



Simultaneous determination of 4-ethylphenol and 4-ethylguaicol on C₆₀ modified dual screen-printed electrochemical sensors

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ABSTRACT

4-ethylphenol and 4-ethylguaicol levels in wine are associated to organoleptic defects that cause consumer rejection accompanied by significant economic losses for producers. Thus, electrochemical sensors based on screen-printed carbon electrodes (SPCEs) modified with activated fullerene C₆₀ (AC₆₀) have been developed for the analysis of both phenols by direct headspace amperometric measurements. Upon optimization of the experimental variables affecting the sensors performance, the AC₆₀/SPCE sensors presented linearity ranges from 9.9 to 65.4 µg/L and from 19.6 to 107.1 µg/L for 4-ethylphenol and 4-ethylguaicol, respectively. The achieved detection capacities were 10.3 µg/L (4-ethylphenol) and 19.6 µg/L (4-ethylguaicol), with a reproducibility of 6.3 % and 9.1 % (n = 3), respectively. In addition, dual-working AC₆₀/SPCE devices were developed for the simultaneous analysis of both phenols using different working potentials for each electrode. The dual systems were successfully applied in the analysis of different spiked wine samples, obtaining good recoveries ranging from 94 to 108 %.

1. Introduction

The organoleptic characteristics of a wine significantly influence its marketing, considering their great effect on the consumer. Therefore, characterizing a wine in relation to its aromatic composition can be an ideal method to ensure not only its good commercialization but also its correct production and packaging, even avoiding fraud and falsifications. Among the numerous species involved in the aroma of wines, different volatile phenols contribute, depending on their level of concentration, to the quality of the final aroma [1,2]. Within these phenols, compounds such as 4-ethylphenol and 4-ethylguaicol stand out in relation to organoleptic disorders that cause unpleasant odours that sometimes remind stables or smoked [3–7], being their simultaneous detection in wine interesting to avoid their harmful effects. The characterization of the aroma of a wine has traditionally been carried out through simple sensory analysis, establishing perception thresholds from which wines were considered unsuitable of 95 µg/L and 600 µg/L for 4-ethylguaicol and 4-ethylphenol, respectively, and 450 µg/L for the sum of both analytes. However, this type of analysis is subject to the partiality of the taster and does not offer enough information about the chemical composition of the wine sample, which makes also difficult to find the causes of possible alterations and their possible solution. Thus,

different instrumental methods have been used in the joint detection of 4-ethylguaicol and 4-ethylphenol, being chromatographic techniques, including gas chromatography [8–11] and high-resolution liquid chromatography (HPLC) [12–14], the most prominent. Although, these methods present high selectivity and sensitivity, they require long sampling times, in addition to expensive and voluminous equipment that prevents the implementation of on-site measurements to monitor the quality of wines during the different stages of the production process. These problems may be solved using electrochemical techniques, which imply reduced and cheaper instrumentation, shorter sampling times and also allow *in situ* analysis [15–22].

The analysis of 4-ethylphenol and 4-ethylguaicol has already been performed by means of different electrochemical techniques and modified electrodes (Table 1) [16–29]. Nevertheless, only a few of these works have been applied in the determination of these compounds in wine [16,22,23,25], being the simultaneous determination of 4-ethylguaicol and 4-ethylphenol described in just one of them [25]. This joint determination is based on complex array systems combined with multivariate analysis with limits of detection higher than the perception thresholds of both analytes. Thus, the simultaneous electrochemical analysis of both volatile phenols in wine samples still needs the development of novel selective electrochemical devices. In this way, the

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Table 1
Electrochemical sensors for 4-ethylguaicol and 4-ethylphenol

Analyte	Technique	Electrode	LOD ($\mu\text{g/L}$)	Reprod.	Sample	Recov. (%)	Ref.	
4-ethylphenol	Amp	SPCE modified with Tyr	1.4	7.0 %	Water	–	[27]	
		GCE modified with CNTs and Tyr	12.2	–	Synthetic cocktail	108	[28]	
		AC ₆₀ /SPCE	10.3	6.3	Wine	99–104	This work	
	CV	GCE modified with CNTs and Tyr	25.7	–	Synthetic cocktail	–	[28]	
		DPV	GCE	–	–	–	–	[29]
	4-ethylguaicol	Amp.	GCE modified with a MIP of polypyrrol	24.4	3.0 %	Wine	101	[23]
			AuE	290	–	–	–	[17]
		AuE modified with a MIN of 4-vinylpyridine	70	–	–	–	[17]	
		AuE modified with a MIP of 4-vinylpyridine	68	17.4 %	–	–	[18]	
		AC ₆₀ /SPCE	36	10.0 %	–	–	[19]	
AC ₆₀ /SPCE		700	5.4 %	Wine	100.3–101.8	[16]		
AC ₆₀ /SPCE		19.6	9.1 %	Wine	96–97	This work		
4-ethylphenol and 4-ethylguaicol	CV	SPCE modified with SnO ₂ nanoparticles	12.5	–	–	–	[20]	
		SPCE modified with TiO ₂ nanoparticles	19.2	–	–	–	[21]	
		CPE	16.9	–	–	–	[21]	
	DPV	CPME-CNT	16.1	–	–	–	[21]	
		CPME-AB	14.3	–	–	–	[21]	
		SPCE modified with SnO ₂ nanoparticles	9.4	2.48 %	Simulated chemical mixture of volatiles	91.6–108.8	[20]	
		SPCE modified with TiO ₂ nanoparticles	5.3	4.85 %	–	91.0–101.8	[20]	
	SWV	AC ₆₀ /SPCE	200	7.6 %	Wine	96–106	[22]	
		Nafion-modified BDDE	15.2	–	Whiskey samples	–	[24]	
	Amp.	Dual AC ₆₀ /SPCE	–	–	Wine	94–108	This work	
CV		Array of 6 GECEs modified with different materials	5500 (4-ethylguaicol) 1800 (4-ethylphenol)	6.5 % (4-ethylguaicol) 4.6 % (4-ethylphenol)	Wine	–	[25]	
DPV		Array of 5 GECEs modified with MIPs	2400 (4-ethylguaicol) 1300 (4-ethylphenol)	–	–	–	[26]	

AC₆₀/SPCE, activated fullerene-modified screen-printed electrode; Amp., Amperometry; AuE, Gold electrode; BDDE, boron-doped diamond electrode; GCE, Glassy carbon electrode; CPE, carbon paste electrode; CPME-CNT, carbon paste-modified electrode with carbon nanotubes; CPME-AB, carbon paste-modified electrode with activated biochar; CV, cyclic voltammetry; DPV, differential pulse voltammetry; GECEs, graphite epoxy composite electrodes; LOD, limit of detection; MIN, molecularly imprinted nanoparticle; MIPs, molecularly imprinted polymers; SPCE, Screen Printed Carbon Electrode; SWV, square wave voltammetry; Tyr, Tyrosinase.

modification of screen-printed electrodes with nanomaterials leads to sensors that combine the advantages provided by both systems in terms of portability and better sensitivity [15]. Among them, fullerene C₆₀ (C₆₀) can be considered a nanomaterial of special application in the development of sensitive sensors due to the wide potential window and the excellent conductivity and stability of C₆₀-modified electrodes [30]. In fact, this nanomaterial has been successfully used in the electrochemical detection of both volatile phenols in wine [16,22], based on differential pulse voltammetric measurements in solution after a pre-concentration step of the analyte present in the gaseous phase in equilibrium with the liquid sample. Although good results were obtained in the individual analysis of both compounds, the developed sensors have not been applied yet in the joint determination of 4-ethylphenol and 4-ethylguaicol in the same sample. Therefore, this has been the aim of this work.

Moreover, in order to increase the performance and the selectivity of this dual determination avoiding possible interferences from the wine matrix, amperometric measurements were directly performed on the gaseous phase in equilibrium with the sampled matrix, that is, in the headspace.

2. Material and methods

2.1. Reagents, materials and devices

Reagents of analytical grade were used. All solutions were prepared

in Milli-Q water (Milli-pore, Bedford, MA, USA, 18.2 M Ω cm). Britton Robinson buffer (BR) solutions, formed by 0.04 M phosphoric acid (Panreac, Barcelona, Spain), acetic acid 0.04 M (VWR Chemical, Fontenay, France), boric acid 0.04 M (Panreac, Barcelona, Spain) and potassium chloride 0.1 M (Merck, Darmstadt, Germany) were used as supporting electrolyte. NaOH 1.0 M solutions (Ecros, Barcelona, Spain) were used to adjust the pH of the supporting electrolyte. C₆₀ solutions (Acros Organics, Geel, Belgium), prepared in dichloromethane (Panreac, Barcelona, Spain), were used to modify the working electrode surface. 1.0 M KOH solutions (Carlo Erba, Val de Reuil, France) were employed for electrochemical activation of C₆₀. Standard solutions of the analytes were prepared by dissolving 4-ethylphenol (Alfa Aesar, Haverhill, Massachusetts, USA) and 4-ethylguaicol (Alfa Aesar, China) in Milli-Q water.

A potentiostat PalmSens4 (PalmSens BV, Houten, The Netherlands) was employed for the electrochemical measurements, as well as three-electrode based SPCEs, with carbon working, carbon auxiliary and Ag/AgCl reference electrodes (DRP-C11L-SPCEs, Metrohm DropSens, Oviedo, Spain), and dual SPCEs based on four-electrode configurations, with two carbon working, carbon auxiliary and Ag reference electrodes (DRP-X1110-SPCEs, Metrohm DropSens, Oviedo, Spain). A selective deposition lamination-3D-printing machine (Anycubic: Photon Mono SE, AnyCubic, Shenzhen, China) was employed for the fabrication of the appropriate electrochemical cell for amperometric measurements with DRP-X1110 SPCEs, using an Anycubic Grey Colored UV resin.

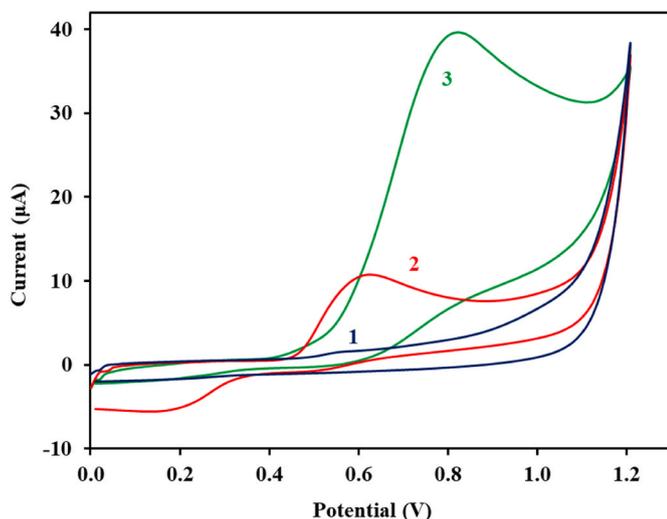


Fig. 1. Cyclic voltammograms obtained by gas phase measurements of (1) a blank solution; (2) a 3.6 g/L 4-ethylguaicol solution and (3) a 1.6 g/L 4-ethylguaicol solution using an $AC_{60}/SPCE$ (Supporting electrolyte pH 3; scan rate 50 mV/s).

2.2. Fullerene modification of carbon working electrodes ($AC_{60}/SPCEs$)

The working electrode modification was performed following the procedure described in previous publications [16,22,31]. Briefly, 40 μL of a solution of 0.1 mg/mL of C_{60} in dichloromethane was deposited on the surface of the SPCEs and left to dry at room temperature. It was then electrochemically activated scanning the potential from 0 to -1.5 V , at 10 mV/s, by cyclic voltammetry in 50 μL of a 1.0 M KOH solution. In this way, the conductive films that were formed allow the registration of higher voltammetric currents of the redox probe ferricyanide (Fig. S1, supplementary material).

2.3. Headspace electrochemical measurements

$AC_{60}/SPCEs$ were immersed in the corresponding supporting electrolyte before using these devices, in such a way that a thin film of this solution was pre-loaded by adsorption. For the gaseous phase amperometric measurements, these devices were then placed on the top of a sealed electrochemical cell (Metrohm DropSens, Oviedo, Spain), avoiding the contact with the stirred solution placed at the bottom [32]. 1 mL of supporting electrolyte pH 3.6 or 2.0 and an applied potential of $+0.56\text{ V}$ or $+0.86\text{ V}$ were used in the case of the analyses of 4-ethylguaicol and 4-ethylphenol, respectively, except for the optimization process.

Simultaneous analyses of both compounds were performed using

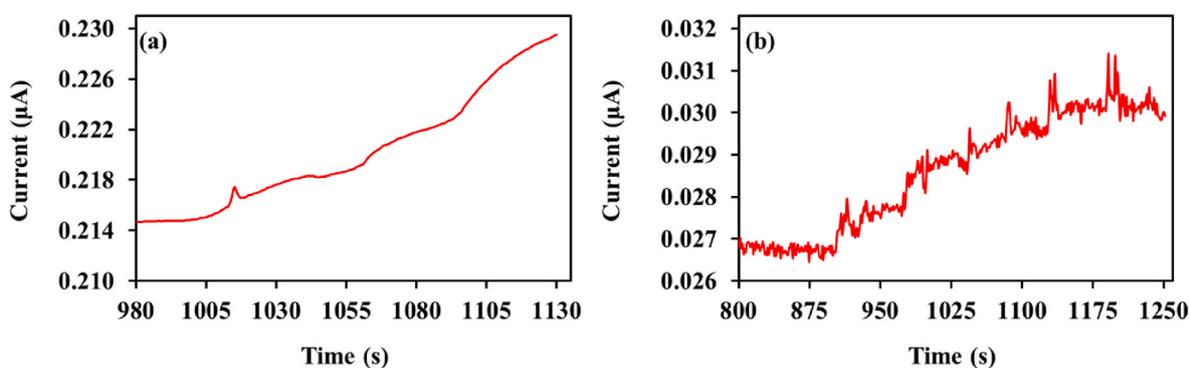


Fig. 2. Headspace amperograms registered for consecutive additions of 10 μL of an 11 mg/L 4-ethylphenol solution in 1 mL of supporting electrolyte under a) optimum conditions (pH 2.0; working potential, $+0.86\text{ V}$) and b) non-optimum conditions (pH 5; working potential, $+0.50\text{ V}$).

dual $AC_{60}/SPCEs$. The dual devices were first immersed in the supporting electrolyte and covered with a polyamide membrane (DRP-MEMB, DropSens, Oviedo, Spain) to improve the wettability of the four-electrode system. In this case, a homemade sealed 3D printed resin cell was used (Fig. S2, supplementary material), which allows the addition of samples from the lateral side, containing 1 mL of stirred supporting electrolyte pH 2.0. Potentials of $+0.86\text{ V}$ and $+0.56\text{ V}$ were applied to each working electrode of the dual devices.

3. Results

The electrochemical response of 4-ethylphenol and 4-ethylguaicol has been described as an oxidation process that takes place through a quinone generation, according to the scheme shown in Fig. S3 (Supplementary material) [29]. This redox process has been studied by means of gaseous phase cyclic voltammetric measurements using different transducers. Fig. 1 shows well defined oxidation peaks for both phenols when $AC_{60}/SPCEs$ were used, being the redox peak achieved significantly higher than those obtained when SPCEs (Fig. S4, supplementary material) or $C_{60}/SPCEs$ (Fig. S5, supplementary material) were used. Although $AC_{60}/SPCEs$ -based electrochemical sensors have showed to be sensitive to the presence of the target analytes by direct headspace measurements, in order to achieve a greater sensitivity and selectivity in the analysis of both compounds, effective and simple gaseous phase amperometric sensors were first individually optimized to find the best conditions of the experimental variables that would lead to the simultaneous detection of 4-ethylphenol and 4-ethylguaicol in wine samples.

3.1. 4-ethylphenol determination using $AC_{60}/SPCEs$

The current generated by the oxidation of 4-ethylphenol can be easily recorded by amperometry, being considerably affected by the pH value of the supporting electrolyte and the applied potential. Thus, an optimization process of these variables, which is mandatory in order to improve the performance of the sensor, was then carried out by using the experimental design methodology. Consequently, a 2^2 central composite design including all the possible combinations of these variables was performed, taking as response the oxidation current of a 9.9 $\mu\text{g/L}$ 4-ethylphenol solution. The analysis of these responses in terms of analysis of the variance (ANOVA), using the Statgraphics software [33], showed that the values that maximized the oxidation response were a potential and pH values of $+0.86\text{ V}$ and 2.0, respectively. Fig. 2 shows the amperometric current recorded under the different experimental conditions, highlighting the improvement at the optimum ones.

The method was then validated in terms of different parameters including, precision (reproducibility and repeatability), sensitivity (capability of detection, limit of decision), trueness (analysis of wines) and specificity (interference analysis). Reproducibility was determined considering the slopes of three calibration curves registered under the

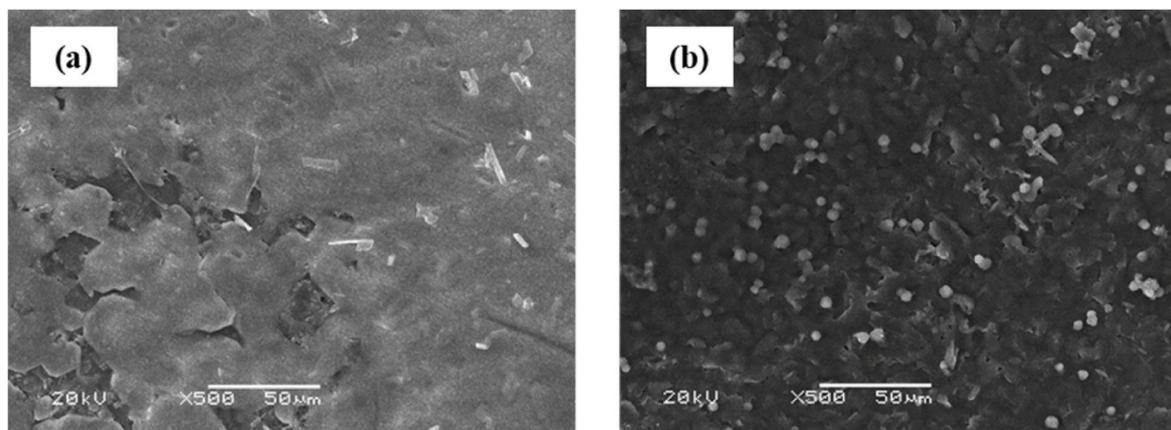


Fig. 3. SEM images of an AC₆₀/SPCE before (a) and after (b) registering a calibration curve in the 4-ethylphenol concentration range from 9.9 to 65.42 μg/L (pH 2.0; working potential, +0.86 V).

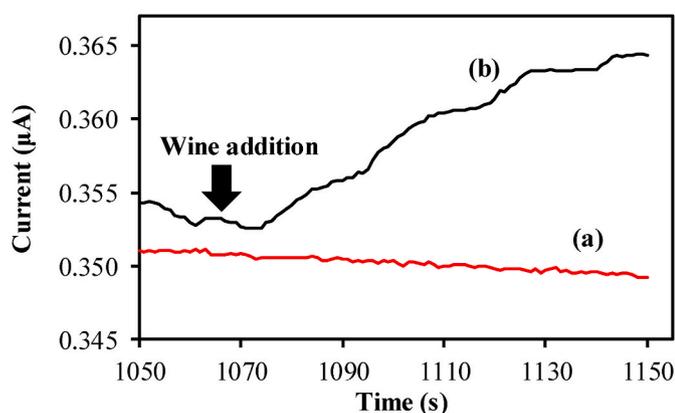


Fig. 4. Amperograms registered in the gas phase using an AC₆₀/SPCE for a) untreated wine and b) spiked white wine and consecutive additions of 10 μL of a 1.0 mg/L 4-ethylphenol solution in 1 mL of supporting electrolyte (pH 2.0; working potential, +0.86 V).

Table 2
Amperometric analysis of 4-ethylphenol in wine samples using AC₆₀/SPCEs.

Sample	Concentration Added (μg/L)	Concentration Found (μg/L)	Recovery (%)
White wine	–	Not detected	–
1	19.61	19.41 ± 2.67	99
White wine	–	Not detected	–
2	19.61	19.47 ± 3.17	99
Red wine 1	–	Not detected	–
	19.61	20.30 ± 2.81	104
Red wine 2	–	Not detected	–
	19.61	20.43 ± 2.62	104

optimum experimental conditions with different AC₆₀/SPCEs, in the concentration range from 9.9 to 65.4 μg/L. The relative standard deviation (RSD) value found for these calibration sets was of 6.3 % (n = 3). However, an important loss in sensitivity was observed when using the same AC₆₀/SPCE (Repeatability), which is insignificant considering the disposable features of the electrodes used. This lack of repeatability was explained by the analysis of the electrode surface by SEM (Fig. 3). The thin layer of activated nanomaterial that covered the electrode (Fig. 3a) disappeared as the measurements were made, leaving the fullerene deactivated and preventing further measurements with the same electrode (Fig. 3b).

Capability of detection (CC_β) and limit of decision (CC_α) values were

also determined by means of a validated regression model [34] according to ISO 11.843 [35] for $\alpha = \beta = 0.05$, obtaining values of 4.2 and 10.3 μg/L for CC_α and CC_β, respectively.

Trueness analysis was performed by means of the analytical determination of 4-ethylguaicol in different red and white wine samples. Firstly, untreated wine samples were measured for which no oxidation signal related to the presence of 4-ethylphenol was observed (Fig. 4). Next, recovery experiments were performed by spiking four wine samples with a known concentration of analyte, obtaining good recovery values ranging from 99 to 104 % (Table 2) by means of the standard addition method.

Finally, the specificity of the developed AC₆₀/SPCEs towards 4-ethylphenol was also studied by examining the analyte response in presence of interfering species. In this way, ethanethiol and 4-ethylguaicol, volatile compounds also present in wine matrices, were selected as possible interferents. Amperometric currents were recorded under optimal 4-ethylphenol measurement conditions, in the concentration range between 20 and 100 μg/L for ethanethiol and, from 10 to 100 μg/L, for 4-ethylguaicol. While no amperometric response was obtained for ethanethiol, an oxidation response was observed for 4-ethylguaicol even at low concentration levels (Fig. S6, supplementary material). Thus, when 4-ethylguaicol is also present in the sample, the analytical method developed is not capable of distinguishing between both phenols, when operating under the optimized experimental conditions described. Hence, optimal conditions for the analysis of 4-ethylguaicol were next optimized with the aim of achieving selectivity towards this analyte.

3.2. 4-ethylguaicol determination using AC₆₀/SPCEs

The amperometric response obtained for 4-ethylguaicol using AC₆₀/SPCEs was analogously optimized using the experimental design methodology. Thus, the two influential experimental variables, pH of the supporting electrolyte and applied oxidation potential, were optimized a central composite design 2². The results were treated with the Statgraphics program [33], obtaining as optimal values that maximized the response a value of 3.6 for the pH and, of +0.56 V, for the applied potential (Fig. S7, supplementary material). Under these measurement conditions, a well-defined amperometric signal for the oxidation of 4-ethylguaicol was obtained.

The precision of the developed method was estimated by reproducibility and repeatability determinations. For this, three different calibration curves were built for a concentration range between 19.6 and 107.1 μg/L of 4-ethylguaicol. An RSD value of 9.1 % (n = 3) was obtained for the reproducibility, considering the slopes of the calibration curves, as well as low repeatability values due to the activated layer

Table 3

Amperometric determination of 4-ethylguaicol in wine samples using AC₆₀/SPCEs.

Sample	Concentration Added (µg/L)	Concentration Found (µg/L)	Recovery (%)
White wine 1	19.61	19.11 ± 1.68	97
White wine 2	19.61	18.90 ± 2.04	96

falling as it has been above-mentioned. Moreover, a value of 4.1 µg/L was reached for CC_α and a value inferior that the lowest of the concentrations used in the construction of the calibration set for CC_β. 19.6 µg/L was then selected as the capability of detection of the developed method [36].

Finally, the application of the described electrochemical sensor was tested by direct determination of 4-ethylguaicol in wine samples. Since,

no analytical response was obtained in wine samples, recovery experiments were also carried out by analysing spiked wine samples, obtaining good results for the two varieties of white wine analysed (Table 3), which indicates that the method can be successfully applied in the analysis of complex samples such as wine. However, a high matrix effect was detected for red wines that prevented the analytical quantification of 4-ethylguaicol without a sample pretreatment [22].

With the aim of studying the selectivity of the method, the effect of the presence of 4-ethylphenol was also analysed. Thus, the amperometric response achieved for this compound, under the above described optimized experimental conditions, was studied. No significant results were observed for this species; therefore, it can be considered non-interfering in the amperometric measurement of 4-ethylguaicol. Considering the above describe results, it can be deduced that the developed AC₆₀/SPCEs were selective for the presence of 4-ethylguaicol when working under optimal pH and potential conditions for this analyte. This selectivity was maintained even in the presence of high

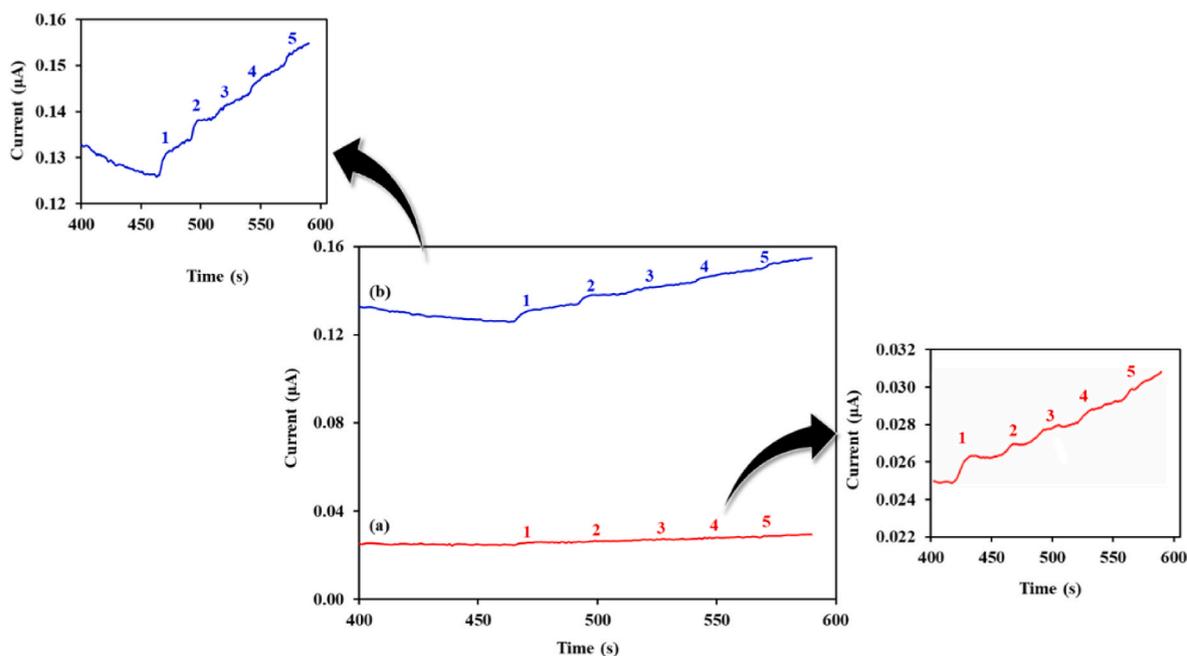


Fig. 5. Amperograms recorded for the simultaneous determination of 4-ethylphenol and 4-ethylguaicol in wine with a dual AC₆₀/SPCE using (a) +0.56 V and (b) +0.86 V as working potential. (1) addition of 200 µL of a spiked wine sample (2–5) successive additions of 10 µL of a 50 mg/L 4-ethylguaicol in 1 mL of supporting electrolyte pH 2.0.

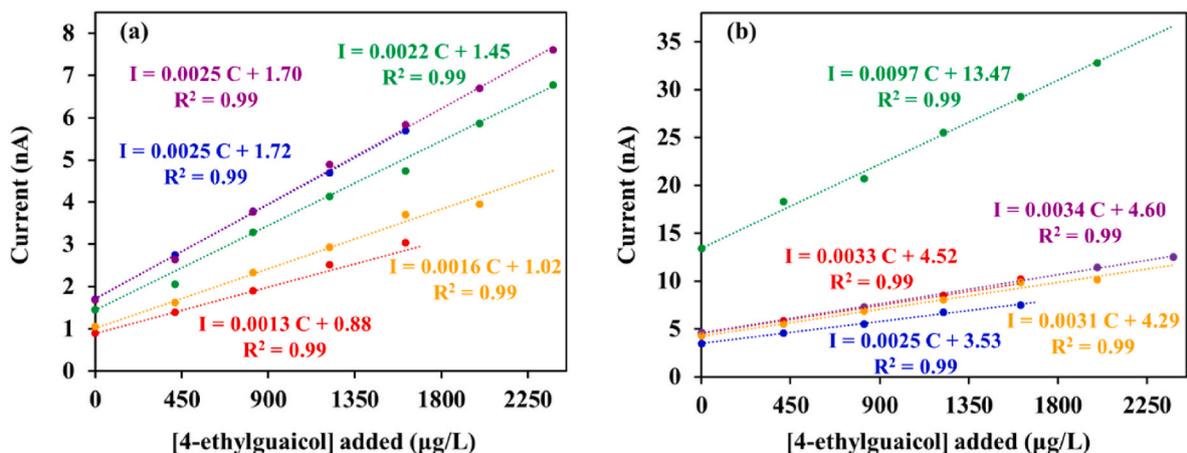


Fig. 6. Experimental points and calibration plots obtained using dual AC₆₀/SPCEs for (a) the 4-ethylguaicol determination at +0.56 V and (b) 4-ethylguaicol and 4-ethylphenol determination at +0.86 V in different spiked wine samples by means of the standard addition method (Supporting electrolyte pH 2).

Table 4

Determination of 4-ethylguaiaicol and 4-ethylphenol in different wine samples by amperometry using a dual AC₆₀/SPCE.

Sample	Analyte	Concentration Added (µg/L)	Concentration Found (µg/L)	Recovery (%)
White wine 1	4-ethylguaiaicol	694.4	687.8 ± 21.3	99
	4-ethylphenol		747.4 ± 57.9	108
White wine 2	4-ethylguaiaicol	694.4	664.5 ± 23.7	96
	4-ethylphenol		725.4 ± 85.5	104
White wine 3	4-ethylguaiaicol	694.4	652.6 ± 25.5	94
	4-ethylphenol		725.9 ± 70.5	105
White wine 4	4-ethylguaiaicol	694.4	694.4 ± 37.1	100
	4-ethylphenol		672.8 ± 66.6	97
White wine 5	4-ethylguaiaicol	694.4	660.7 ± 27.3	95
	4-ethylphenol		705.0 ± 49.3	102

concentrations of 4-ethylphenol.

3.3. Simultaneous determination of 4-ethylphenol and 4-ethylguaiaicol using AC₆₀/SPCEs

The use of dual systems based on the two working electrodes described above could therefore lead to the simultaneous determination of 4-ethylguaiaicol and 4-ethylphenol. Selective results for 4-ethylguaiaicol could be achieved when working at a potential of +0.56 V and for both compounds at +0.86 V in supporting electrolyte pH 2. Thus, amperometric measurements were made in the gas phase at supporting electrolyte pH 2 using dual screen-printed electrodes according to the procedure described in section 2.3.

The developed electrochemical dual sensor was applied to the direct and simultaneous determination of 4-ethylguaiaicol and 4-ethylphenol in wine samples (Fig. 5). Five samples of white wine and two samples of red wine, different in terms of grape variety and origin, were analysed by standard addition. In no case an analytical response was obtained due to the presence of analyte. Recovery experiments were then also carried out by analysing spiked wine samples (Fig. 6), obtaining good analytical values ranging between 94 and 108 % for the different commercial white wines, which indicates the good performance of the described analytical method (Table 4).

4. Conclusions

A new electrochemical method for the simultaneous determination of 4-ethylphenol and 4-ethylguaiaicol has been developed. The method is based on the modification of dual screen-printed carbon electrodes with C₆₀, combining the advantages of this type of electrodes in terms of disposability with the higher sensitivity provided by the nanomaterial. The developed AC₆₀/SPCEs has shown greater sensitivity than previous described electrochemical devices for the analysis of these phenols [16, 22, 23, 25], being the capacities of detection achieved adequate for the analysis of both phenol levels in wine samples. In addition, carrying out the measurements directly in the gas phase improves the selectivity of the method, allowing the simultaneous analysis of both phenols in complex samples such as wine. Thus, the method is presented as an interesting, sensitive and low-cost alternative to the traditional methods of analysis used in wineries.

CRedit authorship contribution statement

Paula Portugal-Gómez: Formal analysis, Validation. **M. Asunción Alonso-Lomillo:** Investigation, Supervision, Writing - review & editing, Conceptualization. **Olga Domínguez-Renedo:** Conceptualization, Investigation, Supervision, Writing - original draft.

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.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.talanta.2023.125543>.

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