Disposable screen-printed carbon-based electrodes in amperometric detection for simultaneous determination of parabens in complex-matrix personal care products by HPLC

Sergio Lucas-Sánchez, Lucía Abad-Gil [*], Carmen Isabel-Cabrera, M. Jesús Gismera, M. Teresa Sevilla, Jesús R. Procopio

Departamento de Química Analítica y Análisis Instrumental, Facultad de Ciencias, Universidad Autónoma de Madrid, Avda. Francisco Tomás y Valiente, 7, E-28049, Madrid, Spain

ARTICLE INFO

ABSTRACT

Parabens are chemicals widely used as preservatives in different types of industrial products. In recent years, the concern about the safety of these compounds has increased due to their endocrine disrupting activity. For this reason, their use is highly regulated and even some of them have already been banned. Thus, methods for the sensitive and selective detection of these compounds are required to control their presence in food, cosmetic, and pharmaceutical products. This paper presents an HPLC method with electrochemical detection using disposable screen-printed electrodes (SPE) for simultaneous determination of 6 different parabens in personal care products. Electrochemical behaviour of parabens was studied on SPE with different carbon-based materials as working electrode: carbon, ordered mesoporous carbon and graphene. From these studies, pH, detection potential, and the most adequate SPE were chosen. Due to the wide range of textures and viscosities (e.g., liquid, solid, and semi-solid) of personal care products, adequate sample pretreatments are required before chromatographic measurement. Here, a fast ultrasound-assisted extraction method was applied to simultaneously extract 6 parabens (methyl-, ethyl-, isopropyl-, propyl-, butyl-and benzyl-paraben) from different complex-matrix cosmetic products. Instrumental limits of detection between 20 and 115 $\mu g\ L^{-1}$ were obtained applying +1.0 V (*vs.* Ag) as detection potential on carbon-based SPE. The total analysis time, including sample extraction and HPLC run, was shorter than 35 min. The proposed method is more versatile and faster than the current available methods and has been successfully applied to determine parabens in commercial samples such as shampoos, body creams, facial tonics, and toothpastes.

1. Introduction

Parabens, esters of *p*-hydroxybenzoic acid, are widely used as preservatives in cosmetic, food, and pharmaceutical industries due to their low cost, broad-spectrum antimicrobial activity, and chemical stability [1]. Parabens were considered as low toxicity compounds. However, recent investigations have indicated that these compounds are endocrine disruptors, and can cause negative effects on human health such as reproductive dysfunctions, carcinogenic effects, and allergic contact dermatitis [1–4]. It is well-known that parabens are among the most abundant substances added to cosmetics and pharmaceuticals, so these products are considered the principal way of human exposure to parabens. In addition, eco-toxicity studies have demonstrated the negative

effects of parabens on the aquatic media [5], being detected in natural waters, wastewaters, sediments and sewage sludges [2,6–9].

The most common parabens are methylparaben (MP), ethylparaben (EP), propylparaben (PP), isopropylparaben (iPP), butylparaben (BP), isobutylparaben (iBP), and benzylparaben (BzP). To ensure the safety of the consumers, the European Union has regulated the content of these compounds in cosmetics. The EU Regulation No 1223/2009 [10] specifies a maximum concentration (expressed as 4-hydroxybenzoic acid) of 0.4% for single paraben and 0.8% for mixtures of parabens in cosmetic products. This regulation was later amended to ban the use of iPP, iBP, BzP, pentylparaben and phenylparaben in cosmetics due to the growing concern about these compounds, their high risk to health and the daily, extended, and increasing use of personal care products [11]. The use of

PP and BP is also banned in leave-on products designed for application on the nappy area of children under three years of age. In addition, the sum of the individual concentrations of PP and BP in cosmetics has been limited to 0.14% (expressed as 4-hydroxybenzoic acid) [12].

The development of adequate methods to determine and control the concentration of parabens in commercial products, natural systems or biological samples is currently of great importance in analytical chemistry. In fact, review papers on analytical methods to extract and determine parabens and other endocrine disruptors in cosmetics, environmental, and biological samples proof the current interest on this topic [7–9,13–16]. The most used methods for the determination of parabens are based on liquid chromatography (HPLC) coupled with diode-array (DAD), mass spectrometer (MS) or fluorescence detectors [7–9,16–21]. Due to the electrochemical properties of parabens [22,23], electroanalytical methodologies based on unmodified [24,25] and modified electrodes [26–38] for the individual determination of these compounds have been developed. The state-of-the-art electroanalytical sensors are not selective enough to determine one paraben in the presence of others [39], thus they can only provide the total paraben content [40,41]. This is an important drawback since combination of different parabens is usually used to prevent degradation of products. Alternatively, chromatographic methods coupled to an electrochemical detector (ECD) are an excellent option for the individual determination of parabens. The use of ECD presents some advantages compared to DAD such as better selectivity and sensitivity. ECD-based methods also outstand due to their reduced cost and portability over MS detectors. Despite these interesting features, there are not many publications dealing with methods based on HPLC coupled to ECD in amperometric [42–44] or coulometric modes [42,45], UPLC-ECD [46] and capillary electrophoresis-ECD [47] to determine parabens in cosmetic products. The incorporation of screen-printed electrodes (SPEs) to HPLC-ECD systems is an attractive option to determine all parabens that can be present in cosmetics since these devices are economical and can easily be replaced, achieving an increase on the reproducibility of the measurements [48,49]. In addition, surface passivation of working electrode and polishing processes are avoided.

Prior to the determination of parabens, a sample pretreatment step is usually needed, specially, when complex matrix samples are analysed. Extraction methods based on solid phase extraction and ultrasound-assisted extraction (UAE) are among the most used to determine parabens in cosmetic, environmental and biological samples [13–17,50]. New sorbent materials based on metal-organic frameworks, nanocomposite materials and QuEChERS have been also investigated to develop more efficient extraction methods [19,51–53].

The aim of this work is to develop a simple and fast method for simultaneous determination of different parabens in consumer products. A HPLC method with ECD detection has been optimized to determine MP, EP, iPP, PP, BP and BzP. The electrochemical detection was performed in amperometric mode using a SPE. Commercial SPEs with working electrodes of different carbon materials, such as carbon (SPCE), ordered mesoporous carbon (SPCE-OMC) and graphene (SPCE-GPH), were evaluated to get the optimal detection. UAE was optimized as pretreatment procedure for the simultaneous extraction of parabens from cosmetic samples prior the chromatographic measurement. The suitability of the method was tested by analysing a variety of commercial personal care products with different matrices and textures.

To the best of our knowledge, there is only one publication on an HPLC method with amperometric detection for paraben determination using SPE [44]. In that work a SPCE is modified with a nanocomposite of graphene, polyvinylpyrrolidone and polyaniline. The here proposed method is easier to implement as a complex previous procedure to modify the electrode is not required since commercial devices are directly used.

2. Experimental section

2.1. Reagents

MP, EP, iPP, PP, BP and BzP (purity >99%) were obtained from Sigma-Aldrich (Darmstadt, Germany). Individual stock solutions of 1000 mg L^{-1} were prepared by dissolving 10 mg of each paraben in 10.0 mL of acetonitrile. Working standard solutions were prepared by mixing appropriate amounts of individual standard solutions and diluting in the adequate media. All solutions were kept at 4 °C in the darkness.

HPLC-grade acetonitrile and methanol (Scharlab, Barcelona, Spain) were used as organic modifiers of the mobile phase and extraction solvents. *O*-phosphoric acid (84–85% purity) and potassium and sodium phosphate salts, used to prepare phosphate solutions at pH ranging from 2 to 8, were acquired from Scharlab (Barcelona, Spain) and Fluka (Buchs, Switzerland), respectively. Potassium ferrocyanide (K$_4$[Fe(CN)$_6$]·3H$_2$O) and potassium chloride used in the characterization of SPEs were acquired from Panreac (Barcelona, Spain) and Sigma-Aldrich (Darmstadt, Germany), respectively. All aqueous solutions were prepared using ultrapure water Type I (resistivity $\geq$18.2 MΩ) obtained from a Milli-Q Direct (Millipore, Merck KGaA, Germany) water purification system.

2.2. Instrumentation

Electrochemical measurements were performed with the µSTAT 400 bipotentiostat (DropSens, Oviedo, Spain), controlled by the "Drop-View 8400" Software. Disposable SPEs (Metrohm-Dropsens, Oviedo, Spain), used in voltammetric measurements and for the amperometric detection, consisted of a ceramic substrate (L 3.4 x W 1.0 x H 0.05 cm) with electric contacts made of silver, a silver pseudo-reference electrode and a carbon auxiliary electrode. The working electrode (4 mm diameter) was of carbon in the SPCE (ref. DRP-110), ordered mesoporous carbon/carbon in the SPCE-OMC (ref. DRP-110 MC), and graphene/carbon in the SPCE-GPH (ref. DRP-110 GPH). Specific connectors (ref. DRP-CAST, Methrom-DropSens, Oviedo, Spain) were used to connect the SPEs to the µSTAT 400.

The chromatographic system consisted of a quaternary gradient pump (Jasco PU-2089 Plus, Tokyo, Japan) equipped with a vacuum degasser, an automatic sample injection system (Jasco AS-2055, Tokyo, Japan), and a thermostatically controlled oven (Jasco CU-2067, Tokyo, Japan). For the spectrophotometric detection, a MD-2010 Plus Multiwavelength Detector (Jasco, Tokyo, Japan) was used. Chromatographic data obtained with DAD were acquired and handled using a LC-NetII/ADC interface controlled with the Jasco ChromPass Chromatography data system.

A Gilson Minipulse 3 peristaltic pump (Gilson, Middleton, USA) and a sample injection valve 21939–18 (Omnifit) with a loop of 100 µL volume were used in the hydrodynamic voltammetric measurements performed with different SPE devices. To carry out the in-flow electrochemical measurements, the SPEs were coupled to the HPLC or Flow Injection Analysis (FIA) systems with a thin layer flow cell (ref. DRP-HPLCELL 70022, Methrom-DropSens, Oviedo, Spain). The amperometric data were acquired with the µSTAT 400 bipotentiostat (DropSens, Oviedo, Spain), controlled by the Drop-View 8400 Software when the FIA system was used, or with the µAutolab potentiostat controlled by the software General Purpose Electrochemical System (GPES Manager 4.9007 version) using the HPLC system.

A pH meter GLP 22 (Crison, Barcelona, Spain) was used to measure pH values. An Elmasonic P30HS model ultrasonic bath (ELMA, Singen, Germany), a Universal 16 centrifuge (Hettich, Westfalia, Germany) and a Wizard Vortex mixer (Velp Scientifica, Monza, Italy) were used for sample pretreatment.

2.3. Electrochemical measurement procedures

The electrochemical behaviour of parabens on the SPEs was studied by cyclic voltammetry. For this purpose, individual solutions of 200 mg L^{-1} were prepared in a 0.10 mol L^{-1} phosphate solution at different pH values containing 10% acetonitrile. The voltammetric measurements were performed by adding 100 µL of the tested solution covering the three electrodes of the three types of SPEs. Voltammograms were recorded from +0.30 to +1.50 V at a scan rate of 0.100 V s^{-1}. All measurements were performed in triplicate at room temperature.

The in-flow electrochemical response of MP on the different SPEs were obtained in the described FIA system by injecting 100 µL of a 20 mg L^{-1} solution of paraben in 35% acetonitrile-0.010 mol L^{-1} pH 6 phosphate solution. Hydrodynamic curves of all the assayed parabens were obtained on SPCE in the HPLC system by injecting 20 µL of a 10 mg L^{-1} multi-analyte solution using as mobile phase the mixture 35% acetonitrile-0.010 mol L^{-1} pH 6 phosphate solution.

2.4. Chromatographic conditions

A Kromasil C18 (150 mm length x 4.6 mm inner diameter and 5 µm particle size) column (Scharlab, Barcelona, Spain) thermostated at 40 °C, was used to carry out the chromatographic separation. A mixture of 0.010 mol L^{-1} phosphate at pH 6 solution containing 35% acetonitrile was used as mobile phase at a flow rate of 1.5 mL min^{-1} in isocratic elution mode. All parabens standard solutions and sample extracts were filtered using 0.45 µm nylon syringe filters (Scharlau, Barcelona, Spain) before their introduction in the chromatographic system. An injection volume of 20 µL was used. Parabens were detected at 257 nm with DAD [13]. The ECD was operated in amperometric mode using SPCE at +1.0 V (*vs.* Ag).

2.5. Analysed samples and pretreatment procedures

Samples of commercial cosmetic products containing at least one of the studied parabens were purchased from local supermarkets. Two facial tonics, two toothpastes, two shampoos, and two body creams from different brands were analysed. The sample pretreatment was selected according to the complexity of the sample matrix. A simple 1:200 dilution with methanol was required for samples with aqueous matrices, such as, facial tonics. Parabens from cosmetic products containing fatty acids, abrasives, or surfactants such as body creams, toothpastes or shampoos were extracted using a simple and fast sample pretreatment based on the following UAE procedure: 9.0 mL of methanol were added to 1.00 g of weighed sample and the mixture was sonicated for 10 min at 25 °C in an ultrasonic bath operated at 80 kHz of frequency and 100% power. After sonication, the mixture was centrifuged at 2500 rpm for 5 min. Prior to the analysis, 1.0 mL of the extract was diluted to 5.0 mL with methanol.

Before the chromatographic analysis all extracts were filtered throughout a 0.45 µm nylon and the samples were analysed by triplicate.

2.5.1. Sample treatment procedure according to European Directive

Parabens were extracted using the sample treatment indicated in the European Directive [57]. In short, approximately 1.0 g of sample was weighted into a 100 mL glass tube with screw cap. After that, 1.0 mL of 2.0 mol L^{-1} sulphuric acid solution and 50.0 mL of 9:1 ethanol: water mixture were added into the tube. Then, the tube was closed and shaken vigorously for at least 1 min until a homogeneous suspension was obtained. To facilitate the extraction of parabens in the ethanolic phase, the tube was placed in a water bath at 60 ± 1 °C for 5 min. After extraction, the tube was immediately cooled in a stream of cold water and the extract was stored in the refrigerator for 1 h, and then filtered through a filter paper. The extracts were stored at 4 °C and the HPLC determination was performed within 24 h.
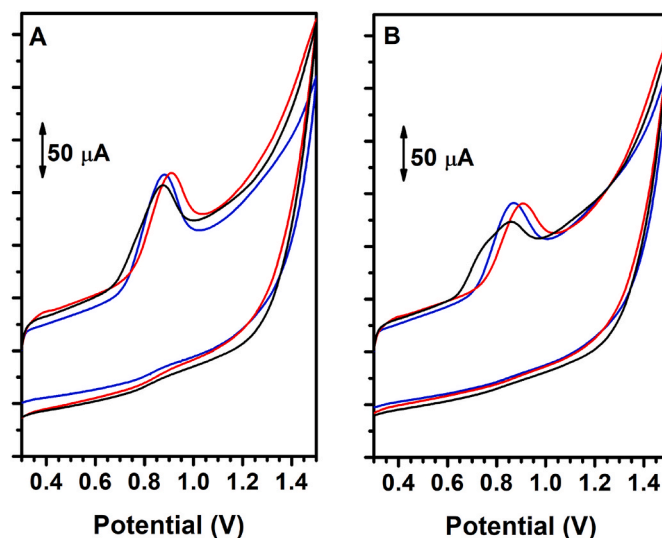

Fig. 1. Cyclic voltammograms of (A) MP and (B) BzP at 200 mg L^{-1} obtained on SPCE (blue line), SPCE-OMC (red line) and SPCE-GPH (black line) in 0.10 mol L^{-1} pH 6 phosphate solution containing 10% of acetonitrile. Other conditions: 0.100 V s^{-1} scan rate. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3. Results and discussion

3.1. Optimization of chromatographic conditions

Prior the optimization of the electrochemical detection, the best conditions for chromatographic separation were found by injecting replicates of a standard solution containing all parabens at 10 mg L^{-1} concentration level using DAD at 257 nm. Percentages of acetonitrile between 35% and 75% in 0.010 mol L^{-1} phosphate solution at pH 6 were assayed. The analysis time was shortened as the acetonitrile percentage was increased, but a diminution in the resolution was also observed. This decrease in the resolution was more pronounced for the most retained compounds (i.e., iPP, PP, BP and BzP) obtaining resolutions below 1 for the highest acetonitrile percentages. Adequate resolutions (R values > 1.5) for these compounds were obtained with 35% of acetonitrile at 1.0 mL min^{-1} flow rate. Flow rates between 1.0 and 1.5 mL min^{-1} were evaluated to diminish the analysis time. A significant decrease in the analysis time without changes in the resolution was obtained at 1.5 mL min^{-1} flow rate. Under optimal mobile phase composition and flow rate, the retention times for MP, EP, iPP, PP, BP and BzP were 2.49 ± 0.02, 3.9 ± 0.1, 6.2 ± 0.1, 6.7 ± 0.1, 12.5 ± 0.3, 13.4 ± 0.4 min, respectively. The separation of the six analytes was completed in less than 14 min.

3.2. Voltammetric behaviour of parabens on SPEs: optimization of electrochemical detection

Before the evaluation of the electrochemical behaviour of parabens on the SPEs, the working electrode surface of the SPCE, SPCE-OMC and SPCE-GPH was characterized by cyclic voltammetry using ferrocyanide as electrochemical probe (Section 1S in Electronic Supplementary Material, ESM, for details on experimental conditions and results). According to the obtained results, carbon nanomaterials based SPCE, especially SPCE-OMC, were a good choice for amperometric detection of parabens. Fig. 1 shows the electrochemical response of parabens with different length of the alkyl chain (e.g., MP and BzP) on SPCE, SPCE-OMC and SPCE-GPH. As can be observed, both parabens showed an irreversible oxidation process and the anodic peak potential shifted to lesser positive values as the length of the alkyl chain increases. Only slight differences were observed in the response of MP and BzP on SPCE-
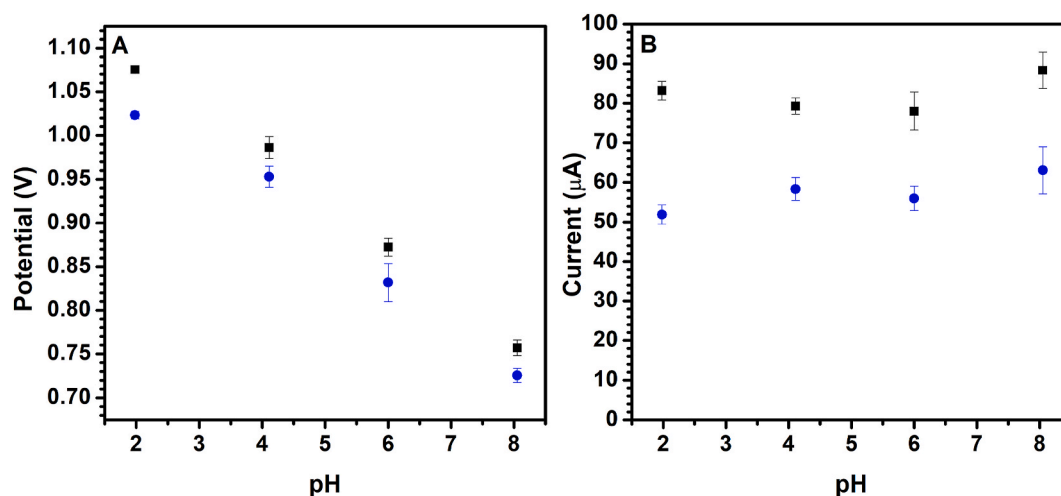
Fig. 2. (A) Anodic peak potential and (B) anodic peak current of MP (black squares) and BzP (blue circles) at 200 mg L^{-1} in 0.10 mol L^{-1} phosphate solutions at different pH values, ($n = 3$). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)
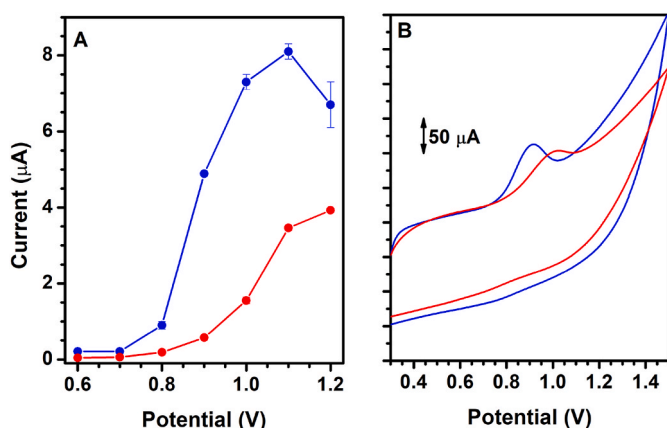

Fig. 3. (A) FIA responses of a 20 mg L^{-1} solution of MP obtained using 35% acetonitrile-0.010 mol L^{-1} pH 6 phosphate solution as carrier, ($n = 3$). (B) Cyclic voltammograms of 200 mg L^{-1} of MP in 0.10 mol L^{-1} phosphate solution at pH 6 containing 35% of acetonitrile. SPCE (blue line) and SPCE-OMC (red line). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Fig. 4. Chromatogram obtained with ECD in amperometric mode and using the SPCE at +1.0 V for a 10 mg L^{-1} multi-analyte solution of parabens. Mobile phase: 35% acetonitrile-0.010 mol L^{-1} phosphate solution at pH 6. Flow rate: 1.5 mL min^{-1}.

OMC and SPCE-GPH in comparison to that obtained using the unmodified SPCE. No improvement in the voltammetric response of parabens was observed on SPCE-OMC despite of the greater roughness that can be considered for this SPE due to the presence of ordered mesoporous carbon. A similar effect was reported in a previous published study using a glassy carbon electrode modified with mesoporous carbon and Q10 for paraben detection [41]. In that paper a poor definition of the anodic peak was observed when the electrode was only modified with mesoporous carbon. Here, a rapid deterioration of the working electrode of the SPCE-GPH with loss of the ink that constitutes the electrode surface was observed during the voltammetric studies. Due to this low stability, SPCE-GPH devices were not considered adequate to carry out flow measurements.

Since no differences were observed on the electrochemical response of parabens on SPCE and SPCE-OMC, the effect of pH on the anodic peak current and potential was evaluated for MP and BzP using SPCE. As can be seen in Fig. 2A, for each paraben, the oxidation peak potential value diminishes as the pH value increases, suggesting that protons and electrons are exchanged in the oxidation process. These results are in accordance with those previously published [23]. No significant differences were observed in the anodic peak current in the studied pH range
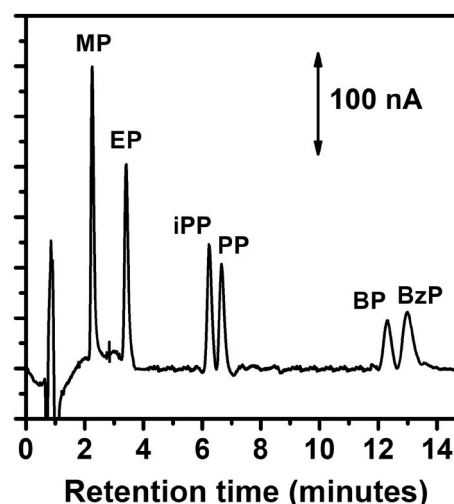
(Fig. 2B). The same behaviour was observed for EP, iPP, PP and BP, thus pH 6 was selected as pH of the mobile phase to obtain adequate electrochemical responses.

To select the most adequate SPE for the EC detection, the in-flow electrochemical response of 20 mg L^{-1} of MP on SPCE and SPCE-OMC was evaluated using the FIA system in the potential range from +0.60 to +1.20 V (*vs*. Ag) with a 0.010 mol L^{-1} phosphate solution at pH 6 containing 35% of acetonitrile as carrier. Fig. 3A shows FIA responses for MP using SPCE and SPCE-OMC. As can be observed, the electrochemical signals obtained with SPCE-OMC were much lower than those observed using SPCE. This deterioration of the voltammetric response on SPCE-OMC could be due to (i) the percentage of acetonitrile in the carrier and/or (ii) an abrasive effect of the continuous flow on the electrode surface. To confirm the influence of acetonitrile on this worsening, cyclic voltammograms of a MP solution containing 35% of acetonitrile were registered using both SPEs (Fig. 3B). Comparing the voltammograms obtained on SPCE and SPCE-OMC for MP in presence of 10% (Figs. 1A) and 35% (Fig. 3B) of acetonitrile in solution, it was observed a diminution of the anodic signal when the acetonitrile percentage was increased, being this decrease higher on the SPCE-OMC.

Table 1
Analytical parameters for the determination of parabens using the HPLC- ECD method.

Compound	Sensitivity[a]	r^2	ILD[b], µg L^{-1}	Repeatability RSD, %	Reproducibility RSD, %
MP	373 ± 8	0.9990	20	1.8	2.6
EP	328 ± 8	0.9990	40	2.3	3.5
iPP	228 ± 9	0.9960	60	1.4	2.1
PP	246 ± 5	0.9992	60	2.8	3.3
BP	208 ± 9	0.9960	80	3.9	4.2
BzP	155 ± 4	0.9984	115	3.1	4.4

[a] Sensitivity expressed as nA·min·L·mg^{-1}.

[b] Instrumental limits of detection.

According to this result, the SPCE-OMC was considered not adequate for EC detection. The SPCE was used in the HPLC-ECD method to determine parabens.

To stablish the optimal detection potential, the hydrodynamic curves of all parabens were registered using the HPLC system with the SPCE for amperometric detection and 35% acetonitrile- 0.010 mol L^{-1} phosphate solution at pH 6 as mobile phase. As expected, all parabens showed a similar behaviour with an increase in peak current as the applied potential increases (Figure S2 in ESM). Although the highest peak currents were observed at potential of +1.2 V, the best signal-to-noise ratio was obtained at +1.0 V, thus this potential was selected as the optimal working potential for amperometric detection. A typical chromatogram obtained at the optimal separation and detection conditions is shown in Fig. 4.

3.3. Analytical parameters of the HPLC-ECD method

Calibration plots for MP, EP, iPP, PP, BP and BzP were obtained at the optimal working conditions, using standard solutions containing the six parabens at concentrations ranging from 0.010 mg L^{-1} to 30 mg L^{-1} prepared in the optimal mobile phase (35% acetonitrile- 65% 0.010 mol L^{-1} phosphate solution at pH 6). The analytical parameters obtained for the six parabens are presented in Table 1.

Good linear relationships (r^2 > 0.995) between peak area and concentration were obtained up to 20 mg L^{-1} for all parabens. Precision was calculated in terms of repeatability and reproducibility. For repeatability, five replicates of a 3.0 mg L^{-1} multi-analyte solution were injected throughout the same day. Reproducibility was calculated by injecting the multi-analyte solution daily along five days. The values of repeatability and reproducibility, expressed as relative standard deviation RSD%, were very similar and below 5% for all parabens.

To evaluate the robustness of the method, 1.0 mg L^{-1} multi-analyte standard solution was analysed by the HPLC method but introducing slight modifications in experimental parameters such as mobile phase, flow rate and temperature. No significant changes in retention times, resolutions and peak areas were observed when the acetonitrile percentage of the mobile phase, the temperature and flow rate were varied ±0.5%, ± 1 °C and ±0.01 mL min^{-1}, respectively.

Instrumental limits of detection (IDLs) and quantification (IQLs) were calculated as signal-to-noise ratio of 3:1 (S/N = 3) and 10:1 (S/N = 10), respectively. IDL between 20 and 115 µg L^{-1} were achieved with the proposed method. As was indicated in the Introduction Section, there are very few publications on paraben determination using HPLC methods with amperometric detection. Two of those publications use boron-doped diamond (BDD) electrodes for the ECD [43,46]. The IDLs values obtained in the present work are better or in the same order of magnitude than those reported in the UPLC-BDD method (30 µgL^{-1}) [46] and three orders of magnitude lower than the values indicated in the publication using HPLC-BDD (0.01% w/w) [43]. The IDLs obtained here are worse than those obtained using a glassy carbon electrode (1.5–2.5 µgL^{-1}) [45], but in that method BzP was not analysed. The IDL values published for a HPLC-ECD method using a SPCE modified with a graphene/polyvinylpyrrolidone/polyaniline-based nanocomposite [44] are of the same order of magnitude (between 10 µgL^{-1} and 30 µgL^{-1})

than the obtained ones in this work using an unmodified SPCE. Therefore, we consider that the here proposed method is an excellent, easier, and cheaper to implement option for paraben determination compared to the reported methods, since commercial SPCE are directly used without the need of additional time and reagents to modify the working electrode surface.

3.4. Optimization of sample pretreatments

Different methods for the extraction of parabens from liquid, semisolid and solid cosmetics have been optimized. After the sample pretreatment step, all extracts were analysed in triplicate using the HPLC system. For validation purposes, these results were compared to those obtained using the official extraction method [54] described in the Experimental Section 2.5.1.

3.4.1. Liquid cosmetics based on aqueous matrices

Liquid samples based on aqueous matrices, such as, facial tonics, were simply diluted and the suitability of different solvents to carry out this dilution was evaluated. Acetonitrile, methanol, water, and 35% acetonitrile-water mixture (organic modifier percentage in the mobile phase) were evaluated as solvents to dilute this type of cosmetics. These studies were carried out with the sample denoted as Facial Tonic 1 that according to the label contains MP and EP. The lowest concentration for both parabens were detected (Figure S3 in ESM) when water was used. This can be expected due to the low solubility of parabens in this solvent. No significant differences (95% confidence level) were observed between MP and EP concentration obtained following the official method and using methanol as solvent for the sample treatment. Thus, methanol was selected as the most adequate solvent for the dilution of cosmetics with liquid aqueous matrices.

3.4.2. Solid and liquid with semi-solid texture cosmetic samples

For this type of samples, such as shampoos and body creams, a method based on UAE was optimized. UAE parameters (e.g., mass to volume ratio, extraction solvent, temperature and time used for sonication) were optimized to obtain the highest efficiency in paraben extraction. Acetonitrile, methanol and 35% acetonitrile-water were assayed as extraction solvents. According to the results obtained for MP and EP extraction from Shampoo 1 (Figure S4 in ESM) the best conditions to perform the extraction of parabens from this type of samples were a mass to volume ratio of 1:9 (1.0 g–9.0 mL) using methanol as solvent, and sonication for 10 min at 25 °C applying 80 kHz of frequency and 100% power. Under these UAE conditions, no significant differences (95% confidence level) were observed for the concentrations of parabens in Shampoo 1 obtained using the UAE and the official method. This UAE method was also applied to an oil-based cosmetic sample containing MP, EP, PP and BP (Body Cream 1). No significant differences were observed (Figure S5 in ESM) in paraben concentrations using both the UAE procedure and the official method. The obtained results indicate that the proposed extraction method is adequate for the extraction of parabens from cosmetics with different compositions.

Table 2
Concentration (mean value and standard deviation of three replicated *(n = 3))* of parabens in cosmetic products determined using the UAE-HPLC-ECD and HPLC-DAD methods.

Sample	Concentration (wt. % ± SD, n = 3)							
	MP		EP		PP		BP	
	HPLC-ECD	HPLC-DAD	HPLC-ECD	HPLC-DAD	HPLC-ECD	HPLC-DAD	HPLC-ECD	HPLC-DAD
Facial Tonic 1	0.062 ± 0.001	0.063 ± 0.001	0.056 ± 0.002	0.060 ± 0.001	*	*	*	*
Facial Tonic 2	0.288 ± 0.003	0.29 ± 0.01	*	*	*	*	*	*
Shampoo 1	0.047 ± 0.002	0.046 ± 0.002	0.022 ± 0.001	0.022 ± 0.001	*	*	*	*
Shampoo 2[a]	0.292 ± 0.002	0.290 ± 0.001	0.285 ± 0.002	0.287 ± 0.001	*	*	*	*
Body Cream 1	0.081 ± 0.004	0.078 ± 0.003	0.025 ± 0.001	0.030 ± 0.001	0.015 ± 0.001	0.0125 ± 0.0004	0.031 ± 0.001	0.026 ± 0.001
Body Cream 2	0.081 ± 0.003	0.087 ± 0.001	*	*	0.029 ± 0.001	0.030 ± 0.001	*	*
Toothpaste 1	0.069 ± 0.002	0.069 ± 0.001	*	*	0.051 ± 0.002	0.054 ± 0.001	*	*
Toothpaste 2	0.11 ± 0.01	0.11 ± 0.01	*	*	0.08 ± 0.01	0.08 ± 0.01	*	*

*Not declared in the label.
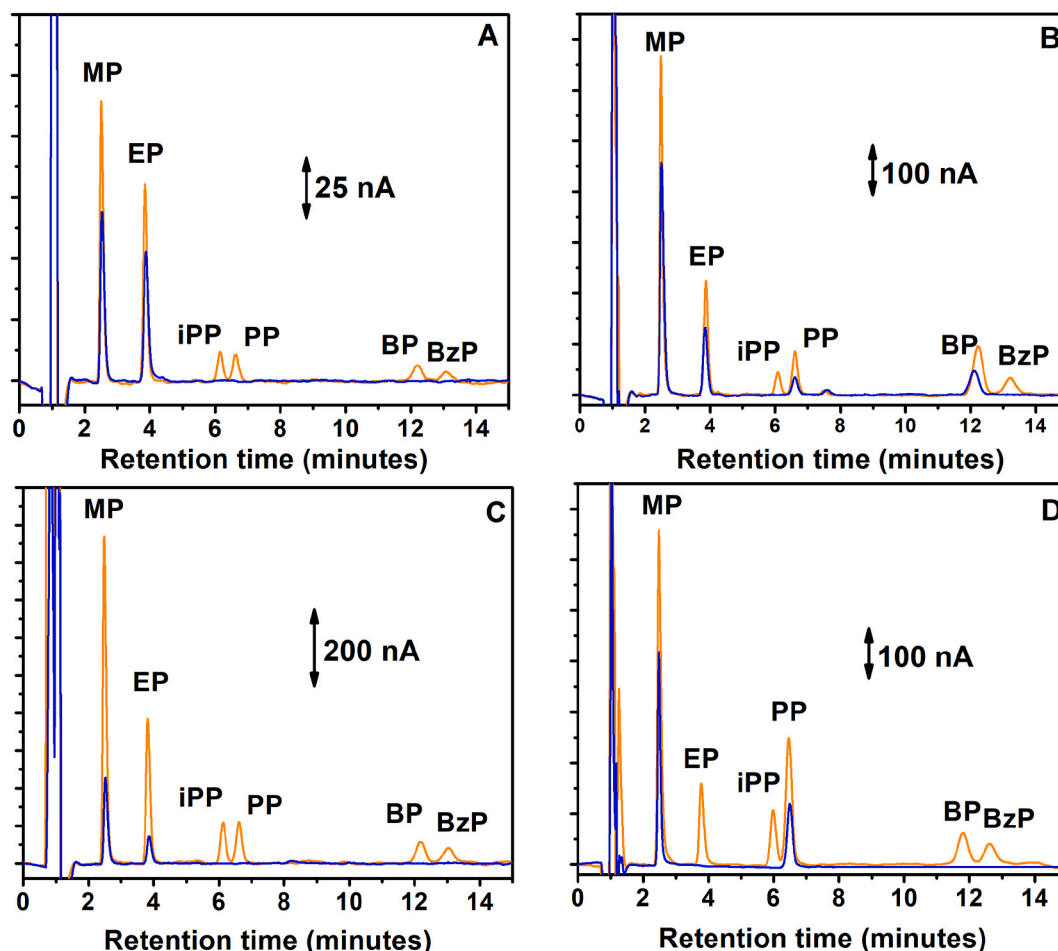[a] Additional 1:10 dilution.

Fig. 5. Chromatograms of (A) Facial tonic 1, (B) Body cream 1, (C) Shampoo 1 and (D) Toothpaste 1 obtained before (blue lines) and after (orange lines) fortification with MP, EP, iPP, PP, BP and BzP. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3.5. Analysis of real samples

The HPLC-ECD method was applied for the determination of MP, EP, iPP, PP, BP and BzP in eight cosmetic samples. Two facial tonics, two shampoos, two body creams, and two toothpastes, containing at least one of the studied parabens, were analysed. Prior to chromatographic analysis, liquid samples as facial tonics were diluted with methanol. Parabens from solid and liquid with semi-solid texture samples (i.e., shampoos, body creams and toothpastes) were extracted following the optimized UAE procedure described in the experimental section. An

external standard calibration method was used to determine the concentration of parabens. Concentrations (mean value and standard deviation of three replicates) of parabens in the samples are shown in Table 2. These results were compared with those obtained with DAD. In general, according to the Student's *t*-test at a 95% confidence level, no significant differences were obtained between the concentrations of all parabens calculated using DAD and ECD. MP was found in all samples in a higher content than the other parabens, indicating that MP is the most used paraben for cosmetic preservation. As could be expected, iPP and BzP were not found in the analysed samples as these parabens are

Table 3

Comparison of some analytical features with those obtained for other liquid chromatographic methods for paraben determination.

Analytes	Cosmetic products	Sample pre-treatment	Method	LOD[a]	Precision (RSD, %)	Total analysis time[b]	Reference
MP, EP, PP, BP, BzP	Liquid cosmetics based on aqueous matrices	Dilution + FPSE	HPLC-UV	7.6–17 µg L^{-1}	<5%	80 min	[18]
MP, EP, PP, BP, BzP	Cream samples	UAE + FPSE	HPLC-UV	0.025–0.058 µg g^{-1}	<5%	110 min	[18]
MP, BP and phthalate esters	Cream samples	DµSPE	HPLC-DAD	21–22 µg g^{-1}	<9%	50 min	[19]
MP, EP, PP, BP	Tonics, micellar waters and eau de toilettes	Dilution	HPLC-FLD	7–14 mg L^{-1}	<2.5%	15 min	[21]
MP, EP, PP, iBP, BP	Makeup remover	UAE	HPLC-ECD	0.04–0.11 mg L^{-1}	<12%	33 min	[44]
MP, EP, PP	Liquid cosmetics based on aqueous matrices	UAE	UPLC-ECD	8 mg L^{-1}	<5%	<20 min	[46]
MP, EP, PP	Cosmetics with solid and semi-solid texture	UAE	UPLC-ECD	15 µg g^{-1}	<5%	<20 min	[46]
MP, EP, PP, BzP, and bisphenol A	Shampoos and Hair Conditioners	UAE + SPE	HPLC-MS	0.8–2.3 µg g^{-1}	<5%	30 min	[50]
MP, PP, BP	Cosmetics with solid and semi-solid texture	UAE + FPSE	HPLC-DAD	0.072 µg g^{-1}	<15%	80 min	[20]
MP, EP, PP, BP and isothiazolinones	Cosmetics with solid and semi-solid texture	SPE	HPLC-DAD	6.7–13.3 µg L^{-1}	<6%	45 min	[55]
MP, EP, iPP, PP, BP, BzP	Liquid cosmetics based on aqueous matrices	Dilution	HPLC-ECD	4–23 mg L^{-1}	<5%	<20 min	This work
MP, EP, iPP, PP, BP, BzP	Cosmetics with solid and semi-solid texture	UAE	HPLC-ECD	0.9–5.2 µg g^{-1}	<9%	<35 min	This work

FPSE: Fabric-phase sorptive extraction.

DµSPE: dispersive magnetic micro solid-phase extraction.

[a] LOD estimated from the instrumental LOD reported in the work and the described procedure for sample preparation.

[b] Time estimated including sample preparation procedure and paraben determination.

banned in cosmetics since 2014. The concentration of parabens in all the analysed cosmetic samples meets the requirements stablished in the European Regulations [10–12].

For validation purposes, one cosmetic sample of each type (Facial Tonic 1, Shampoo 1, Body Cream 1, and Toothpaste 1) was fortified with the six parabens and analysed by triplicate. Prior to apply the HPLC-ECD method, the liquid sample was diluted with methanol and, for the other samples, the UAE procedure was carried out. Fig. 5 shows the chromatograms obtained for these samples before and after their fortification. Recoveries within 81%–116% with RSD values between 1% and 9% were obtained (Table S1 in ESM). These results demonstrate the accuracy of the HPLC-ECD method. The obtained recoveries also indicate the suitability of the proposed extraction procedure joint to the HPLC-ECD method for the determination of parabens in cosmetic samples with very different compositions and textures.

Table 3 shows a comparison between some characteristics of the method proposed in this work and those reported in other papers devoted to paraben determination in cosmetics. As can be seen, the precision and limits of detection (LODs) obtained in liquid and solid or semi-solid products are very similar to those reported for other authors in HPLC and UPLC methods with different detection modes. The lower LODs obtained by some authors [18,20,55] were achieved thanks to the preconcentration sample technique used. Apart from its good sensitivity, more selective detection is achieved with ECD than with DAD. In chromatograms obtained with DAD for some of the analysed samples, an additional peak due to an interference appears close to MP peak (Figure S6 in ESM), whereas this interference disappears when ECD is used (Fig. 5B). Moreover, as can be seen in Table 3, the methods indicated above include sample pretreatment approaches that are similar or more complicated (include more steps) than the proposed in this work. This fact is reflected in the total analysis time that was estimated including sample preparation procedure and HPLC paraben determination. As shown in Table 3, the total analysis times obtained in this work for liquid, solid, and semi-solid products are shorter or very similar to those achieved for methods previously published that even determine a minor number of parabens in the cosmetic products.

4. Conclusions

The good results obtained in this work show the utility and advantages of using disposable and commercial SPCE for paraben determination by HPLC-ECD. Analytical parameters of the method are comparable or better than other published for HPLC-ECD methods using modified electrodes for the amperometric detection. This method is cost effective, and easy and quick to implement since a previous modification of the electrode is not required. Sample treatment procedures have been optimized to extract parabens from cosmetics products with very different characteristics, from aqueous liquid samples to semi solid or even solid with oily components products. The maximum efficiency of paraben extraction is achieved using a short sample pretreatment, a low consumption of reagent and avoiding the decomposition of parabens. MP, EP, PP and BP are successfully determined in different commercial products such as two facial tonics, two shampoos, two body creams and two toothpastes using the HPLC-ECD method in a total analysis time lower than 20 min for facial tonics and 35 min for shampoos, body creams and toothpastes. Finally, the good recoveries obtained in validation studies on fortified samples show the suitability of the proposed method to ensure the compliance of different types of personal care products with regulations.

CRediT author statement

Lucía Abad-Gil: visualization, supervision, writing-original draft, writing-review and editing. Sergio Lucas-Sánchez: investigation, writing-review and editing. Carmen Isabel-Cabrera: investigation. Mª Jesús Gismera: supervision, writing-original draft, writing-review and editing. Mª Teresa Sevilla: writing-original draft, writing-review and editing. Jesús Rodríguez Procopio: conceptualization, supervision, writing-review and editing.

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.

Acknowledgements

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.talanta.2022.123459.

References

[1] A.F. Fransway, P.J. Fransway, D.V. Belsito, E.M. Warshaw, D. Sasseville, J. F. Fowler, J.G. DeKoven, M.D. Pratt, H.I. Maibach, J.S. Taylor, J.G. Marks, C.G. T. Mathias, V.A. DeLeo, J.M. Zirwas, K.A. Zug, A.R. Atwater, J. Silverberg, M. J. Reeder, Parabens. Dermatitis 30 (2019) 3–31, https://doi.org/10.1097/DER.0000000000000429.

[2] D. Bledzka, J. Gromadzinska, W. Wasowicz, Parabens. From environmental studies to human health, Environ. Int. 67 (2014) 27–42, https://doi.org/10.1016/j.envint.2014.02.007.

[3] F. Wei, M. Mortimer, H. Cheng, N. Sang, L.H. Guo, Parabens as chemicals of emerging concern in the environment and humans: a review, Sci. Total Environ. 778 (2021) 14615, https://doi.org/10.1016/j.scitotenv.2021.146150.

[4] M. Bilal, H.M.N. Iqbal, An insight into toxicity and human-health-related adverse consequences of cosmeceuticals- A review, Sci. Total Environ. 670 (2019) 555–568, 10.10167j.scitotenv.2019.03.261.

[5] Y. Nagar, R.S. Thakur, T. Parveen, D.K. Patel, K.R. Ram, A. Satish, Toxicity assessment of parabens in Caenorhabditis elegans, Chemosphere 246 (2020) 125730, https://doi.org/10.1016/j.chemosphere.2019.125730.

[6] D. Sadutto, R. Alvarez-Ruiz, Y. Pico, Systematic assessment of extraction of pharmaceuticals and personal care products in water and sediment followed by liquid chromatography-tandem mass spectrometry, Anal. Bioanal. Chem. 412 (2020) 113–127, https://doi.org/10.1007/s00216-019-02207-0.

[7] M.T. Garcia-Corcoles, R. Rodriguez-Gomez, B. Alarcon –Gomez, M. Cipa, L. Martín-Pozo, J.M. Kauffmann, A. Zafra-Gomez, Chromatographic methods for the determination of emerging contaminants in natural water and wastewater samples: a review, Crit. Rev. Anal. Chem. 49 (2019) 2 160–186, https://doi.org/10.1080/10408347.2018.1496010.

[8] L. Martín-Pozo, B. Alarcon-Gomez, R. Rodriguez-Gomez, M.T. Garcia-Corcoles, M. Cipa, A. Zafra-Gomez, Analytical methods for the determination of emerging contaminants in sewage sludge samples. A review, Talanta 192 (2019) 508–533, https://doi.org/10.1016/j.talanta.2018.09.056.

[9] N. Perez-Lemus, R. Lopez-Serna, S.I. Perez-Elvira, E. Barrado, Analytical methodologies for the determination of pharmaceuticals and personal care products (PPCPs) in sewage sludge: a critical review, Anal. Chim. Acta 1083 (2019) 19–40, https://doi.org/10.1016/j.aca.2019.06.044.

[10] (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on Cosmetic Products. http://data.europa.eu/eli/reg/2009/1223/2019-08-13 (accesed june 2021).

[11] Commission Regulation (EC) No 358/2014 of 4 April 2014 Amending Annex II and V to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on Cosmetic Products. http://data.europa.eu/eli/reg/2014/358/oj (accesed june 2021).

[12] Commission Regulation (EC) No 358/2014 of 18 September 2014 Amending Annex V to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on Cosmetic Products. http://data.europa.eu/eli/reg/2014/1004/oj (accesed june 2021).

[13] J.A. Ocaña-Gonzalez, M. Villar-Navarro, M. Ramos-Payan, R. Fernandez-Torres, M. A. Bello-Lopez, New developments in the extraction and determination of parabens in cosmetics and environmental samples. A review, Anal. Chim. Acta 858 (2015) 1–15, https://doi.org/10.1016/j.aca.2014.07.002.

[14] N. Cabaleiro, I. de la Calle, C. Bendicho, I. Lavilla, An overview of sample preparation for the determination of parabens in cosmetics, Trac. Trends Anal. Chem. 57 (2014) 34–46, https://doi.org/10.1016/j.trac.2014.02.003.

[15] V. Alampanos, V. Samanidou, An overview of sample preparation approaches prior to liquid chromatography methods for the determination of parabens in biological matrices, Microchem. J. 164 (2021) 105995, https://doi.org/10.1016/j.microc.2021.105995.

[16] L. Martin-Pozo, M.C. Gomez-Regalado, I. Moscoso-Ruiz, A. Zafra-Gomez, Analytical methods for the determination of endocrine disrupting chemicals in cosmetics and personal care products: a review, Talanta 234 (2021) 122642, https://doi.org/10.1016/j.talanta.2021.122642.

[17] G. Alvarez-Rivera, M. Llompart, M. Lores, C. Garcia-Jares, A. Salvador, A. Chisvert, Preservatives in Cosmetics: Regulatory Aspects and Analytical Methods in Analysis of Cosmetics Products, Elsevier, 2018.

[18] R. Kaur, Kaur R. Heena, A. Grover, S. Rani, A.K. Malik, A. Kabir, K.G. Furton, Trace determination of parabens in cosmetics and personal care products using fabric phase sorptive extraction and high-performance liquid chromatography with UV detection, J. Separ. Sci. 43 (2020) 2626–2635, https://doi.org/10.1002/jssc.201900978.

[19] N. Jalilian, H. Ebrahimzadeh, A. Asgharinezhad, Preparation of magnetite/multiwalled carbon nanotubes/metal –organic framework composite for dispersive magnetic micro solid phase extraction of parabens and phthalate esters from water samples and various types of cream for their determination with liquid chromatography, J. Chromatogr. A 1608 (2019) 460426, https://doi.org/10.1016/j.chroma.2019.460426.

[20] S. Gülle, H.I. Ulusoy, A. Kabir, A. Tartaglia, K.G. Furton, M. Locatelli, V. F. Samanidou, Application of a fabric phase sorptive extraction high performance liquid chromatography-photodiode array detection method for the trace determination of methyl paraben, propyl paraben and butyl paraben in cosmetic and environmental samples, Anal. Methods 11 (2019) 6136–6145, https://doi.org/10.1039/c9ay02260k.

[21] A. Zgota-Grzeskowiak, J. Werner, M. Jeszka-Skowron, B. Czarczynska-Goslinska, Determination of parabens in cosmetic products using high-performance liquid chromatography with fluorescence detection, Anal. Methods 8 (2016) 3903–3909, https://doi.org/10.1039/c6ay00521g.

[22] S. Michalkiewicz, Anodic oxidation of parabens in acetic acid–acetonitrile solutions, J. Appl. Electrochem. 43 (2013) 85–97, https://doi.org/10.1007/s10800-012-0502-5.

[23] E. de S. Gil, C.H. Andrade, N.L. Barbosa, R.C. Braga, S.H.P. Serrano, Cyclic voltammetry and computational chemistry studies on the evaluation of the redox behavior of parabens and other analogues, J. Braz. Chem. Soc. 23 (3) (2012) 565–572, https://doi.org/10.1590/S0103-50532012000300025.

[24] K.M. Naik, S.T. Nandibewoor, Electroanalytical method for the determination of methylparaben, Sens. Actuator A-Phys. 212 (2014) 127–132, https://doi.org/10.1016/j.sna.2014.03.033.

[25] M.S.R. Dantas, A.S. Lourenço, A.C. Silva, K.M. Bichinho, M.C.U. Araujo, Simultaneous determination of methyl, ethyl, propyl, and butyl parabens in sweetener samples without any previous pretreatment using square wave voltammetry and multiway calibration, Food Chem. 365 (2021) 130472, https://doi.org/10.1016/j.foodchem.2021.130472.

[26] P. Luo, J. Liu, Y. Li, Y. Miao, B. Ye, Voltammetric determination of methylparaban in cosmetics using a multi-wall carbon nanotubes/nafion composite modified glassy carbon electrode, Anal. Lett. 45 (2012) 2445–2454, https://doi.org/10.1080/00032719.2012.691589.

[27] J.R. Steter, R.S. Rocha, D. Dionísio, M.R.V. Lanza, A.J. Motheo, Electrochemical oxidation route of methyl paraben on a boron-doped diamond anode, Electrochim. Acta 117 (2014) 127–133, https://doi.org/10.1016/j.electacta.2013.11.118.

[28] L. Wang, Y. Li, G. Li, B. Ye, A new strategy for enhancing electrochemical sensing from MWCNTs modified electrode with Langmuir-Blodgett film and used in determination of methylparaben, Sensor. Actuator. B Chem. 211 (2015) 332–338, https://doi.org/10.1016/j.snb.2015.01.056.

[29] C.D. Mendonça, T.M. Prado, F.H. Cincotto, R.T. Verbinnen, S.A.S. Machado, Methylparaben quantification via electrochemical sensor based on reduced graphene oxide decorated with ruthenium nanoparticles, Sensor. Actuator. B Chem. 251 (2017) 739–745, https://doi.org/10.1016/j.snb.2017.05.083.

[30] W.E.F.W. Khalid, M.N.M. Mohamad Nasir Mat Arip, L. Jasmani, Y.H. Lee, A new sensor for methyl paraben using an electrode made of a cellulose nanocrystal–reduced graphene oxide nanocomposite, Sensors 19 (2019) 2726, https://doi.org/10.3390/s19122726.

[31] L.F. de Lima, C.M. Daikuzono, C.M. Miyazaki, E.A. Pereira, M. Ferreira, Layer-by-Layer nanostructured films of magnetite nanoparticles and polypyrrole towards synergistic effect on methylparaben electrochemical detection, Appl. Surf. Sci. 505 (2020) 144278, https://doi.org/10.1016/j.apsusc.2019.144278.

[32] J.A. Rather, A.J. Al Harthi, E.A. Khudaish, A. Qurashi, A. Munam, P. Kannan, An electrochemical sensor based on fullerene nanorods for the detection of paraben, an endocrine disruptor, Anal. Methods 8 (2016) 5690–5700, https://doi.org/10.1039/c6ay01489e.

[33] A.K. Baytak, T. Teker, S. Duzmen, M. Aslanoglu, A novel electrochemical platform based on carbon nanofibers and tri-metallic nanoparticles of gold, nickel and cobalt for the quantification of ethyl paraben, Mater. Sci. Eng. C-Mater. Biol. Appl. 72 (2017) 301–307, https://doi.org/10.1016/j.msec.2016.11.080.

[34] J.A. Rather, A. Al Abri, P. Kannan, Electrochemical sensing of parabens in solubilized ionic liquid system at polyaniline decorated gold nanoparticles constructed interface, Microchem. J. 159 (2020) 105379, https://doi.org/10.1016/j.microc.2020.105379.

[35] L.A. Goulart, T.T. Guaraldo, M.R.V. Lanza, A novel electrochemical sensor based on printex L6 carbon black carrying CuO/Cu2O nanoparticles for propylparaben determination, Electroanalysis 30 (2018) 2967–2976, https://doi.org/10.1002/elan.201800549.

[36] G. Manasa, R.J. Mascarenhas, B.M. Basavaraja, Sensitively-selective determination of Propyl Paraben preservative based on synergistic effects of polyaniline-zinc-oxide nano-composite incorporated into graphite paste electrode, Colloids Surf. B Biointerfaces 184 (2019) 110529, https://doi.org/10.1016/j.colsurfb.2019.110529.

[37] S.A. Qurashi, J.A. Rather, T. Yamazaki, M. Sohail, K. De Wael, B. Merzougui, A. S. Hakeem, Swift electrochemical detection of paraben an endocrinedisruptor by In2O3 nanobricks, Sensor. Actuator. B Chem. 221 (2015) 167–171, https://doi.org/10.1016/j.snb.2015.06.026.

[38] M.A. Lorenzo, A. Sánchez Arribas, M. Moreno, E. Bermejo, M. Chicharro, A. Zapardiel, Determination of butylparaben by adsorptive stripping voltammetry

at glassy carbon electrodes modified with multi-wall carbon nanotubes, Microchem. J. 110 (2013) 510–516, https://doi.org/10.1016/j.microc.2013.05.018.

[39] L. Wang, Y. Li, G. Li, Y B, A new strategy for enhancing electrochemical sensing from MWCNTs modified electrode with Langmuir-Blodgett film and used in determination of methylparaben, Sensor. Actuator. B Chem. 211 (2015) 332–338, https://doi.org/10.1016/j.snb.2015.01.056.

[40] C. Radovan, D. Cinghită, F. Manea, M. Mincea, C. Cofan, V. Ostafe, Electrochemical sensing and assessment of parabens in hydro- alcoholic solutions and water using a boron-doped diamond electrode, Sensors 8 (2008) 4330–4349, https://doi.org/10.3390/s8074330.

[41] A. Kannan, K.S.S. Devi, B. Dinesh, U.M. Krishnan, S. Gandhi, Tailoring the electrochemical interface of mesoporous carbon with ubiquinone for detection of parabens in cosmetics, ChemistrySelect 5 (2020) 4628–4636, https://doi.org/10.1002/slct.202000185.

[42] K. Murakami, H. Watanabe, T. Tateno, J.-M. Kauffmann, Comparative study of the determination of parabens in shampoos by liquid chromatography with amperometric and coulometric detection, Electroanalysis 22 (15) (2010) 1702–1706, https://doi.org/10.1002/elan.201000042.

[43] I. Martins, F. Cristiani Carreira, L.S. Canaes, F.A. de Souza Campos Junior, L.M. da Silva Cruz, S. Rath, Determination of parabens in shampoo using high performance liquid chromatography with amperometric detection on a boron-doped diamond electrode, Talanta 85 (2011) 1–7, https://doi.org/10.1016/j.talanta.2011.04.047.

[44] S. Kajornkavinkul, E. Punrat, W. Siangproh, N. Rodthongkum, N. Praphairaksit, O. Chailapakul, Graphene/polyinylpyrrolidonde/polyaniline nanocomposite-modified electrode for simultaneous determination of parabens by high performance liquid chromatography, Talanta 148 (2016) 655–660, https://doi.org/10.1016/j.talanta.2015.05.044.

[45] M.B. Hicks, L. Salituro, I. Mangion, W. Schafer, R. Xiang, X. Gong, C.J. Welch, Assessment of coulometric array electrochemical detection coupled with HPLC-UV for the absolute quantitation of pharmaceuticals, Analyst 142 (2017) 525–536, https://doi.org/10.1039/c6an02432g.

[46] M. Chuto, S. Chaiyo, W. Siangproh, O. Chailapakul, A rapid separation and highly determination of paraben species by ultra-performance liquid chromatography-electrochemical detection, Detection 1 (2013) 21–29, https://doi.org/10.4236/detection.2013.12004.

[47] S. Sheng, L. Zhang, G. Chen, Low-cost fabrication of graphene ball electrodes for the amperometric detection of capillary electrophoresis, Electrochem. Commun. 24 (2012) 13–16, https://doi.org/10.1016/j.elecom.2012.08.001.

[48] A.L. Squissato, R.A.A. Muñoz, C.E. Banks, E.R. Richter, An overview of recent electroanalytical applications utilizing screen-printed electrodes within flow systems, Chemelectrochem 7 (2020) 2211–2221, https://doi.org/10.1002/celc.202000175.

[49] A. García-Miranda Ferrari, S.J. Rowley-Neale, C.E. Banks, Screen-printed electrodes: transitioning the laboratory in-to-the field, Talanta Open 3 (2021) 100032, https://doi.org/10.1016/j.talo.2021.100032.

[50] H. Shaaban, A. Mostafa, W. Alhajri, L. Almubarak, K. Alkhalifah, Development and validation of an eco-friendly SPE-HPLC-MS method for simultaneous determination of selected parabens and bisphenol A in personal care products: evaluation of the greenness profile of the developed method, J. Liq. Chromatogr. Relat. Technol. 41 (2018) 1–8, https://doi.org/10.1080/10826076.2018.1499527.

[51] E. Ghasemi, M. Sillanpaa, Ultrasound-assisted solid-phase extraction of parabens from environmental and biological samples using magnetic hydroxyapatite nanoparticles as an efficient and regenerable nanosorbent, Microchim. Acta 186 (2019) 622, https://doi.org/10.1007/s00604-019-3720-2.

[52] R. Perestrelo, P. Silva, P. Porto-Figueira, J.A.M. Pereira, C. Silva, S. Medina, J.S. Câmaea, QuEChERS- Fundamentals, relevant improvements, applications and future trends, Anal. Chim. Acta 1070 (2019) 1–28, https://doi.org/10.1016/j.aca.2019.02.036.

[53] R.A. Gonzalves, N. Nagata, P.G. Peralta-Zamora, Optimizacao e validacao de método baseado em QuEChERS para determinacao de conservantes em cosméticos por HPLC-DAD, Quim. Nova 43 (2020) 175–180, https://doi.org/10.21577/0100-4042.20170471.

[54] Seventh Commission Directive 96/45/EC of 2 July 1996 Relating to Methods of Analysis Necessary for Checking the Composition of Cosmetic Products. http://data.europa.eu/eli/dir/1996/45/oj (accesed june 2021).

[55] H.M. Ali, I.H. Alsohaimi, M.R. Kha, M. Azam, Simultaneous determination of isothiazolinones and parabens in cosmetic products using solid-phase extraction and ultra-high performance liquid chromatography/diode array detector, Pharmaceuticals 13 (11) (2020) 412, https://doi.org/10.3390/ph13110412.