Simultaneous Electrochemical Determination of Articaine HCl and Epinephrine

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Abstract

A simple, precise, accurate and inexpensive voltammetric method was developed for the simultaneous determination of articaine HCl and epinephrine in bulk, pharmaceutical formulations and human urine at carbon paste electrode in Britton-Robinson buffer of pH 7 and 40 µL of 10^{-2} mol L^{-1} sodium dodecyl sulphate. Several factors were studied such as buffer type, pH, surfactant, scan rate, and accumulation time to obtain the optimum conditions for analysis. The method showed linearity in concentration range of 1.0×10^{-6}-2.6×10^{-5} mol L^{-1}. The limits of detection and quantitation were found 2.88×10^{-7} mol L^{-1} and 8.72×10^{-7} mol L^{-1} for articaine HCl and 5.10×10^{-8} mol L^{-1} and 1.56×10^{-7} for epinephrine, respectively. The proposed voltammetric method was successfully applied for simultaneous determination of articaine HCl and epinephrine in bulk, injections and urine. The results obtained from the proposed method were statistically compared with those of a reported method and showed no significant difference. Thus, it can be used as quality control in laboratories.

Keywords: Articaine HCl; Epinephrine; Sodium dodecyl sulphate; Carbon paste; Voltammetry; Bulk; Urine

Introduction

Articaine HCl is a white or almost white crystalline powder, freely soluble in water, methanol and ethanol [1]. It is an intermediate-potency, short-acting amide local anesthetic with a fast metabolism due to an ester group in its structure. It is effective with local infiltration or peripheral nerve block in dentistry, when administered as a spinal, epidural, ocular, or regional nerve block, or when injected intravenously for regional anesthesia. Local anesthetic drugs are administered to the areas around the nerves to be blocked as the skin, subcutaneous tissues, retrobulbar, intrathecal, and epidural spaces. Articaine has a half-life of 60 minutes after entering the circulation and is quickly metabolized via hydrolysis into its inactive metabolite articainic acid, which is partly metabolized in the kidney into articainic acid glucuronide. Seventy-five percent of articainic acid is excreted unchanged; the rest is glucuronidated by the kidneys before excretion [2]. It is an amino-amide anesthetic having a thiophene, rather than a benzene ring, as well as an additional ester group that is subject to metabolism by plasma esterases. It has a widespread popularity in dental anesthesia, where it is generally considered to be more effective, and possibly safer, than lidocaine, the prior standard [3]. Epinephrine greatly increases the duration of the local anesthesia

by producing vasoconstriction at the site of injection. This allows the local anesthetic to persist at the injection site before being absorbed into the systemic circulation [4].

Literature survey reveals that several different analytical techniques have been developed for the determination of articaine HCl and epinephrine including high performance liquid chromatographic methods [5-7], thin layer chromatographic methods [8], gas chromatographic methods [9] and spectrophotometric methods [10] for articaine HCl and high performance liquid chromatographic methods [11-15], thin layer chromatographic methods [16,17], gas chromatographic methods [18,19], spectrophotometric methods [20-24] and electrochemical methods [25-30] for epinephrine. Carbon based electrodes are currently in widespread use in electroanalytical chemistry, because of their broad potential window, low cost, rich surface chemistry, low background current and chemical inertness. Carbon paste electrode (CPE) has some special

characteristics and benefits such as the ease of surface renewal, individual polarizability, and easy to apply modifications. The disadvantage of CPE is the tendency of the organic binder to dissolve in solutions containing an appreciable fraction of organic solvent [31].

In this study articaine HCl and epinephrine were determined simultaneously using differential pulse voltammetry (DPV) at carbon paste electrode in bulk, pharmaceutical formulations and human urine.

Materials and Methods

Experimental preparations

Pure and market samples: Articaine HCl and epinephrine bitartrate were kindly supplied by Inibsa Laboratories, Spain. Their purity was 100% as stated by the supplier.

Artinibsa ampoules; batch no. K-3, labeled to contain 40 mg Articaine HCl and 0.01 mg Epinephrine per ampoule, product of Inibsa Laboratories, Spain.

Standard solutions: Standard solutions of articaine HCl and epinephrine bitartarate were prepared in methanol. For cyclic voltammetry (CV) 1.0×10^{-2} mol L^{-1} solutions were prepared by dissolving 32.1 mg of articaine HCl and 33.3 mg of epinephrine bitartarate, each in 10 mL volumetric flask and diluted with methanol. For DPV, one mL of each 1.0×10^{-2} mol L^{-1} solution was taken and diluted to 10 mL with the same solvent to obtain 1.0×10^{-3} mol L^{-1} working solution.

Chemicals and reagents: All reagents used were of analytical grade and solvents were of spectroscopic grade. Distilled water was used throughout the work.

    (i) Methanol, HPLC grade (Fischer Chemical, UK).

    (ii) Sodium hydroxide (Qualikems fine chemical Pvt. Ltd).

    (iii) Sodium dodecyl sulphate (SDS) (Sigma-Aldrich, Germany).

    (iv) Dioctyl sodium sulfosuccinate (DSS) (Sigma-Aldrich, Germany).

    (v) Hexane Sulfonic acid sodium salt monohydrate (HSA) (Sharlab S.L., Spain).

    (vi) Potassium dihydrogen o-phosphate (El Nasr Pharmaceutical Chemicals, Egypt).

    (vii) Phosphoric acid (Sigma-Aldrich, Germany).

    (viii) Britton-Robinson (BR) buffer was prepared by mixing 0.04 mol L^{-1} of phosphoric acid (Sigma-Aldrich), acetic acid (Loba Chemie Co., India) and boric acid (Sigma-Aldrich).

Buffer solutions were adjusted with the appropriate amount of 0.2 mol L^{-1} NaOH (Qualikems fine chemical Pvt. Ltd) to get the desired pH 2-11 [32].

Phosphate buffer was prepared by adding 34.7 mL of 0.2 mol L^{-1} NaOH to 50 mL of 0.2 mol L^{-1} monobasic potassium phosphate solution (prepared by dissolving 27.22 g monobasic potassium phosphate in water and dilute with water to 1000 mL) and complete to 200 mL with water [32].

Instruments: All voltammetric measurements were carried out using a computer-driven analytical electrochemical workstation (model AEW2) with ECProg3 electrochemistry software (Sycopel, England) in combination with a three-electrode configured C-3 stand. The working electrode was a carbon paste electrode (MF-2010, BAS model), the reference electrode Ag/AgCl/ 3 mol L^{-1} NaCl (MW-2063, BAS model) and a platinum wire counter electrode (MW-1032, BAS model). A digital pH-meter (Jenway pH meter, UK) with combined glass electrode was used to carry out the pH measurements. All electrochemical experiments were performed at an ambient temperature of 25 ± 0.2°C.

Procedures

Preparation of working electrode: In a mortar 0.5 g graphite powder and 0.3 mL paraffin oil were mixed thoroughly with a pestle. The paste was packed into the hole of the electrode body and smoothed on a filter paper until it acquired a shiny appearance; the paste was carefully removed and replaced by a new one after each measurement [33].

Linearity: Aliquots of working standard articaine HCl and epinephrine solutions (1.0×10^{-3}) were added separately to the electrolytic cell containing 5 mL of Britton-Robinson buffer of pH 7 and 40 µL of 1.0×10^{-2} mol L^{-1} SDS, the solutions were stirred for 5 s at open circuit conditions, voltammetric analyses were carried out and voltammograms were recorded at a scan rate 20 mV s^{-1}.

Calibration curve was constructed by plotting anodic peak current against drug concentrations in molarity; and the regression equation was computed.

Accuracy and precision: Three different concentrations covering the linearity range of articaine HCl and epinephrine were analyzed in triplicates within the same day for intraday and for three successive days for interday using the procedure detailed under linearity part. Accuracy was calculated as precision (Relative standard deviation (%RSD)).

Application to pharmaceutical formulations

An aliquot (0.8 mL) containing 32.1 mg articaine HCl and 0.0144 mg epinephrine bitartarate was transferred to 10 mL volumetric flask, 33.286 mg pure standard epinephrine bitartarate was transferred to the volumetric flask and volume completed with methanol to obtain 1.0×10^{-2} mol L^{-1} solution of each drug. One mL of the prepared 1.0×10^{-2} mol L^{-1} solution was taken and diluted to 10 mL with the same solvent to obtain 1.0×10^{-3} mol L^{-1} working solution to be analyzed by the proposed electrochemical method using the procedure detailed under linearity part. The drug concentrations were calculated from the corresponding regression equation; the proposed method was further validated by using the standard addition technique.

Analysis of articaine HCl and epinephrine in urine: For the analysis of articaine HCl and epinephrine in urine, 1.0 mL of urine was mixed with 9.0 mL BR buffer of pH 7.0, then successive additions of 1.0×10^{-3} mol L^{-1} working standard solutions (covering the linearity range) were added to the voltammetric cell containing 5.0 mL of the previously diluted urine.

Results and Discussion

Electrochemical oxidation of articaine HCl

The reversibility of the oxidation process of articaine HCl at CPE was studied by CV, the cyclic voltammogram showed one well defined anodic peak in BR buffer of pH 7.0 (anodic peak current (I)=19.58 µA at 1.095 V), and the reverse scan showed no cathodic peak indicating that articaine HCl oxidation is irreversible **(Figure 1a)**. The proposed oxidation mechanism was shown in **Figure 1b.**

Optimization of experimental conditions

Effect of pH: CV at CPE and scan rate of 100 mV s⁻¹ was used to investigate the effect of pH upon the oxidation of articaine HCl. 4.5 mL of BR buffer (2-11) and 0.5 mL of 1.0×10^{-2} mol L⁻¹ articaine HCl standard solution were added to the electrochemical cell, and the respective voltammetric response was recorded **(Figure 2a)**. This experiment was repeated using phosphate buffer **(Figure 3a)** to obtain the optimum buffer with the optimum pH value.

Figures 2a and 3a show that the anodic peak potential (E) was shifted negatively by increasing pH indicating that articaine HCl oxidation at CPE is pH dependant and those protons are involved in the reaction. **Figures 2c and 3c** show that higher peak current was achieved using BR buffer of pH 7.0.

The anodic peak current at pH 7 (BR buffer) was found 19.58 µA and at pH 6.8 (Phosphate buffer) was 15.10 µA. The linear relations between pH and peak potential (E) observed in the pH range 7-11 (BR) buffer, and 6.4-8.0 phosphate buffer was used to apply Nernest equation as shown in **Figures 2b and 3b** with a regression equation: E(V)=−0.053 pH+1.465, R² (correlation coefficient=0.9974 and E(V)=−0.0695 pH+1.548, R²=0.9977 in case of BR and phosphate buffers, respectively. Applying Nernst equation using the formula ΔEp/ΔpH (Slope)=0.059x/n, where x and n is the number of protons and electrons involved in the reaction, respectively. It can be concluded that number of electrons transferred is equal to the number of protons, thus n=x [34,35].
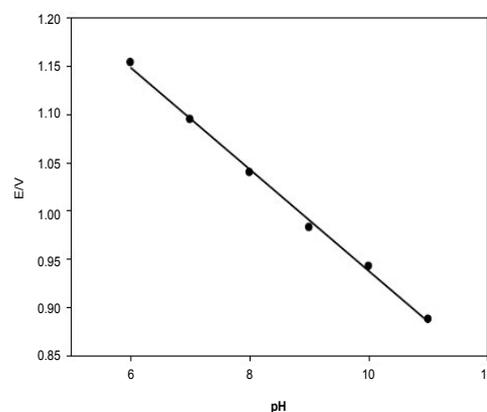
Effect of surfactant: A surface-active agent (surfactant) is one which tends to accumulate at a surface or interface. A prerequisite for surfactants to be surface active is the property of
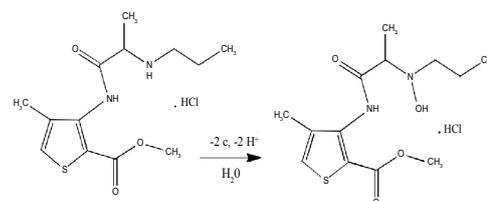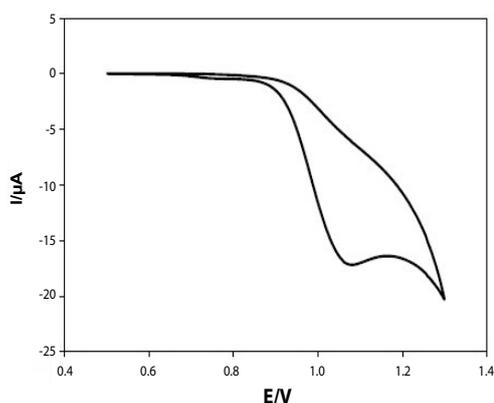

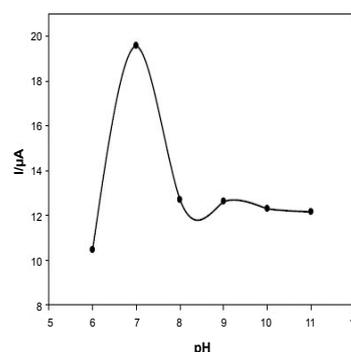**Figure 1b** Oxidation mechanism of articaine HCl.
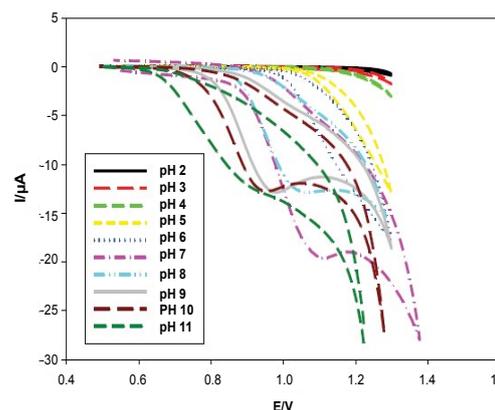
Figure 2a Cyclic voltammograms of 1.0×10^{-3} mol L⁻¹ articaine HCl in BR buffer pH (2-11) at CPE, scan rate 100 mV s⁻¹.
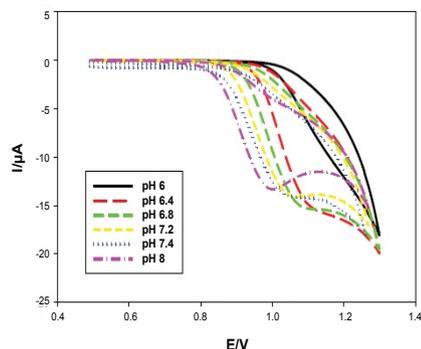

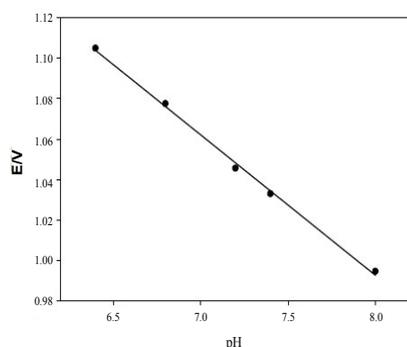**Figure 2b** Plot of the anodic peak potential as a function of pH (BR buffer).

Figure 1a Cyclic voltammogram of 1.0×10^{-3} mol L⁻¹ articaine HCl in BR buffer of pH 7.0 at CPE, scan rate 100 mVs⁻¹.

Figure 2c Plot of the anodic peak current as a function of pH (BR buffer).

Figure 3a Cyclic voltammograms of 1.0×10^{-3} mol L^{-1} articaine HCl in phosphate buffer pH (6-8) at CPE, scan rate 100 mV s^{-1}.

Figure 3b Plot of the anodic peak potential as a function of pH (Phosphate buffer).

these molecules to adsorb at the interface between bulk phases, such as air and water, oil and water or electrode and solution. The distinct structural feature of a surfactant is the hydrophilic region of the molecule or the polar head group which may be positive, negative, neutral or zwitterionic and the hydrophobic region or the tail that consists of one or more hydrocarbon chains, usually with 6-22 carbon atoms, thus they are also called amphiphiles, i.e., compounds having both polar and nonpolar regions in their molecules. Depending on the chemical structure of the hydrophilic moiety bound to the hydrophobic portion, the surfactant may be classified as cationic, anionic, non-ionic or zwitterionic.

Two important properties of surfactants, adsorption at interface and aggregation into supramolecular structures are advantageously used in electrochemistry. Surfactants can modify and control the properties of electrode surfaces **(Figure 4)** [36].

Surfactants were widely used in electroanalytical chemistry to improve sensitivity and selectivity and were applied for determination of potassium ferricyanide and dopamine [37], diethylstilbestrol [38], dopamine, uric acid and ascorbic acid [39], uric and ascorbic acids [40], thyroxine [41], moexipril hydrochloride [33], cefdinir [42], drotaverine hydrochloride [43] and atorvastatin [44].

The anodic peak current was found to be 19.58 µA at 1.095 V in BR buffer of pH 7.0 at CPE **(Figure 1a)**, and 39.28 µA at 1.065 V

in presence of 40 µL of 1.0×10^{-2} mol L^{-1} SDS **(Figures 5 and 6)** which enhances the current value and showing catalytic effect. Several surfactants were tried including SDS, DSS, and HSA, where SDS gave the best results with the highest anodic peak current as shown in **Figure 6**.

Effect of SDS concentration: The anodic peak current of articaine HCl increased gradually upon increasing the concentration of SDS, however it decreased when SDS concentration exceeded 8.0×10^{-5} mol L^{-1} (40 µL of 1.0×10^{-2} mol L^{-1} SDS), which was chosen as the optimum concentration of SDS. The relationship between anodic peak current of articaine HCl and SDS concentration was illustrated in **Figures 7a and 7b**.

Effect of scan rate: The effect of different scan rates (υ) ranging from 10 to 250 mV s^{-1} on the cyclic voltammetric response of articaine HCl in BR buffer (pH 7.0) was investigated, with increasing scan rates, the anodic peak was slightly shifted to
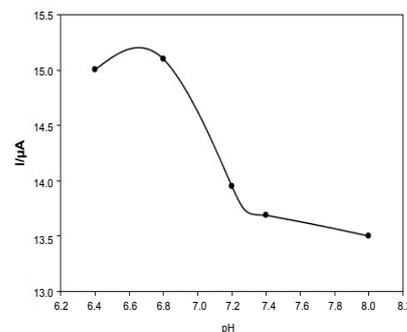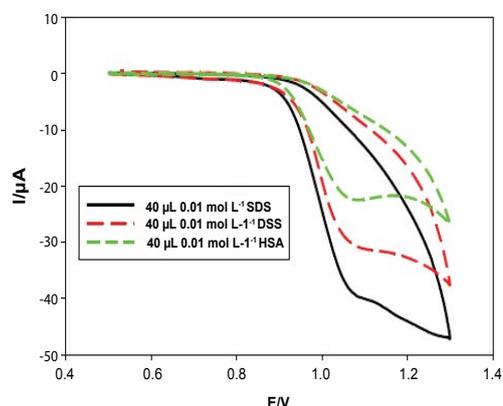

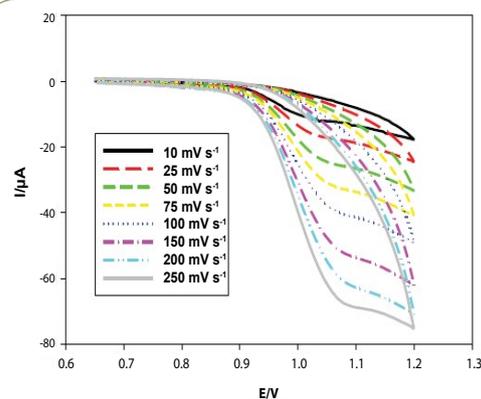**Figure 3c** Plot of the anodic peak current as a function of pH (Phosphate buffer).
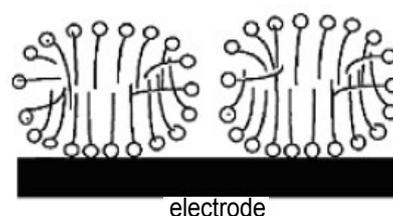
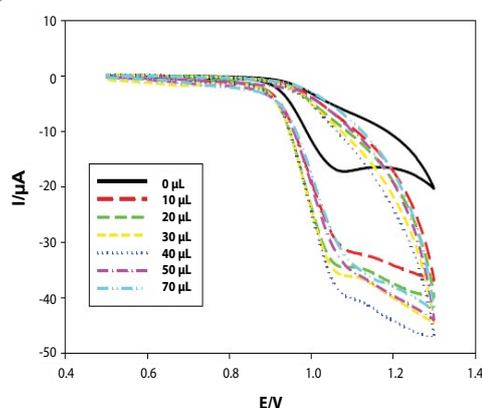**Figure 4** Side views of surface micelles or cylinders.
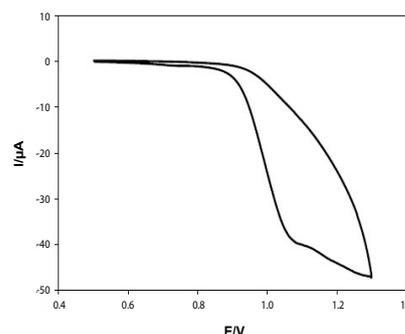
Figure 5 Cyclic voltammogram of 1.0×10^{-3} mol L^{-1} articaine HCl in BR buffer of pH 7.0 with 40 µL of 1.0×10^{-2} mol L^{-1} SDS at CPE, scan rate 100 mV s^{-1}.
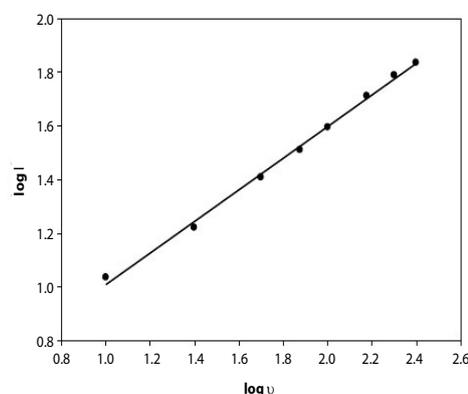
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Figure 6 Comparison of different types of surfactants used.

Figure 7a Cyclic voltammograms of 1.0×10^{-3} mol L^{-1} articaine HCl at CPE in BR buffer of pH 7.0 as a function of SDS concentration at scan rate 100 mV s^{-1}.

Figure 7b Plot of the anodic peak current versus SDS concentration.

Figure 8a Cyclic voltammograms of 1.0×10^{-3} mol L^{-1} articaine HCl at CPE in BR buffer (pH 7.0) and 40 μL SDS (1.0×10^{-2} mol L^{-1}) as a function of scan rate.

Figure 8b Plot of log (I) versus log (υ).

adsorption contribution **(Figure 8b)** [45].
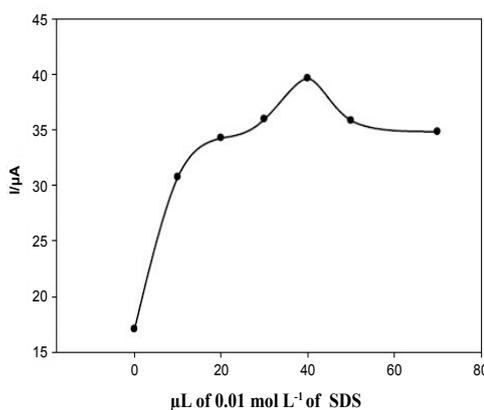
Effect of accumulation time: It was found that the peak current depended on the accumulation time (Tacc) of 1.0×10^{-3} mol L^{-1} articaine HCl at CPE in BR buffer (pH 7.0) and 40 μL SDS (1.0×10^{-2} mol L^{-1}). Sharp increase was observed at 5 s reaching its maximum value, and then decreased with increasing time. 5 s was chosen as the optimum Tacc for determination of articaine HCl **(Figures 9a and 9b)**.

Simultaneous determination of articaine HCl and epinephrine

Figure 10a shows the cyclic voltamogram of 1.0×10^{-3} mol L^{-1} epinephrine at CPE in BR buffer (pH 7.0) containing 40 μL SDS (1.0×10^{-2} mol L^{-1}). **Figure 10b** exhibits the oxidation mechanism of epinephrine [34]. **Figure 10c** presents the cyclic voltammogram of 1.0×10^{-3} mol L^{-1} articaine and epinephrine at CPE using the same conditions referring to well defined separate peaks of articaine and epinephrine were obtained, therefore these drugs can be determined simultaneously.

Method validation

Linearity: Linear relationships were found between the peak currents and concentrations of the two drugs in the range of 1.0×10^{-6}- 2.6×10^{-5} mol L^{-1} (0.320-8.34 μg mL^{-1}) for articaine HCl and (0.183-4.763 μg mL^{-1}) for epinephrine using the proposed method as shown in **Figure 11.** The mean percentage recoveries were of

the positive potential direction and the peak current increased remarkably with increasing scan rates **(Figure 8a)**. It was found that the logarithm of anodic peak current (log I) is linear to the logarithm of scan rate (log υ), with the linear regression equation as log I=0.59 log υ+0.421, R^2=0.9966. From the value of the slope, 0.59, it can be deduced that the electrochemical oxidation process of articaine HCl at CPE is diffusion controlled process with an
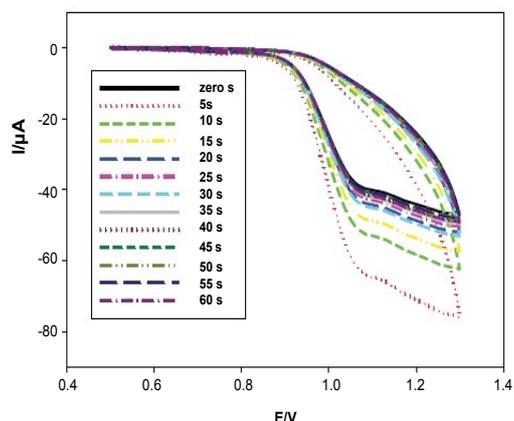
Figure 9a Cyclic voltammograms of 1.0×10^{-3} mol L^{-1} articaine HCl at CPE in BR buffer (pH 7.0) and 40 µL SDS (1.0×10^{-2} mol L^{-1}) at scan rate 100 mV s^{-1} as a function of accumulation time from 0 to 60 s.
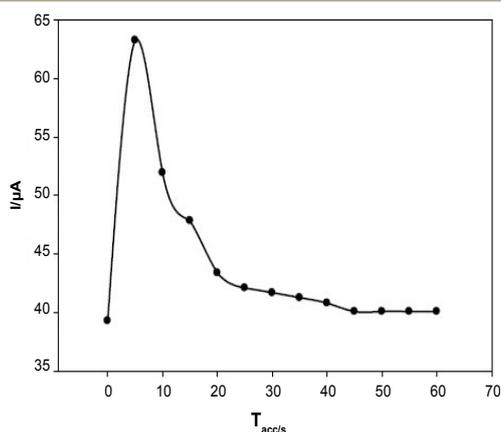
Figure 9b Plot of the anodic peak current versus accumulation time.
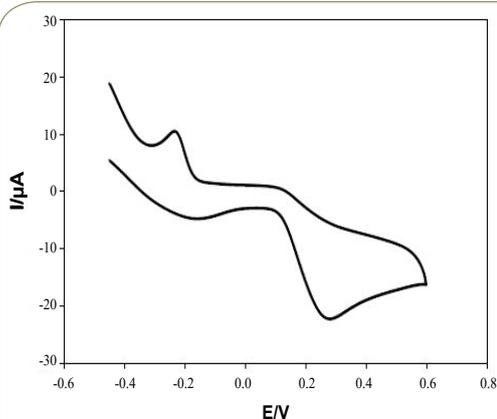
Figure 10a Cyclic voltammogram of 1.0×10^{-3} mol L^{-1} epinephrine in BR buffer of pH 7.0 and 40 µL SDS (1.0×10^{-2} mol L^{-1}) at CPE, scan rate 100 mV s^{-1}.

Figure 10b Oxidation mechanism of epinephrine at CPE
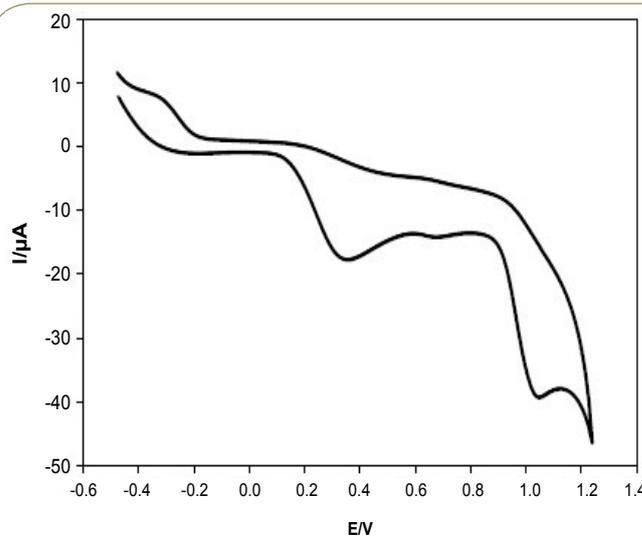
Figure 10c Cyclic voltammogram of 1.0×10^{-3} mol L^{-1} articaine HCl and epinephrine in BR buffer of pH 7.0 and 40 µL SDS (1.0×10^{-2} mol L^{-1}) at CPE, scan rate 100 mV s^{-1}.
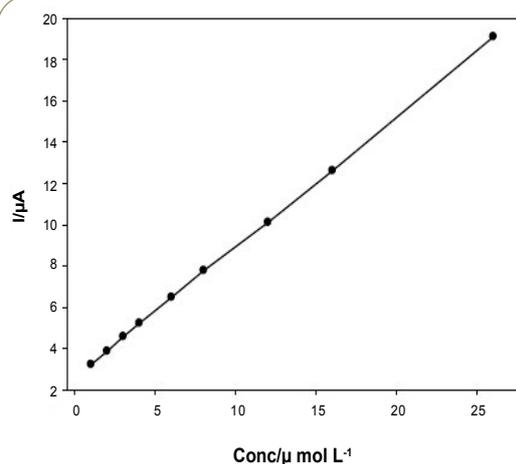
Figure 11a Calibration curve of the anodic peak current to the corresponding concentration of articaine HCl.

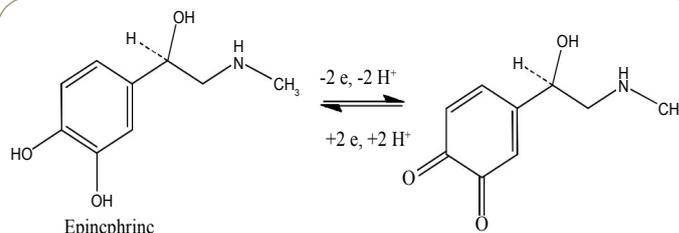98.1 ± 1.96 and 98.2 ± 1.94 for articaine HCl and epinephrine, respectively. The proposed method is more sensitive than spectrophotmetric method for articaine HCl 10-70 µg/mL [10], spectrophotometric methods for epinephrine: 2-20 mg mL^{-1} [20], 1.5-30, 3.0-30, and 1.5- 25 µmol L^{-1} [21], 0.4-12.8 mg mL^{-1} [22], 1.143-142.90 µg mL^{-1} [23], and 1.8-35.3 µg mL^{-1} [24], and electrochemical methods for epinephrine: 3.0-175.0 µmol L^{-1} [26], and 1.0×10^{-5} to 1.0×10^{-3} mol L^{-1} [29]. The regression parameters were computed and presented in **Table 1.**

LOD and LOQ: The limits of detection (LOD) and of quantification (LOQ) were determined according to ICH [46] using the standard deviation of multiple blank samples and the slope of the

Figure 11b Calibration curve of the anodic peak current to the corresponding concentration of epinephrine.
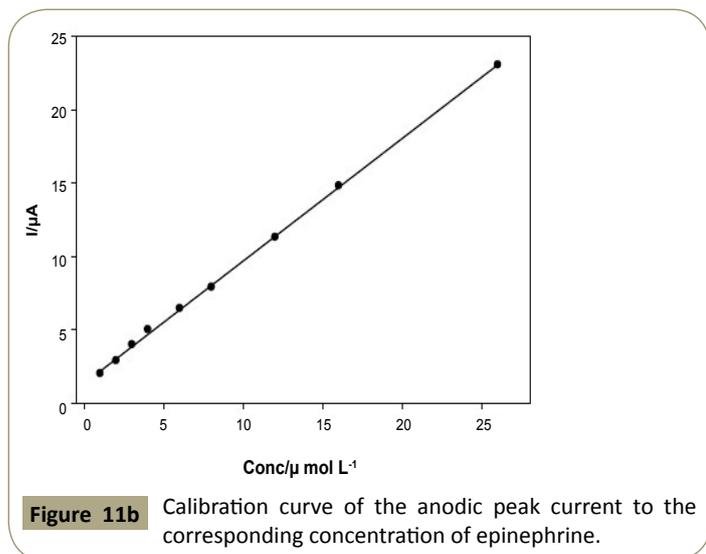
Table 1 Regression parameters for the determination of articaine HCl and epinephrine by proposed electrochemical method.

Parameter	Articaine HCl	Epinephrine
Linearity range (mol L^{-1})	1.0×10^{-6}- 2.6×10^{-5}	1.0×10^{-6}- 2.6×10^{-5}
Slope ± SD*	0.631 ± 0.57	0.834 ± 0.49
Intercept ± SD*	2.637 ± 0.055	1.370 ± 0.013
R^2	0.9998	0.9995
LOD (mol L^{-1})	2.88×10^{-7}	5.10×10^{-8}
LOQ (mol L^{-1})	8.72×10^{-7}	1.56×10^{-7}

*Average of three determinations at each level

calibration curve. The limits of detection and quantification were found 2.88×10^{-7} mol L^{-1} and 8.72×10^{-7} mol L^{-1} for articaine HCl and 5.10×10^{-8} mol L^{-1} and 1.56×10^{-7} for epinephrine, respectively (Table 1).

Robustness

The robustness of proposed DPV method using 6.0×10^{-6} mol L^{-1} of the two drugs was evaluated by variation in the concentration of SDS and pH of BR buffer. The relative standard deviation (%RSD) and Recovery (%R) values listed in Table 2 indicate that the DPV method was not affected by deliberate changes in the optimum parameters of the method.

Accuracy and precision

Intraday and interday accuracy (%R) ranged from 99.3% to 101.7% and precision (%RSD) from 0.23% to 1.49% for articaine HCl and from 98.3% to 101.5% and from 0.58% to 1.78% for epinephrine (Table 3).

Application to pharmaceutical formulation

The proposed method was applied successfully for the determination of articaine HCL and epinephrine in pharmaceutical dosage form in the presence of excipients and additives in the same concentration range as in the bulk without interference with a recovery of 100.4 ± 0.65 and 99.2 ± 0.71, respectively. The standard addition technique was further used to determine the recovery of the proposed method (Table 4).

Statistical analysis of the results obtained by the proposed method compared with a reported method [47] revealed no significant difference between the proposed and reported methods, where the calculated t- and F- values are less than the tabulated ones, confirming accuracy and precision at 95% confidence limit [48]. However, the proposed method allows simultaneous determination of both drugs, the reported method determines both drugs separately (Table 5).

The reported method involved determination of articaine HCl and epinephrine by HPLC; articaine HCl was determined using mobile phase (600 mL acetonitrile and 400 mL [1.3 mL from 1.0 mol L^{-1} sodium phosphate+32.5 mL from 0.5 mol L^{-1} disodium phosphate in 1000 mL with distilled water (pH 8.0)], lichrospher 100 RP-18 (5 μm × 250 mm × 4 mm) as column and wavelength of 240 nm. Epinephrine was determined using gradient mobile phase [A: methanol, B: 0.42% w/v tetramethylammonium hydrogen sulphate+0.116% w/v sodium heptanesulfonate+0.21% v/v disodium edetate at pH 3.5 with 40% NaOH], Kromacil C18 5 μm × 4 mm × 150 mm and wavelength of 205 nm.

Simultaneous determination of articaine HCl and epinephrine in spiked urine samples

Successive additions of articaine HCl and epinephrine solutions (1.0×10^{-3} mol L^{-1}) covering the linearity range of (1.0×10^{-6}- 2.6×10^{-5} mol L^{-1}) were added to the voltammetric cell containing 5 mL of diluted urine and 40 μL of 1.0×10^{-2} mol L^{-1} SDS, the voltammograms were recorded at a scan rate of 20 mV s^{-1} using DPV at carbon paste electrode with percentage recoveries were calculated from regression equation (Table 6).

Conclusion

In the present work a simple, sensitive, accurate and precise electroanalytical voltammetric method was developed for

Table 2 Robustness results of the proposed DPV method.

Parameter	Articaine HCl		Epinephrine	
	%RSD*	%R*	%RSD*	%R*
pH 6.8	0.98	100.8	0.53	99.15
pH 7.2	0.14	98.9	0.38	99.70
38 μ	0.63	101.3	1.21	100.35
42 μ	1.52	100.8	0.85	101.6

*Average of three determinations at each level.

Table 3 Intraday and Interday accuracy and precision for the simultaneous determination of articaine HCl and epinephrine by the proposed electrochemical method.

Procedure	Taken (μmol L^{-1})	Intraday			Interday		
		Found (μmol L^{-1})	%R*	%RSD*	Found (μmol L^{-1})	%R*	%RSD*
Articaine HCl	2	2.03	101.5	1.03	2.01	100.5	1.49
	8	7.94	99.3	1.1	8.07	100.9	1.1
	12	12.04	100.3	1.25	12.2	101.7	0.23
Epinephrine	1	0.991	99.1	0.86	0.983	98.3	1.12
	8	8.04	100.5	1.41	8.12	101.5	0.68
	12	12.15	101.3	0.58	11.8	98.3	1.78

*Average of three determinations at each level.

Table 4 Application of standard addition technique for the simultaneous determination of articaine HCl and epinephrine in Artinibsa® carpules by the proposed electrochemical method.

Articaine HCl				Epinephrine			
Mean ± RSD	**Standard addition**			**Mean ± RSD**	**Standard addition**		
	Claimed taken (µmol L⁻¹)	**Pure added (µmol L⁻¹)**	**%R of added**		**Claimed taken (µmol L⁻¹)**	**Pure added (µmol L⁻¹)**	**%R of added**
Artinibsa® carpules	6.0	2	100.6	Artiniba® carpules	1.0	1	99.8
		4	100.6			3	98.8
		6	100.3			5	98.8
		8	101.3			7	98.5
		12	99.4			11	99.6
		18	99.9			15	98.2
						25	100.2
Mean ± RSD	100.4 ± 0.65			Mean ± RSD	99.2 ± 0.71		

Table 5 Results obtained by the proposed electrochemical method compared with the reported method for the analysis of articaine HCl and epinephrine in Artinibsa®carpules.

Parameters	Articaine HCl		Epinephrine	
	Proposed method	**Reported method [47]**	**Proposed method**	**Reported method [47]**
Linearity range (µg mL⁻¹)	0.32-8.34	20-70	0.183-4.763	1.5-4.0
N (number of replicates)	9	6	9	6
Mean %	98.1	99.8	98.2	99.5
SD*	1.96	1.38	1.94	1.17
Variance	3.84	1.9	3.76	1.37
t-test	1.95 (2.77)		1.61 (2.77)	
F-test	1.95 (6.39)		2.74 (6.39)	

*Average of three determinations at each level; Figures in parenthesis are theoretical t and F values at 95% confidence level.

Table 6 Simultaneous determination of articaine HCl and epinephrine in spiked urine samples.

Concentration (µmol L⁻¹)	%R Articaine HCl	%R Epinephrine
2	102.2	98.4
3	97.3	101.2
4	99.5	97.2
6	100.3	99.2
8	98.5	102.3
12	100.8	101.0
18	99.7	99.3
26	98.5	100.8
Mean ± RSD	99.6 ± 1.53	99.9 ± 1.68

simultaneous determination of articaine HCl and epinephrine in bulk, pharmaceutical dosage forms and spiked human urine based on the electrochemical oxidation of these drugs at carbon paste electrode in BR buffer of pH 7.0 in the presence of sodium dodecyl sulphate, which allows to use the proposed method for routine quality control applications for articaine HCl and epinephrine.

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