



4-ethylphenol detection in wine by fullerene modified screen-printed carbon electrodes

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ABSTRACT

This work shows the potential of modified screen-printed carbon electrodes (SPCEs) for sensitive and selective detection of 4-ethylphenol in wine. Gold nanoparticles (AuNPs) and fullerene C₆₀ (C₆₀), modified sensors have been compared. pH of the supporting electrolyte, deposition time and working temperature have been optimized considering their influence in the voltammetric pulse response of 4-ethylphenol. Under the optimal conditions of measurement, the developed activated C₆₀/SPCE (AC₆₀/SPCE) shows the best performance, with a detection capability of 400 µg/L and 700 µg/L, when using deposition times of 14 min and 6 min, respectively ($\alpha = \beta = 0.05$). The reproducibility of the developed sensor resulted better when a deposition time of 6 min was used (5.4 %, n = 3). The influence of different interferences on the analytical response has been studied, as well as their application in the determination of 4-ethylphenol in different wine samples.

1. Introduction

In wine industry, quality control of the final product is an issue of growing importance for manufacturers to guarantee the obtention of more competitive final products. In this sense, the organoleptic properties of a wine are one of the key parameters to determine its quality. The appearance of compounds that produce unpleasant odours in these products may cause serious economic losses to the wine industry. Among the most common compounds that may reduce wine quality are volatile phenols, including 4-ethylphenol [1,2]. The formation of 4-ethylphenol takes place by decarboxylation of hydroxycinnamic acids by yeasts of the *Brettanomyces/Dekkera bruxellensis* genus, existing in the microflora of grapes [3-5]: they are first converted to hydroxystyrene by the action of hydroxycinnamate decarboxylase enzyme and subsequently reduced to ethyl derivatives by vinylphenol reductase enzyme. Furthermore, the concentration of 4-ethylphenol frequently increases during aging process and even after the wine is bottled, producing undesirable off-flavours to wine, described as animal odours, horse sweat, stable or varnish [1,2]. Thus, different analytical methods have been developed for the determination of this compound in wine quality control, being gas chromatographic techniques the most widely used including mass spectrometry detection [2,6-16] and, in a less extent, flame ionisation detection [17-21]. These chromatographic procedures involve the extraction of 4-ethylphenol from wine matrix using different

approaches, such as liquid-liquid extraction [10,11,19], dispersive liquid-liquid microextraction [8,15,16], solid-phase extraction [12,15], solid phase microextraction [10,14,18-20] or stir bar sorptive extraction [9,13]. Thus, chromatographic procedures result time consuming, using high-cost equipment that is often not useful for real-time or *in situ* analysis. On the contrary, electroanalytical techniques offers an effective approach in biological and environmental analysis due to important advantages such as cost-effectiveness, fast response and ease of miniaturization and portability, keeping a high degree of selectivity and sensitivity [22-27]. Their use for the determination of 4-ethylphenol is currently emerging using different types of electrodes including carbon electrodes [28-33], gold electrodes [34-36] and electrochemical biosensors [32,33]. Nevertheless, only a few of these works have been applied in the determination of this molecule in wine (Table 1). Due to the complex matrix of wine samples, modification of the working electrode with molecularly imprinted polymers [29] or the use of chemometric tools [31] has been attempted in order to obtain selective signals. However, these methods are still characterized by poor sensitivity. It is well-known that both sensitivity and selectivity in the determination of different analytes can be improved by using nanomaterials, such as metallic nanoparticles [37-40] and fullerene C₆₀ (C₆₀) [41-44].

Metallic nanoparticles are characterized by large response surface, high catalytic and mass transfer activities that may increase the selectivity and sensitivity of sensors [45]. Among them, gold nanoparticles

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Table 1
Electrochemical determination of 4-ethylphenol.

Technique	Electrode	Modification	Limit of detection ($\mu\text{g/L}$)	Reprod.	Sample	Recovery	Ref
DPV	GCE	–	–	–	–	–	[28]
		MIP with polypyrrol	24.4	3.0%	Wine	101%	[29]
	GECE	MIP with divinylbenzene	1300	–	–	–	[30]
	Gold	–	290	–	–	–	[34]
		MIN with 4-vinylpyridine	70	–	–	–	[34]
		MIP with 4-vinylpyridine and ethylene dimethacrylate	68	17.4 %	–	–	[35]
CV	GECE	CuNPs, WO ₃ NPs, Cophthalocyanine, Bi ₂ O ₃ NPs and polypyrrole	36	10.0 %	–	–	[36]
			1800	4.6 %	Spiked wine samples	–	[31]
Amp	CNT/GCE	Tyr	25.7	–	Synthetic cocktail	–	[32]
	SPCE	Tyr	1.4	7.0 %	Water	–	[33]
	CNT/GCE	Tyr	12.2	–	Synthetic cocktail	108%	[32]

GCE, Glassy carbon electrode; CNT/GCE, Glassy carbon electrode modified with carbon nanotubes; GECE, Graphite Epoxy Composite Electrode; MIN, molecularly imprinted nanoparticle; MIP, molecularly imprinted polymer; SPCE, Screen Printed Carbon Electrode; Tyr, Tyrosinase.

(AuNPs) are the most used due to their high surface-to-volume ratio and biocompatible and low toxicity [39,40,45,46]. Another alternative for electrode modification is C₆₀, which is a carbon allotrope whose structure is completely different from that of other carbonated compounds. It is an electrochemically attractive material widely used due to its ability to accept and donate electrons [47]. Thus, the present work is focused on the preparation of novel electrochemical sensors for 4-ethylphenol using screen-printed carbon electrodes (SPCEs) modified with C₆₀ and/or AuNPs. These electrodes have been selected considering their exceptional properties compared to those of conventional electrodes, including low cost and mass production, disposability, high versatility to modification and high ability to connect to portable devices that make them useful for *in situ* analysis [24,48-50]. The performance of the developed method has also been studied in terms of reproducibility, capability of detection, as well as by its application to the quantification of 4-ethylphenol in different commercial wine samples.

2. Material and methods

2.1. Reagents

Analytical-reagent grade chemicals were used. Type-I water (Millipore, Bedford, MA, USA), 18.2 M Ω cm, was used for the preparation of all solutions. Britton Robinson (BR) buffer solutions, containing 0.04 M phosphoric acid (Panreac, Barcelona, Spain), 0.04 M acetic acid (VWR Chemical, Fontenay, France) and 0.04 M boric acid (Panreac, Barcelona, Spain), were used as supporting electrolyte for the electrochemical measurements. 1 M NaOH (Ecos, Barcelona, Spain) solutions were used to adjust the pH value of the buffer solutions.

H₂AuCl₄ solutions were prepared by dissolving the appropriate amount of hydrogen tetrachloroaurate(III) trihydrate (Acros Organics, Geel, Belgium) in 0.5 M sulfuric acid (Merck, Darmstadt, Germany). C₆₀ solutions were prepared from fullerene (Acros Organics, Geel, Belgium) using dichloromethane (Panreac, Barcelona, Spain) as solvent.

Stock standard solutions of 4-ethylphenol (Alfa Aesar, Haverhill, Massachusetts, USA) were prepared by dissolving the adequate amount in Milli-Q water.

2.2. Preparation of AuNPs/SPCEs

The electrochemical deposition of AuNPs was performed in a 100 μL drop of a 0.1 mM H₂AuCl₄ solution prepared in 0.5 M H₂SO₄, applying a potential of +0.18 V, according to a previously described procedure [48,51]. The optimum deposition time for the AuNPs formation was estimated by means of cyclic voltammetric measurements performed in a 0.05 M H₂SO₄ solution in the potential range from 0 to +1.5 V, at a scan rate of 100 mV/s. It was observed a well-defined reduction peak at +0.50 V as AuNPs were deposited on the electrode surface, which can be associated to the reduction of gold surface oxide. Longer deposition

times led to higher intensities of this peak. In the case of using deposition times higher than 350 s, an oxidation peak gave rise at +1.0 V approx. This oxidation peak was related to the formation of a gold film on the electrode surface [52,53], which leads to the loss of the unique properties provided by the modification with nanoparticles [38-40,46]. Thus, a value of 350 s was selected as the optimum to guarantee the formation of AuNPs on the SPCE surface.

2.3. Preparation of AC₆₀/SPCEs

The modification of the SPCE surface by C₆₀ was performed following a previous reported method [42]. Briefly, 40 μL of 0.1 mg mL⁻¹ solution of C₆₀ in dichloromethane, except for the optimization process, was deposited on the SPCE surface and left to dry at room temperature.

The C₆₀/SPCE surface was then activated by means of cyclic voltammetry. 50 μL of a 1.0 M KOH solution were deposited on the working electrode surface and the C₆₀ film was partially reduced by ranging the potential from 0 to +1.5 V, for 1 cycle at a scan rate of 10 mV s⁻¹. After this partial reduction, the activated C₆₀/SPCE (AC₆₀/SPCE) becomes sufficiently conductive to be used as a sensitive working electrode [43,54,55].

2.4. Electrochemical measurements

Electrochemical measurements were carried out using a PalmSens4 potentiostat (PalmSens BV, Houten, The Netherlands) using SPCEs (DRP-C11L, Metrohm DropSens, Oviedo, Spain) modified with C₆₀ and/or AuNPs.

The accumulation of 4-ethylphenol on the AC₆₀/SPCE surface was performed at the headspace of a sealed cell [56]. 1.0 mL of the corresponding concentration of the target analyte solution, prepared in BR pH 5.8, were placed into a sealed cell, with the AC₆₀/SPCE on set the top, as far as possible from the solution. The accumulation of the 4-ethylphenol, present in the headspace of the sample, was carried out under stirring during a deposition time of 360 s. The temperature was also controlled during this accumulation step and a value of 54 °C was settled, except for the optimization process. The accumulation of 4-ethylphenol on AuNPs/SPCEs was performed following a similar procedure by means of the stirred deposition of the analyte in BR pH 5.0 during 650 s.

After the incubation process, the electrochemical sensor was carefully removed from the cell and rinsed with Milli-Q water. Next, 100 μL of a BR solution of pH 5.8 for AC₆₀/SPCEs or pH 5.0 for AuNPs/SPCE, were placed on the electrode and differential pulse voltammograms (DPVs) were recorded from -0.2 V to +0.8 V, at room temperature. Other instrumental parameters were pulse potential, +0.01 V; step potential, +0.02 V; pulse time, 0.02 s and scan rate, 50 mV s⁻¹.

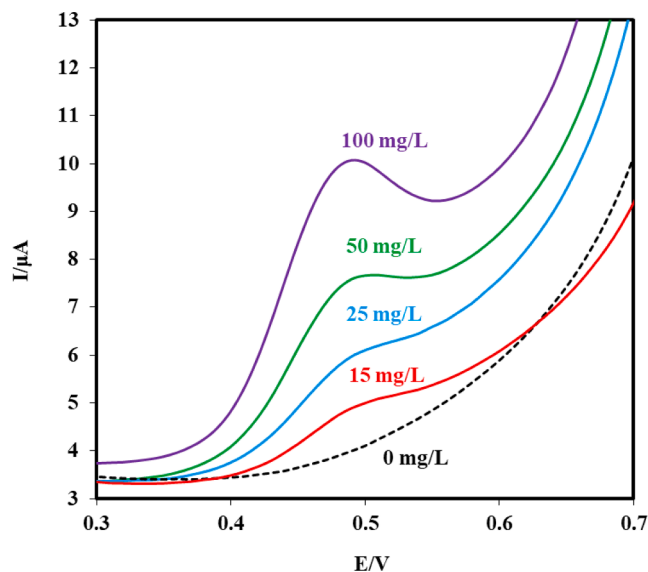


Fig. 1. Differential pulse voltammograms for 4-ethylphenol solutions of concentrations ranging from 0 to 100 mg/L using a AuNPs/SPCE (BR pH 5.0, deposition time, 650 s; pulse potential, +0.01 V; step potential, +0.02 V; pulse time, 0.02 s and scan rate, 50 mV s^{-1}).

3. Results

The electrochemical response of 4-ethylphenol has been described as an oxidation process in the ortho position of the molecule, giving rise to the corresponding quinone [28]. This oxidation response may be used for the quantitative analysis of 4-ethylphenol, so it is very important that it is sensitive and selective enough. Different nanomaterial modified electrodes, including AuNPs and AC_{60} , have been tested with this aim.

3.1. DPV determination of 4-ethylphenol using AuNPs/SPCEs.

The DPV oxidation behaviour of 4-ethylphenol using a AuNPs/SPCE was first studied. The AuNPs/SPCE used for this aim was constructed following the procedure defined in section 2.2, based on the electrodeposition of AuNPs on the SPCE surface applying a potential of + 0.18 V during 350 s.

In order to ensure the quality of the analytical results, the experimental parameters that may have influence in the oxidation response of 4-ethylphenol, using the described AuNPs/SPCEs, were optimized. Thus, the joint optimization of pH of BR solutions and deposition time of 4-ethylphenol on the electrode surface was performed using the experimental design methodology. A central composite design 2^2 , in which the oxidation intensity of a 10 mg/L 4-ethylphenol solution was taken as response variable, was carried out. Eleven experiments were performed to analyse five levels for each of the factors, obtaining a maximum in the response surface for pH and deposition time values of 5.0 and 650 s, respectively. Under these experimental conditions, a well-defined oxidation peak at + 0.48 V, useful for quantitative determination of 4-ethylphenol, was observed (Fig. 1). Hence, different calibrations curves were constructed, which were used to validate the analytical method in terms of precision and capability of detection.

The dispersion of the results was evaluated in terms of the relative standard deviation (RSD) of the slopes associated with different calibration curves. This procedure avoids obtaining incorrect results when considering just a single concentration, since the dispersion may be usually stabilized at high concentration values. Therefore, three calibrations were made in the concentration range from 3 to 25 mg/L of 4-ethylphenol, using a AuNPs/SPCE to estimate the reproducibility. Outliers points with a studentized residual above 2.5 in absolute value were removed in order to provide a correct evaluation of the calibration

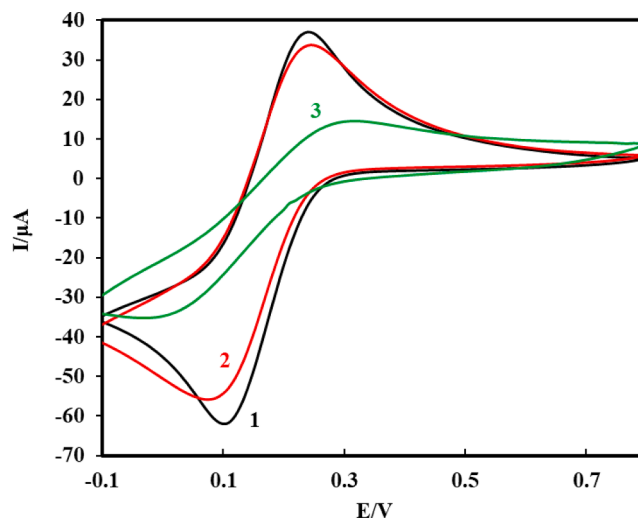


Fig. 2. Cyclic voltammograms obtained for 1 mM $\text{Fe}(\text{CN})_6^{3-}$ solution in BR pH 6 using AC_{60} /SPCEs modified with C_{60} solutions prepared in different solvents: (1) dichloromethane; (2) toluene; (3) dimethylformamide.

parameters, obtaining a RSD value of 8.2 %.

Decision limit ($\text{CC}\alpha$) and capability of detection ($\text{CC}\beta$) were estimated using also the validated calibration curves. $\text{CC}\alpha$ of the procedure is defined as the lowest concentration level at which the method can discriminate if the analyte of interest is in the sample with a probability of $1-\alpha$, where α is the false positive. In the same way, $\text{CC}\beta$ is estimated as the lowest concentration level of analyte, with a probability of $1-\beta$ (β , false negative), that the method is able to detect [57]. When using and an $\alpha = \beta = 0.05$ value, a $\text{CC}\alpha$ of 2.78 mg/L was obtained, while $\text{CC}\beta$ resulted to be lower than the concentration of the first calibration point. Therefore, a concentration of 3 mg/L was taken as the capability of detection of the developed method.

3.2. DPV detection of 4-ethylphenol using an AC_{60} /SPCE.

In order to improve the selectivity and sensitivity of the above

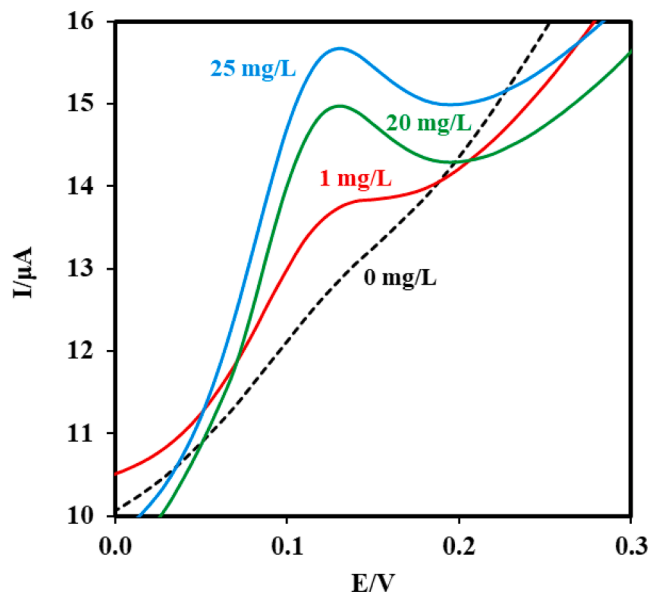


Fig. 3. Differential pulse voltammograms for 4-ethylphenol solutions of concentrations ranging from 0 to 25 mg/L using an AC_{60} /SPCE (BR pH 5.8, deposition time, 14 min; deposition temperature, 54 $^{\circ}\text{C}$; pulse potential, +0.01 V; step potential, +0.02 V; pulse time, 0.02 s and scan rate, 50 mV s^{-1}).

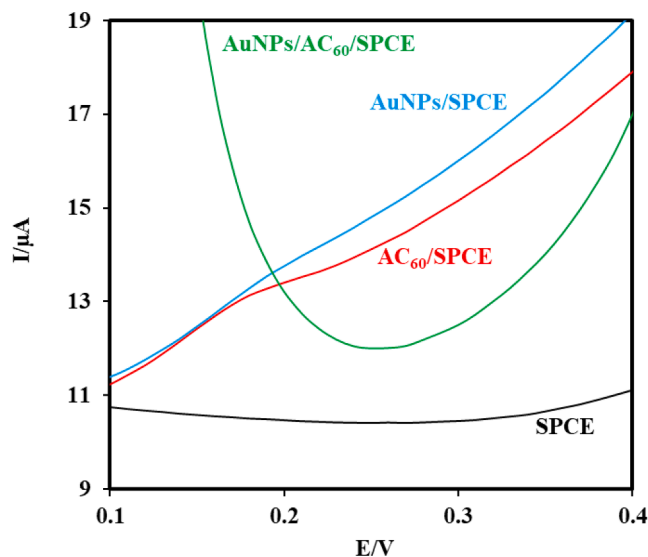


Fig. 4. Differential pulse voltammograms for a 1000 µg/L 4-ethylphenol solution using different electrodes (BR pH 5.8, deposition time, 6 min; deposition temperature, 54 °C; pulse potential, +0.01 V; step potential, +0.02 V; pulse time, 0.02 s and scan rate, 50 mV s⁻¹).

electrochemical method, a modification of the electrode surface with AC₆₀ was also performed. The optimization of this electrochemical response began through a series of experiments to find the best experimental conditions for the modification of the electrode surface. Thus, different solvents were first tested, named dichloromethane, toluene and dimethylformamide, for the preparation of C₆₀ solutions [41,42,44]. The electrochemical response of the different modified electrodes was characterized by cyclic voltammetry using Fe(CN)₆^{3-/4-} as redox probe, achieving the best results when C₆₀ was solved in dichloromethane (Fig. 2).

Next optimization experiments, consisted of finding the best values of the experimental variables that may have significant influence on the analytical response, were performed. For this reason, pH of the supporting electrolyte and deposition time of 4-ethylphenol were optimized. Moreover, in this case, the working temperature was also considered as an influence factor in the deposition of 4-ethylphenol on the electrode surface. The joint optimization of the influence of these variables in the analytical response of a 10 mg/L 4-ethylphenol solution, using central composite designs, led to an optimum value for pH of 5.8 and, 14 min and 54 °C for time and temperature of incubation, respectively. Under these optimized conditions, the electrochemical response of 4-ethylphenol by DPV showed an oxidation peak at + 0.2 V (Fig. 3). Thus, C₆₀ modification of the working electrode led to significantly lowering of peak potential improving the selectivity.

The precision and the capability of the detection of the procedure based on the use of AC₆₀/SPCEs were also calculated, by means of the construction of different validated calibration curves in the range from 400 to 800 µg/L. The reproducibility was calculated in terms of RSD for the slopes of 3 calibration sets using different electrode surfaces, obtaining a value of 9.4 %. CC_α (101.9 µg/L) and CC_β values were also calculated according to ISO 11,843 for $\alpha = \beta = 0.05$ [57]. The value obtained for CC_β was lower than the concentration of the first calibration point, so 400 µg/L was considered as the capability of detection of the method, leading to a higher sensitivity than the previously described AuNPs/SPCEs.

An incubation time of 14 min implies spending a long time for each calibration analysis, which is incompatible with real-time analysis. Therefore, a study of the influence of this parameter on the sensitivity of the method was carried out. Thus, calibration curves using different deposition times ranging from 4 to 14 min were constructed in the

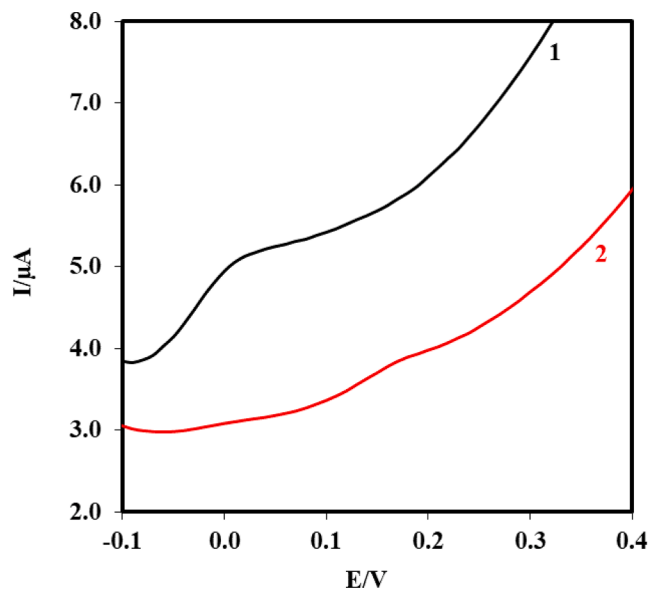


Fig. 5. Differential pulse voltammograms for [4-ethylphenol], 700 µg/L; [4-ethylguaicol], 900 µg/L (1) and [4-ethylphenol], 700 µg/L; [4-ethylguaicol], 1100 µg/L (2) using an AC₆₀/SPCE (BR pH 5.8, deposition time, 360 s; deposition temperature, 54 °C; pulse potential, +0.01 V; step potential, +0.02 V; pulse time, 0.02 s and scan rate, 50 mV s⁻¹).

concentration range from 700 to 1300 µg/L. The analysis of the slopes, obtained for the different analysed times, shown that a deposition time of 6 min gave rise to a similar sensitivity value to that obtained for 14 min, reducing the analysis time to less than half. The capability of detection obtained using this shorter time was 700 µg/L, slightly higher than that obtained for 14 min. However, the reproducibility of the method (RSD, 5.4 %; n, 3) was better than that obtained with longer deposition times. Therefore, 6 min can be selected as good enough for the determination of 4-ethylphenol in real samples.

Moreover, a study of the possible improvement that the presence of AuNPs could exert on the described AC₆₀/SPCEs was also carried out. Thus, AC₆₀/SPCEs were modified with AuNPs by means of the electro-deposition procedure described in section 2.2. The electrochemical response obtained for the developed AuNPs/AC₆₀/SPCEs together with the analytical responses obtained for SPCEs, AuNPs/SPCEs and AC₆₀/SPCEs can be observed in Fig. 4. This figure shows that a higher sensitivity was obtained when the SPCEs were just modified with C₆₀, following the optimized method described above. Bearing in mind these analytical results AC₆₀/SPCEs were selected as working electrodes for next experiments.

3.3. Interference studies.

The selectivity of the developed AC₆₀/SPCEs was analysed by studying the influence of the presence of 4-ethylguaicol on the analytical response of 4-ethylphenol. This interferent was selected considering its simultaneous presence in wine and similar chemical structure to that of 4-ethylphenol. Thus, the influence of different concentrations of the interfering compound, ranging from 700 to 1300 µg/L, in the analytical signal of a 700 µg/L 4-ethylphenol solution was analysed. The obtained results shown no significant interference by 4-ethylguaicol concentration levels lower than 1100 µg/L (Fig. 5). Therefore, this compound cannot be considered as an interferent, taking into account that the concentration of 4-ethylguaicol in wine is often lower [10,13,16].

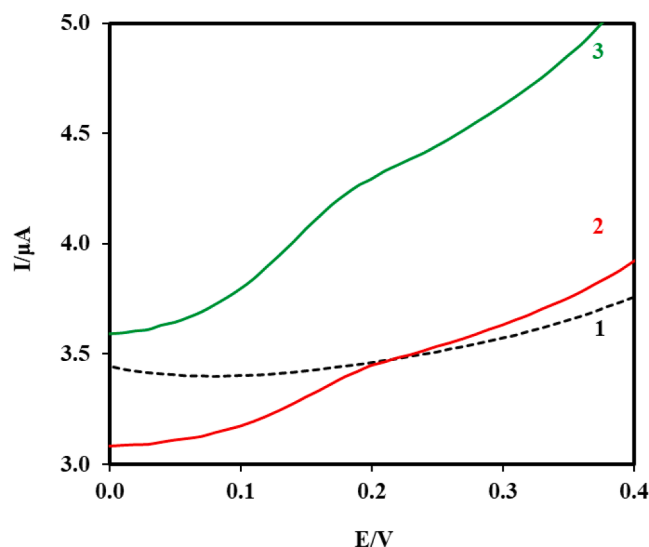


Fig. 6. Differential pulse voltammograms obtained in BR solution (1), spiked red wine (2) addition of 400 $\mu\text{g/L}$ (3) using an $\text{AC}_{60}/\text{SPCE}$ (BR pH 5.8, deposition time, 360 s; deposition temperature, 54 $^{\circ}\text{C}$; pulse potential, +0.01 V; step potential, +0.02 V; pulse time, 0.02 s and scan rate, 50 mV s^{-1}).

Table 2

Determination of 4-ethylphenol in different wine samples by DPV using an $\text{AC}_{60}/\text{SPCE}$.

Sample	Concentration Added ($\mu\text{g/L}$)	Concentration Found ($\mu\text{g/L}$)	Recovery (%)
Wine 1	–	No detected	–
	700	705 ± 248	100.7%
Wine 2	–	No detected	–
	700	713 ± 124	101.8%
Wine 3	–	No detected	–
	700	713 ± 105	101.8%
Wine 4	–	No detected	–
	700	702 ± 284	100.3%

3.4. Wine sample analysis.

The performance of the developed electrochemical sensor was analyzed by the direct determination of 4-ethylphenol in different wine samples. The voltammetric responses obtained for these samples are shown in Fig. 6. Four different commercial samples from different origins and different grape variety were studied by the standard addition method, without finding the presence of analyte in any of them (Table 2). Recovery experiments were also performed by the analysis of spiked wine samples obtaining good analytical values from 100.3 to 101.8 %, which indicates a nice applicability and reliability of the developed analytical method.

4. Conclusions

A novel and easy electrochemical method for the determination of 4-ethylphenol in wine has been developed. The modification of SPCEs with C_{60} gave rise to selective and sensitive sensors for the determination of 4-ethylphenol, even in the presence of high concentrations of 4-ethylguaiacol. Under the properly optimized experimental conditions the sensor showed a wide linear range (from 700 to 1300 $\mu\text{g/L}$), as well as good precision (5.4 %) and capability of detection (700 $\mu\text{g/L}$). Additionally, it was successfully applied to the determination of 4-ethylphenol in different wine samples, obtaining good recovery values ranged from 100.3 to 101.8%.

CRediT authorship contribution statement

Paula Portugal-Gómez: Investigation, Methodology. **M. Asunción Alonso-Lomillo:** Conceptualization, Validation. **Olga Domínguez-Renedo:** Conceptualization, Methodology, Validation.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.microc.2022.107599>.

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