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Original article

CuO-nanoparticles modified carbon paste electrode for square wave voltammetric determination of lidocaine: Comparing classical and Box–Behnken optimization methodologies

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ABSTRACT

In this research, copper oxide nanoparticles modified carbon paste electrode was developed for the voltammetric determination of lidocaine. The square wave voltammogram of lidocaine solution showed a well-defined peak between +0.5 and +1.5 V. Instrumental and chemical parameters influencing voltammetric response were optimized by both one at a time and Box–Behnken model of response surface methodology. The results revealed that there was no significant difference between two methods of optimization. The linear range was 1–2500 μmol L^{-1} ($I_p = 0.11C_{LH} + 17.38$, $R^2 = 0.999$). The LOD and LOQ based on three and ten times of the signal to noise (S/N) were 0.39 and 1.3 μmol L^{-1} ($n = 10$), respectively. The precision of the method was assessed for 10 replicate square wave voltammetry (SWV) determinations each of 0.05, 0.5 and 1 mmol L^{-1} of lidocaine showing relative standard deviations 4.1%, 3.7% and 2.1%, respectively. The reliability of the proposed method was established by application of the method for the determination of lidocaine in two pharmaceutical preparations, namely injection and gel.

1. Introduction

Lidocaine (LH) is chemically designated as acetamide, 2-(diethylamino)-*N*-(2,6-dimethylphenyl) and is the common name of an important member of a category of drugs extensively used as local anesthetics. This drug is also widely used as anti-arrhythmic agent. Analysis of pharmaceutical preparations is one of the most important and attractive branches in analytical chemistry. Different methods have been proposed for the determination of LH in the literature. To date chromatographic methods such as high performance liquid chromatography (HPLC) [1–8], gas chromatography [9–12] and electrophoresis [13–16] are most frequently employed for LH determination due to their high sensitivity and excellent selectivity. Spectrophotometric assay [17,18] and the indirect atomic absorption spectrometric determination have also been studied [19]. Most of these methods suffer from limitations. They are expensive, time consuming or need extensive pre-treatment steps and using toxic solvent and reagents.

Electrochemical techniques are useful alternative methods, having important advantages including simplicity, reliability, sensitivity and selectivity. These techniques are more often used in pharmaceutical preparations and biomedical analysis. Little published data are available for electrochemical determination of LH and related compounds [20–24]. Investigation of direct oxidation of LH in order to find a fast, sensitive and reliable electrochemical method for determination of this compound in pharmaceuticals, as well as for the development of lidocaine voltammetric detectors coupled to flow techniques or chromatographic measurements is important. Recently, many studies have been focused on the application of nano-materials in fabrication and modification of different conventional electrodes to improve their sensitivity and selectivity [20,25,26]. Undoubtedly, carbon paste electrodes represent the most convenient working electrode for modification by mixing with a suitable modifier [26,27].

Application of chemometrics in the optimization of analytical parameters has some advantages including: reduction in the number of experiments, lower reagent consumption and considerably less laboratory work. Thus they are faster and more cost effective than classical univariate approaches. These methods enable us to study several parameters simultaneously. In addition

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they can develop mathematical models that interpret the relevance and statistical significance of different factors in an analytical method [28]. Nowadays, response surface methodology (RSM) with a Box–Behnken design (BBD) is widely used for the optimization of analytical factors through a relatively small number of experiments [29–34]. Experimental design methodology has been extensively used in optimization of parameters in analytical chemistry. But, a few reports are available regarding their applications in electrochemical optimization [35,36]. In this work, a laboratory constructed CuO nanoparticle carbon paste electrode (CNCPE) has been introduced for voltammetric determination of LH in pharmaceutical preparations. In addition, RSM with Box–Behnken design and traditional “one factor at a time” optimization protocols were used to identify chemical and instrumental parameters affecting the electrochemical response and their reliability were compared.

2. Experimental

2.1. Chemicals

All common chemicals such as HCl, NaOH and KNO_3 were of analytical grade and obtained from Merck (Darmstadt, Hesse, from Fluka (Milwaukee, USA). Copper oxide nanoparticle powder (40–80 nm) was obtained from Inframat Advanced Material (Farmington, CT, USA).

LH stock solution (0.01 mol L^{-1}) was prepared by dissolving 0.2886 g of LH in distilled water and diluting to the mark in a 100 mL volumetric flask. Working solutions were prepared by appropriate dilution of the stock solution. Doubled distilled water was used throughout this study.

2.2. Apparatus

For voltammetric measurements, a Metrohm (AUTOLAB, model PGSTAT302N) electrochemical device was employed. A three-electrode arrangement was applied throughout. CuO nanoparticles modified carbon paste electrode as a working electrode and a platinum wire as an auxiliary electrode together with an Ag/AgCl reference electrode were used. Adjustment of pH was carried out using a pH-meter (JENWAY model 3320 – UK).

2.3. Fabrication of CNCPE

CNCPE was prepared by mixing graphite powder with paraffin oil and an appropriate amount of CuO nanoparticles for 15 min as cited elsewhere [26]. The paste was then packed into an insulin syringe and a copper wire was put in contact with it for its external electric contact. The electrode surface was rubbed on waxed paper to obtain a smooth electrode surface.

2.4. Voltammetric determination of LH

In order to investigate the oxidation mechanism of LH at CNCPE, cyclic voltammetry (CV) was used. Square wave voltammography (SWV) was chosen as electrochemical tool to determine LH due to its sensitivity and speed. Preliminary CV experiments showed a well-defined irreversible peak related to oxidation of LH. Likewise, the general procedure adopted for obtaining cyclic and square wave voltammograms of LH was as follows: an appropriate amounts of standard LH solution and 5 mL of KNO_3 (1 mol L^{-1}) were added to a 25 mL volumetric flask and diluted to the mark with distilled water. This solution was transferred into the electrochemical cell. The cyclic voltammograms were recorded from +0.5 to +1.4 V at scan rate of 0.10 V s^{-1}. Square wave voltammograms were recorded by scanning the potential in the range of +0.5 to +1.5 V with a scan rate of 0.125 V s^{-1}. In order to regenerate a new and fresh surface on CNCPE, the tip of the electrode was polished on waxed paper.

2.5. Experimental design

A three-level, three-factor Box–Behnken experimental design was used to determine optimum levels for pH (8–12), scan rate (0.2–0.3 V s^{-1}) and percent of CuO nanoparticles (5%–20%) in CNCPE as important parameters affecting the performance of the method. The three selected levels of the variables for the BBD are shown in Table 1. The peak current of the SWV was taken as the response of the system.

To design the experiments, Minitab 15 software was employed. Table 2 shows the experimental design derived from BBD along with their obtained and predicted results, including three center points. Each experiment was performed in triplicate to verify reproducibility. The results were used to calculate the 10 coefficients of the second-order polynomial equation. This equation shows the relation between the desired response and the independent variables (pH, scan rate and CuO nanoparticle percent). Considering all linear, square, and linear-by-linear interaction terms, the second-order polynomial equation can be described as:

$$Y = b_0 + b_1x_1 + b_2x_2 + b_3x_3 + b_{12}x_1x_2 + b_{13}x_1x_3 + b_{23}x_2x_3 + b_{11}x_1^2 + b_{22}x_2^2 + b_{33}x_3^2 \quad (1)$$

where Y is the response (peak current of LH); b_0 is the offset term; b_1, b_2, and b_3 are the linear coefficients; b_{11}, b_{22}, and b_{33} are the quadratic coefficients, and b_{12}, b_{13} and b_{23} are the coefficients of the linear-by-linear interaction effect between independent variables x_1 (pH), x_2 (scan rate), and x_3 (CuO nanoparticle per cent) [37]. The model suitability of fit was assessed using a coefficient of regression (R^2) and analysis of variance (ANOVA).

Table 1
Experimental range and level of independent variables.

Factors range and levels (coded)	−1	0	1
Scan rate (V s^{-1})	0.2	0.25	0.3
pH	8	10	12
CuO% (w/w)	5	10	20

Table 2
Box–Behnken design matrix for three variables-three levels together with observed and predicted values (concentration of LH: 0.4 mmol L^{-1}).

Exp. run	Scan rate (V s^{-1})	pH	CuO% (w/w)	Current (μA)	Predicted current
1	0.3	10	20	20.49	21.798
2	0.3	8	10	6.64	5.566
3	0.25	10	10	14.90	14.900
4	0.2	10	5	8.78	7.241
5	0.2	8	10	4.50	4.120
6	0.25	12	20	55.92	54.359
7	0.3	10	5	10.81	10.196
8	0.25	12	5	22.10	22.207
9	0.3	12	10	29.42	29.800
10	0.2	10	20	16.12	16.965
11	0.25	8	5	12.39	14.435
12	0.25	10	10	14.90	14.900
13	0.2	12	10	23.01	24.084
14	0.25	10	10	14.90	14.900
15	0.25	8	20	4.20	3.608