenolic group. This reaction happens either in unsubstituted *para* position (as PHOH) or phenols which are *para*-substituted by halogen (as PCP), carboxyl, sulfonic acid, hydroxyl, or methoxyl in which this group is expelled during the reaction. But in the cases in which this position is substituted by an alkyl (such as OP and BPA), aryl or others, the reaction is blocked, and no color change can be observed, resulting in underestimated total phenol amount. Because of that, and due to the visual error inherent in the colorimetric read-

out (which can be also influenced by the daylight intensity), the concentration of phenols is very difficult to be accurately predicted by using these commercially available Test Kits. The current electrochemical approach based on SWV detection offers faster results (< 5 minutes) and requires a small amount of sample, without additional harmful reagents, allowing to quickly screen mixtures with sensitivity in sub-micromolar levels and high selectivity between the four phenols (**Table 4**).

Table 4. Analytical parameters for the electrochemical approach and Phenols Test Kit, obtained from the spiked Scheldt river samples of four phenols (PHOH, PCP, OP and BPA) in three different equimolar concentrations.

	SWV		**HI3864 Phenols Test Kit, Hanna Instruments™**	
Detection method	electrochemical oxidation by an applied potential		colorimetric reaction with 4-aminoantipyrine[a]	
Analyze time/sample	< 5 minutes		> 12 minutes	
Sample volume needed	< 100 µl		20 ml	
Analyte	PHOH+PCP+OP+BPA mixtures spiked in Scheldt river water			
Real spiked concentration[b]	mixture 1: 39.75 mg l^{-1} (i.e. 50 µM equimolar) mixture 2: 79.51 mg l^{-1} (i.e. 100 µM equimolar) mixture 3: 159.01 mg l^{-1} (i.e. 200µM equimolar)			
Dilution	10 times		50 times	
Linear range[b]	0.99 – 9.94 mg l^{-1}		0.00 – 1.00 mg l^{-1} 0.5 – 5.0 mg l^{-1}	
LOD[b]	0.11 mg l^{-1} (average sensitivity of four phenols)		0.1 mg l^{-1}	
Selective	yes		no	
Samples[b]	**real total concentration (10x diluted)**	**determined total concentration**	**real total concentration (50x diluted)**	**determined total concentration**
Mixture 1	3.98 mg l^{-1}	4.09 mg l^{-1}	0.80 mg l^{-1}	< 0.32 mg l^{-1}
Mixture 2	7.95 mg l^{-1}	8.09 mg l^{-1}	1.59 mg l^{-1}	< 1.20 mg l^{-1}
Mixture 3	15.90 mg l^{-1}	16.36 mg l^{-1}	3.18 mg l^{-1}	< 1.70 mg l^{-1}

[a] Most *para*-substituted phenols do not produce color with the 4-aminoantipyrine.
[b] The units of the values are shown in mg L^{-1} to easily compare with the one provided by the commercial kit.

3.6. Determination of phenols in real samples (Scheldt river water) and accuracy evaluation with HPLC technique

To evaluate the accuracy of the optimized electrochemical detection approach, HPLC-DAD was used as a reference technique allowing the identification and quantification of the different phenols. In addition, to demonstrate the potential application of this approach in real samples, Scheldt river water was spiked with individual phenols (PHOH, PCP, OP and BPA) at three different concentrations (50, 100 and 200 µM). Subsequently, these samples were diluted 10 times in pH 12 buffer for SWV measurements or in ultrapure water for HPLC-DAD measurements. External standard calibration method was used for HPLC-DAD analysis to construct the calibration plots of PHOH, PCP, OP and BPA using the peak areas of the responses of different concentrations (2, 5, 10, 20 and 50 µM) of phenols (N=3). Analytical parameters such as retention times, linear dynamic curves and linear range have been collected in **Table S2**. The average of the recoveries of both SWV and HPLC-DAD measurements of 12 spiked samples, as well as the accuracy of the electrochemical approach *versus* the HPLC-DAD are shown in **Table 4**. Remarkably, PHOH, PCP and BPA indicate that this method has great accuracy compared with HPLC-DAD (values between 99% and 112%) with good recoveries for both methods (values between 90% and 117%). While lower accuracy and recovery (SWV) values are shown for OP, as previously observed and described in **section 3.3**, probably due to the lower solubility of OP in an aqueous medium (**Table S1**) as well as the adsorption-controlled mechanism determined.

Table 4. Recovery values were obtained from the spiked Scheldt river samples of individual phenols (PHOH, PCP, OP and BPA) in three different concentrations (5, 10 and 20 µM) in pH 12 BR buffer for SWV and ultrapure water for HPLC-DAD, and the accuracy values between the electrochemical approach and the standard technique, HPLC-DAD (all measurements, N=3).

	SWV		HPLC-DAD		
Sample	**Concentration (µM)**	**Recovery (%)**	**Concentration (µM)**	**Recovery (%)**	**Accuracy (%)**
PHOH	5.85 ± 0.10	116.96 ± 2.08	5.77 ± 0.44	115.40 ± 8.86	101.35
	11.03 ± 0.05	110.32 ± 0.45	10.23 ± 0.01	102.29 ± 0.05	107.86
	21.96 ± 0.13	109.80 ± 0.63	20.27 ± 0.04	101.35 ± 0.19	108.33
PCP	4.86 ± 0.15	97.28 ± 2.98	4.54 ± 0.00	90.86 ± 0.01	107.07
	10.32 ± 0.15	103.23 ± 1.54	10.14 ± 0.00	101.42 ± 0.03	101.79
	20.92 ± 0.25	104.61 ± 1.26	20.95 ± 0.01	104.76 ± 0.04	99.86
OP	5.01 ± 0.53	100.16 ± 10.62	4.98 ± 0.02	99.59 ± 0.34	100.58
	8.82 ± 0.48	88.19 ± 4.80	11.02 ± 0.03	110.21 ± 0.30	80.02
	19.30 ± 2.46	96.50 ± 12.29	22.45 ± 1.16	111.45 ± 5.53	86.58
BPA	5.29 ± 0.05	105.86 ± 0.93	4.95 ± 0.01	99.09 ± 0.15	106.84

	10.88 ± 0.14	108.76 ± 1.41	10.72 ± 0.01	107.25 ± 0.05	101.41
	20.78 ± 0.90	103.91 ± 4.49	18.56 ± 0.01	92.82 ± 0.00	111.95

Furthermore, real samples containing different mixtures of phenols were also studied (**Table S3**). Therefore, Scheldt water was spiked in equimolar ratios with two binary mixtures (PHOH+OP and PCP+BPA), two tertiary mixtures (PHOH+OP+BPA and PCP+OP+BPA) and the complex mixture (PHOH+PCP+OP+BPA) at two different concentrations (50 and 200 µM) and diluted 10 times in pH 12 (for SWV analysis) or ultrapure water (for HPLC-DAD analysis) to reach a final concentration of 5 and 20 µM of each phenol. Due to shifts of the oxidation peaks of some phenols after mixing, the recovery values of the mixtures in SWV were calculated based on the maximum I_p at the corresponding E_p of the anodic oxidation peak of each phenol in the mixture. As it can be seen in **Table S3**, PHOH can be successfully identified and quantified in all the mixtures, showing the best results in terms of recoveries and accuracy between both methods (SWV and HPLC). For the three phenol derivatives, the situation is more controversial. First of all, the lowest SWV recovery and accuracy values are exhibited for PCP, more specifically in complex mixtures, likely due to the suppression of the oxidation signal caused by PHOH previously described in **section 3.5**. Secondly, and probably influenced by the lower solubility as well as the adsorption-controlled mechanism of OP, its quantification is overestimated as can be seen in the recovery values from both, SWV and HPLC-DAD. Last but not least, the highest SWV recovery and accuracy values are shown for BPA as a result of peak overlap, resulting in the peak broadening and the increase of the peak potential. Hence, the recovery values of each phenol derivative in the mixtures (**Table S3**) are worse than in the case of the single phenols (**Table 4**) due to the influence among them. It is important to highlight that even though this approach cannot be implemented for the quantification of each phenol in complex mixtures, their identification is completely successful. Moreover, the insights revealed during this study are being already used for the improvement of the envisioned sensor. Current efforts are being carried out in this group towards the development of a novel sensor that combines the present electrochemical approach with photoelectrochemical readout to further enhance the sensitivity. This will result in a powerful device able to accomplish not only an accurate differentiation (SWV) but also the highly sensitive quantification (photoelectrochemistry) of the total amount of phenols in industrial wastewaters and process streams ensuring limits of detection in

the sub-nM range. By this combination, the drawbacks of both techniques (in terms of sensitivity and selectivity), when used separately, will be excluded. Using disposable SPEs and integrating both techniques on wireless potentiostats will allow on-site detection and/or monitoring. Resulting in a first-of-its-kind, more reliable and fast sensing application in the analysis of phenolic samples compared to the currently used commercial Phenols Test Kits.

4. Conclusions

The electrochemical detection of four highly relevant phenols as EDC on unmodified SPE via rapid voltammetric detection method in complex and real samples has been presented. Importantly, the electrochemical oxidation and behavior of PHOH, PCP, OP and BPA have been unraveled for the first time using BR buffer including reversibility, mass-transfer, pH screening, stability and degradation studies. Moreover, the analytical performance of the SPEs and their capability for the accurate identification of different hazardous phenols in complex mixtures simultaneously are shown by the performed calibration curves. A reliable identification and quantification of real samples from spiked Scheldt river water (Belgium) in comparison with the commercially available Phenols Test Kit is offered by the current method based on SWV detection. Finally, the accuracy of the methodology was evaluated using real samples and comparing with the lab-bench standard method (HPLC-DAD). Overall, the potential of the electrochemical approach for providing rapid and reliable screening of the most important phenolic EDCs during on-site testing has been demonstrated. The advances presented in this article will pave the way for the development of a new generation of electrochemical sensors aiming for on-site detection and degradation of phenols in industrial processes and/or wastewater.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

‡ Hanan Barich and Rocío Cánovas contributed equally to this work.

Hanan Barich: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing - original draft, review & editing. **Rocío Cánovas**: Conceptualization; Formal analysis; Methodology; Supervision; Validation; Visualization; Writing - original draft, review & editing. **Karolien De Wael**: Conceptualization; Funding acquisition; Project administration; Resources; Supervision; Validation; Visualization; Writing - review & editing.

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