

Dual Electrochemical Methods for Determination of Anesthetic Procaine: Square Wave Voltammetry and Differential Pulse Polarography

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Abstract—Procaine belongs to a type of medicine in which excessive dosage form creates cardiac problems and many allergic reactions. Thus, continuous monitoring of this drug and its metabolite is crucial for sustainable health management during treatment. In this study, electrochemical techniques such as square wave voltammetry (SWV) and differential pulse polarography (DPP) are utilized for assaying procaine amounts in standard and pharmaceutical formulations. In SWV, the reduction of diazotized procaine gives a reduction peak at -0.05 V which is directly proportional with procaine hydrochloride concentration, whereas in DPP, the interaction of the drug with lead cation at -0.4 V is followed by the decrease in peak current of the lead cation reduction peak, which is directly proportional with the concentration of the drug. Both methods indicate high accuracy, sensitivity and precision. Linear concentration ranges of both methods are 0.0999 – 5.996×10^{-7} M for SWV and 0.1999 – 5.996×10^{-7} M for DPP. The limit of detection (LOD) and limit of quantification (LOQ) are calculated for both SWV and DPP techniques, and found that LOD equals 1.984×10^{-9} M and LOQ equal 6.611×10^{-9} M for SWV, while for (DPP) LOD and LOQ were found to be 3.519×10^{-9} M and 1.173×10^{-8} M, respectively.

Index Terms— Electrochemical techniques, Polarography, Procaine hydrochloride, Voltammetry.

I. INTRODUCTION

Procaine hydrochloride or (2-diethylaminoethyl 4-aminobenzoate hydrochloride) was synthesized for the 1st time in 1905, and it was the first injectable synthetic local anesthetic drug Fig. 1.

Procaine hydrochloride is a group of compounds that, at an appropriate concentration in the nerves reduce pain sensation from particular areas of the body by the reversible block of the impulse conduction throughout nerve axons and other excitable membranes in which use sodium channels

as the primary mean of action potential generation (Dutu, et al., 2014). It can also prevent cardiac ectopic pacing point autoregulation and dilate blood vessels, hence being adopted to cure ischemic cerebrovascular disease, hemiplegia, and acute renal failure (Zhu, Xu and Liu, 2021). This anesthetic drug is also given in combination with penicillin to treat bacterial infections. It is used as a substitute for cocaine because of its ease of production, sterilization, and the fact that it is non-psychoactive. Its length of activity is shorter than cocaine and it is considerably less toxic (Qader, et al., 2023). In spite of that, Excessive dosage of procaine hydrochloride may lead to central nervous system and cardiovascular reactions such as nausea, respiratory distress, and in severe cases, even anaphylaxis and death. Hence, it is vital to establish a simple, efficient and sensitive analytical method for the determination of procaine hydrochloride (Haroon, et al., 2021). There are many techniques used for determination of procaine among such as; UV-vis spectrophotometric methods (Khayoon, 2021, Marin, et al., 2019), polarography (Plotycya, et al., 2018), chemiluminescence (Golshani, et al., 2023), chromatography (Tonooka, et al., 2016), high-performance liquid chromatography (He, et al., 2013), and electrochemical methods (Guan, et al., 2016; Haghghian, Ghoreishi and Attaran, 2023). Voltammetric methods have easily met the needs in this field because they have been providing safe, accurate, sensitive and reproducible results for years (Altunkaynak, Yavuz and Levent, 2021).

Square wave voltammetry (SWV) is a set of matched amplitude pulses implemented under a staircase potential, in each forward pulse the chemical species diffuse to the electrode surface, and it is abruptly reduced or oxidized. During the backward pulse, the chemical species that was just oxidized or reduced returns to the initial state in a reversible reaction, or if the system is irreversible, no reaction will occur. Therefore, the current values are estimated before and at the end of each pulse, and the resulting or net current equals to reversed current minus forwarded current (Megale and Souza, 2023). While, the differential pulse polarography (DPP) the current is determined as a function of time and as a function of the potential between the reference and working electrodes (Alghamdi and Messali, 2018).

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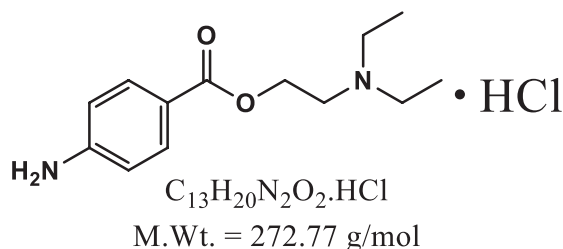


Fig. 1. Chemical structure of procaine hydrochloride.

Innovative electrochemical analysis instrumentation specifically techniques of voltammetry afford reliable and reproducible data for the assay of the analyte (Domergue, et al., 2023).

This study's intention is to evaluate procaine hydrochloride using electrochemical techniques such as SWV and DPP. The performance of the voltammetric techniques is strongly affected by the aspects of the working electrode material, such as the chemical and physical properties of electrode surfaces, applied potential, adsorption, and coatings applied to the electrode surface to enhance detection. Solid electrodes represent the most rapidly growing class of electrodes. In general, solid electrode materials have the advantage of being more mechanically stable, and they provide a larger anodic range than mercury-based electrodes. Furthermore, the handling of solid electrodes is much easier, such that they may readily be applied in flow streams due to their mechanical stability and hardness (Uslu and Ozkan, 2007). The method is simple, sensitive, and rapid.

II. EXPERIMENTAL

A. Apparatus

The measurements were carried out using a voltammetric analysis, model VA Computrace 797, equipped by the Swiss company Metrohm. In addition, the ultrasonic device was used which is of Chinese origin to dissolve solids and pharmaceutical preparations well and to clean the electrode surface using ultrasound waves. A sensitive balance of Japanese origin is also used and a device (Hanna) Model 211, Romanian origin is used to measure the pH.

B. Chemicals and Materials

All chemicals used in this work were at a high degree of purity and were used without any further purification. 1×10^{-4} M of procaine hydrochloride (from Sigma-Aldrich), 1% w/v sodium nitrite solution (from BDH), hydrochloric acid (HCl), 0.2 M boric acid solution (H_3BO_3), Phosphoric acid 0.2 M solution (H_3PO_4), Acetic acid 0.2 M solution (CH_3COOH), Britton-Robinson buffer (BRB) solution (pH 2.0), 250 ppm lead acetate [$Pb(CH_3COO)_2 \cdot H_2O$].

Preparation of pharmaceutical samples

For PenG (300,000 IU) injection powder

One ampoule of PenG is weighed totally (which contains 300,000 IU procaine hydrochloride). An aliquot quantity, that is equivalent to 0.1363 g of procaine hydrochloride, is dissolved in 50 mL of distilled water. An aliquot of the

diluted solution of the injection is analyzed employing the procedures outlined in methods SWV and DPP (Qader, et al., 2023).

For Deva (600,000 IU) injection powder

One ampoule of Deva is weighed totally (which contains 600,000 IU procaine hydrochloride). An aliquot quantity, equivalent to 0.1363 g of procaine hydrochloride, is dissolved in 50 mL of distilled water. An aliquot of the diluted solution of the injection is analyzed employing the procedures outlined in methods SWV and DPP (Qader, et al., 2023).

C. Procedure and Working Steps in SWV

First, 8 mL of BRB is added to the electrochemical cell, and passing nitrogen gas for 5 min for deoxygenation, the applied voltage is -0.05 to 0.0 volts. Then, 1.0 mL of 1% solution of sodium nitrite and 1.0 mL of 1 M hydrochloric acid under the same conditions are added, and nitrous acid is produced in the electrochemical cell instantaneously. To measure and determine the amount of procaine hydrochloride, $5 \mu L$ of 1×10^{-3} M is added to the electrochemical cell, and all the data are collected under instrument conditions (Alallaf, Al-Tae and Othman, 2024).

D. Procedure and Working Steps in DPP

10 mL of BRB was added to the electrochemical cell. Then, passing nitrogen gas for 5 min for deoxygenation, and a silver electrode was used as a WE. After that, 200 μL of lead acetate was added, and optimization of the parameters was carried out. After completing the optimization, the procaine hydrochloride was added to the electrochemical cell, its interaction with lead acetate were observed and the decrease in reduction current of lead acetate was followed (Alhazmi et al., 2020).

III. RESULTS AND DISCUSSION

A. Principle of the Proposed Method SWV

SWV offers an attractive alternative in which the participation of non-faradaic current could be minimized in the voltammogram. As an alternative to linearly sweeping the potential with a defined sweep rate, the potentials are applied as a waveform of specific pulse amplitude (E_{amp}) and width (t_p) in a staircase fashion, in the first cycle a positive E_{amp} is followed by an oppositely directed negative E_{amp} of equal magnitude, immediately after that a next cycle starting at an increased potential according to Estep value (Pilz and Kielb, 2023).

SWV method includes an indirect determination of procaine hydrochloride in its pure form and pharmaceutical preparations by following the reduction of diazotized procaine hydrochloride prepared simultaneously inside the electrochemical cell. Indirect methods provide higher sensitivity and selectivity than direct methods, with the sharper peak shape of the voltammogram (Jones, et al., 2018).

Salts of Diazonium are a large group of organic compounds with the general formula $R-N_2^+X^-$, that R can be alkyl or

aryl and X is an organic or inorganic anion such as halogen (Tavakkoli, et al., 2021).

The aryl diazonium grafting mechanism involves a reductive electron transfer to the diazonium salt, occurring concurrently with the removal of dinitrogen and the subsequent formation of aryl radicals. These radicals subsequently attach to the surface of the electrode. It is generally accepted that aryl diazonium molecules form a covalent carbon-carbon or metal-carbon bond on carbon-based materials and silver substrates, respectively (Mezour, et al., 2018).

The reaction occurs between the amine group and the nitrite, Scheme 1, as a first step to form the corresponding diazonium salt. The azo group in diazonium salt is reduced to the -NHOH group and it will further reduce to NH_2 and give rise to a reduction current as a result of the procaine hydrochloride concentration added.

Study of the electrochemical behavior of procaine hydrochloride using SWV

The electrochemical behavior of procaine hydrochloride was studied using SWV, BRB solution (pH 2.0) by scanning the potential between -0.5 to 0.0 volt, no peak has appeared within the studied range of the buffer solution, Fig. 2. Nitrous acid was produced in the electrochemical cell. To measure and determine the amount of procaine hydrochloride, $5 \mu\text{L}$ of $1 \times 10^{-3} \text{ M}$ was added to the electrochemical cell. The diazotized procaine hydrochloride gives a reduction peak which is appeared at 0.06 volts, Fig. 2, with the current value of the peak $25.4 \mu\text{A}$.

B. Optimization of Parameters in SWV

Effect of NaNO_2

To determine the optimal amount of sodium nitrite and hydrochloric acid that have effect on the formation of diazonium salt and voltammogram, different volumes of 0.5 – 3.0 mL with a concentration of 1% were taken to a fixed amount of hydrochloric acid 1.0 mL. The voltammogram was

recorded for each volume and the current was measured as shown in the results of Fig. 3 It is noted that the amount of 2 mL of sodium nitrite gave the highest current so the ratio of $\text{HCl}:\text{NaNO}_2$ is $1:2$ whereas more than this ratio cause noise in voltammogram shape and gave rise to bubble gas NO liberated (Binnewies, et al., 2010).

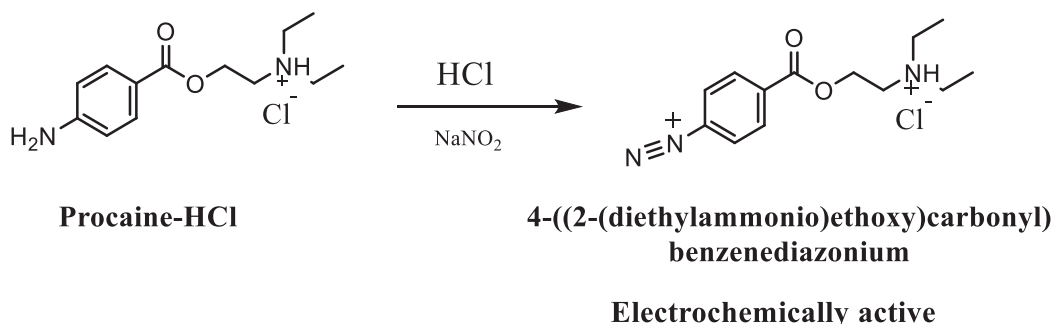
To enhance the shape and the reduction current of the peak that produced in Fig. 2, different parameters that affect the voltammogram shape and the reduction current value has been studied. The parameters under instrument condition and after optimized condition are listed in Table I. The square wave voltammogram of the blank solution and reduction of diazotized procaine hydrochloride measured after optimized condition Fig. 4.

Calibration curve of SWV

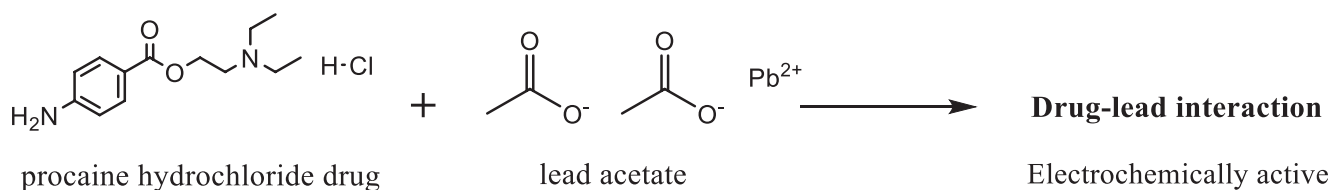
The SW-Voltammograms were recorded at $E_p = -0.05\text{V}$ for sequence additions of procaine hydrochloride ($1 \times 10^{-4} \text{ M}$) to the voltammetric cell containing 1 mL of 1M HCl and 2 mL of 1% NaNO_2 , under the fixed optimum conditions. A plot of I_p versus concentration of procaine hydrochloride added gives two straight lines, first at low concentration range (0.0999 – 0.4997) $\times 10^{-7} \text{ M}$ by a calibration equation $Y = 48.125x + 3.0101$ and second, at high concentration range (0.9999 – 5.996) $\times 10^{-7} \text{ M}$, (Fig. 5) by calibration equations $Y = 4.3491x + 23.836$ with regression coefficient $R^2 = 0.9842$ and 0.9727 , respectively.

C. Principle of the Proposed Method DPP

DPP is an effective and fast electroanalytical technique with many advantages, including low detection limits and good discrimination against background currents (Yilmaz, et al., 2015). The proposed method was based on the principle of drug–metal ion interaction, where the ionizable moieties of the drug molecules complexed with certain metal ions. As a result of their complexation, the reduction current was changed. Procaine hydrochloride interacts with Pb^{2+} ion to produce procaine-Pb complex (Alhazmi, et al., 2020). So, in this method



Scheme 1. Proposed reaction mechanism of reduction of diazonium ion (Alallaf, Al-Tae, and Othman, 2024).



Scheme 2. Proposed reaction of the interaction of procaine hydrochloride with Pb^{2+} in DPP.

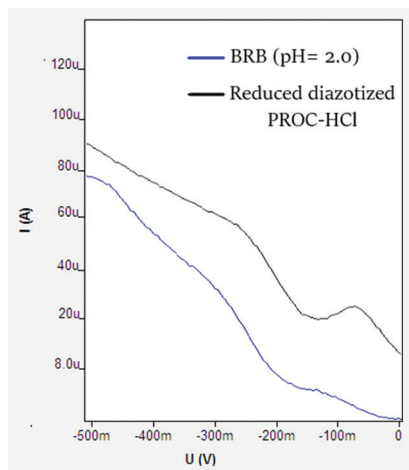


Fig. 2. Square wave voltammogram of reduced diazotized procaine HCl under instrument condition.

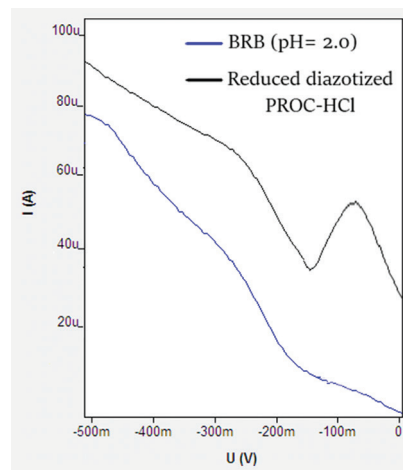


Fig. 4. Square wave voltammogram of reduced diazotized procaine HCl after optimum condition.

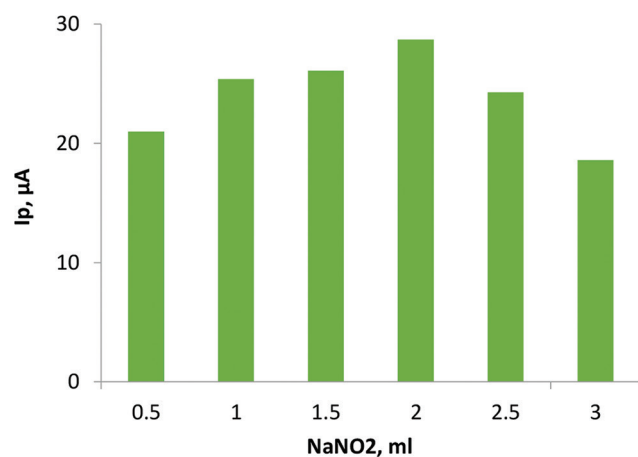


Fig. 3. Effect of amount of sodium nitrite.

procaine hydrochloride is determined indirectly. Scheme 2 shows the proposed interaction of the drug with Pb^{2+} .

Study of the electrochemical behavior of lead acetate

The applied voltage was -0.6 to 0.0 V, no peak has appeared within the studied range of the buffer solution, see Fig. 6. Then, $250 \mu\text{L}$ of 250 ppm lead acetate (electrochemical active) is added to the electrochemical cell, as a result, a peak appeared at a potential of -0.35 V, with the current value of $401 \mu\text{A}$. The differential pulse voltammogram is recorded (Fig. 6) for the BRB solution ($\text{pH} = 2$) and for the lead acetate under instrument condition.

D. Optimization of Parameters in DPP

The applied voltage was -0.6 to 0.0 V, no peak has appeared within the studied range of the buffer solution, Fig. 7. $250 \mu\text{L}$ of 250 ppm lead acetate (electrochemical active) is added to the electrochemical cell, as a result, a peak appeared at a potential of -0.35 V, with the current value of $401 \mu\text{A}$. The differential pulse voltammogram is recorded (Fig. 7) for the BRB solution ($\text{pH} = 2$) and for the lead acetate under instrument and optimized conditions listed in Table II.

TABLE I
STUDY OF THE OPTIMUM CONDITION APPLIED FOR REDUCTION OF DIAZONIUM ION AT PH 2

Parameters	Studied range	Instrument condition	Optimized condition
Start potential (V)	----	-0.05	-0.05
End potential (V)	----	0.0	0.0
Voltage step (V)	$0.0005-0.007$	0.003	0.005
Frequency (Hz)	$40-70$	50	50
Pulse amplitude (V)	$0.01-0.07$	0.03	0.05
Deposition potential (V)	$(-0.2)-(-0.6)$	-0.4	-0.5
Deposition time (s)	$10-60$	60	40
Equilibration time (s)	$1-5$	5	3
No. of cycles	$1-6$	5	5
Cleaning potential (V)	$0.0-0.3$	-0.3	-0.1
Cleaning time (s)	$0-5$	5	3
Sweep rate (V/s)	$0.025-0.3500$	0.1500	0.2500

TABLE II
INITIAL CONDITIONS OF THE INSTRUMENT APPLIED FOR LEAD ACETATE PEAK

Parameters	Studied range	Instrument condition	Optimum condition
Start potential (V)	----	-0.6	-0.6
End potential (V)	----	0.0	0.0
Pulse amplitude (V)	$0.09-0.35$	0.1	0.3
Pulse time (s)	$0.003-0.04$	0.01	0.005
Voltage step (V)	$0.001-0.025$	0.015	0.025
Voltage time (s)	$0.2-0.4$	0.4	0.4
Deposition potential (V)	$(-0.3)-(-0.7)$	-0.5	-0.4
Deposition time (s)	$10-50$	50	40
Equilibration time (s)		5	3
No. of cycles	$1-7$	5	5
Cleaning potential (V)	$1-5$	-0.1	-0.5
Cleaning time (s)	$0-4$	4	3
Sweep rate (V/s)	$0.0250-0.0417$	0.0375	0.0625

During the optimization process, the complexation behavior of certain metal ions including Cd^{2+} , Zn^{2+} , Cu^{2+} , and Pb^{2+} with procaine hydrochloride was investigated. After remarkable efforts, Pb^{2+} was selected for the current analysis because Pb^{2+} exhibited superior binding interaction with procaine drug molecule, and intense sharp peak was

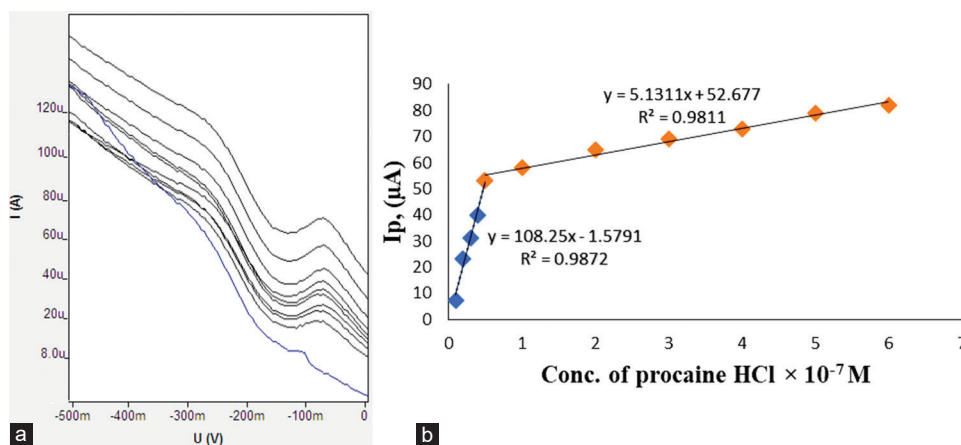


Fig. 5. (a) Voltammogram of serial addition of procaine hydrochloride, (b) Plot of calibration curve for evaluation of procaine HCl, in SWV technique.

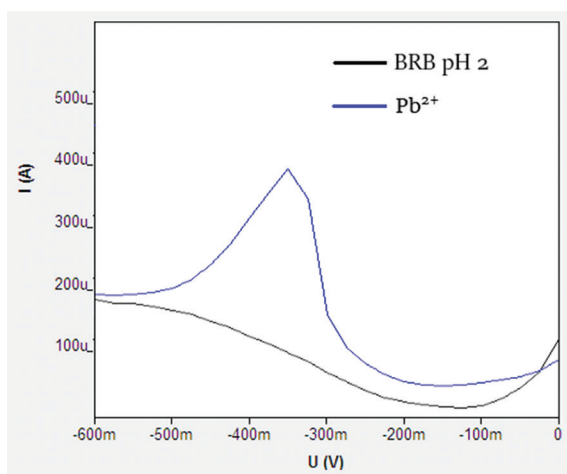


Fig. 6. Differential pulse voltammogram of the buffer and lead acetate (Pb^{2+}) under instrument condition.

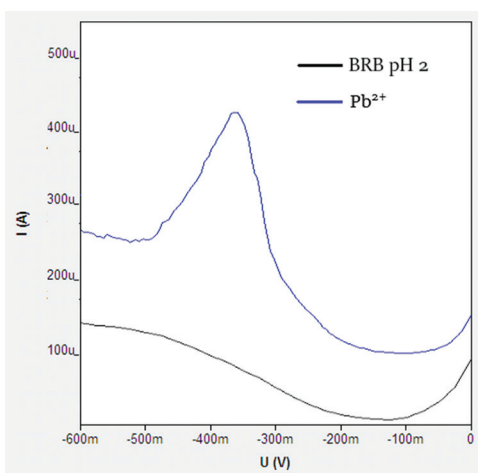


Fig. 7. Differential pulse voltammogram of the lead acetate (Pb^{2+}) under optimum condition.

observed, while for other metal ions, no peak has observed that belong to the procaine-metal interaction. Lead ion has the least negative peak potential does not require greater range of deposition potential. The lead signal increased as the deposition potential became less negative, and vice versa (Van Staden and Matoetoe, 2000).

After completion of the studying optimization of the parameters, 10 mL of BRB (pH = 2) is added to the electrochemical cell. After ensuring no peak of the blank is observed 250 μL of 250 ppm lead acetate is added. The enhanced shape of the lead acetate peak can be noticed in Fig. 7.

Electrochemical behavior of procaine hydrochloride and procaine-Pb complex

The electrochemical behavior of procaine hydrochloride was studied by adding 10 mL of BRB (pH = 2) in a glass cell as a supporting electrolyte. The voltammograms were recorded under the optimum conditions (Table II) for BRB and procaine hydrochloride as depicted in (Fig. 8a) one broad peak was observed ($E_p = 1.21$ V) for procaine hydrochloride. While, under the similar condition the voltammogram of procaine-Pb complex was recorded, in which a sharp and intense peak was observed at -0.4 V for the complex (Fig. 8b).

The most interesting behavior was revealed for the procaine-Pb complex. DP-voltammograms showed higher current intensity and modified shapes for the reduction peak found approximately at -0.4 V. In spite of the fact that the oxidation potential registered with free procaine shifted to lower values, the current intensity diminished, being comparable with that obtained with the complex. It was observed that the potentials of the peaks not only shifted, but that the shapes of peaks also changed, this may due to the high sensitivity of indirect methods over the direct methods.

Calibration curve of DPP

The DP-Voltammograms were recorded at $E_p = -0.4$ V for sequence additions of procaine hydrochloride (1×10^{-4} M) to the voltammetric cell containing 250 μL of 250 ppm lead acetate, under the fixed optimum conditions. A plot of ΔI_p versus concentration of procaine hydrochloride added gives two straight lines, first at low concentration range $(0.0999-0.4997) \times 10^{-7}$ M by a calibration equation $Y = 205.14x + 3.5133$ and second, at high concentration range $(0.9999-5.996) \times 10^{-7}$ M, (Fig. 9) by calibration equations $Y = 15.124x + 99.597$ with regression coefficient $R^2 = 0.9964$ and 0.9906 , respectively.

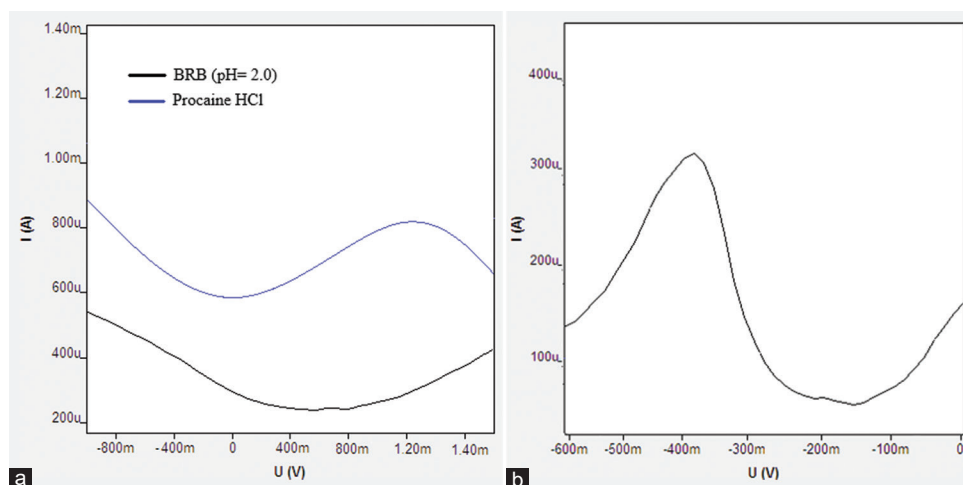


Fig. 8. Differential pulse voltammogram of (a) procaine HCl, (b) procaine-Pb complex.

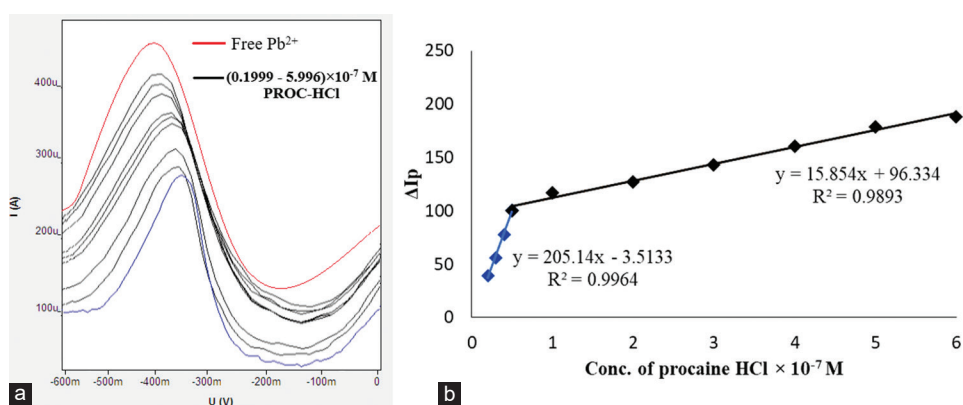


Fig. 9. (a) Voltammogram of serial addition of procaine hydrochloride, (b) Plot of calibration curve for evaluation of procaine HCl, in DPP technique.

E. Analytical Figures of Merit

The accuracy (recovery %), precisions (RSD), and the limits of detection (LOD), and quantitation (LOQ) of the two proposed methods in SWV and DPP techniques are assayed. The accuracy and precision of the proposed procedure in SWV were provided by measuring I_p of procaine HCl after formation of corresponding diazotized procaine of three different concentrations of standard procaine HCl $(0.1999, 0.9999, 4.997) \times 10^{-7}$ M, while in DPP, measuring ΔI_p of procaine-Pb complex after the interaction of procaine with lead acetate of three different concentrations of standard procaine HCl $(0.1999, 1.999, 4.997) \times 10^{-7}$ M, individually in three replicate measurements. The values of recovery% and RSD% were between 97.49% and 99.74%, and 0.413–0.913%, respectively for SWV, while for DPP were 98.85–99.84%, and 0.523–0.951%, respectively. The results are shown in Tables III and IV, indicating that the proposed procedure is valid and applicative. The LOD and LOQ were (1.98433×10^{-9}) M, (6.61144×10^{-9}) M, respectively for SWV, while for DPP were (3.51923×10^{-9}) M, and (1.17307×10^{-8}) M, respectively. Remarkably lower LODs and LOQs for procaine HCl indicated that the proposed method was highly sensitive.

F. Applications

Both methods SWV and DPP were successfully applied to evaluate procaine hydrochloride in its pharmaceutical

TABLE III
ANALYTICAL DATA AND OPTICAL CHARACTERISTICS OF THE PROPOSED METHODS SWV AND DPP

Parameters	Value	
	SWV	DPP
linear range (M)	$(0.0999-5.996) \times 10^{-7}$	$(0.1999-5.996) \times 10^{-7}$
LOD (M)	1.98433×10^{-9}	3.51923×10^{-9}
LOQ (M)	6.61144×10^{-9}	1.17307×10^{-8}
Recovery (%) range*	97.49–99.74	98.85–99.84
RSD%* range	0.413–0.913	0.523–0.951
t_{exp} range	0.219–1.972	0.314–2.945
Determination coefficient (R^2)	0.9842, 0.9727	0.9964, 0.9894
Slope (a) [#]	48.125, 4.3491	205.14, 15.813
Intercept (b) [#]	3.0101, 23.836	3.5133, 96.384

*Average of three determinations, [#]Regression equation ($X=b+ac$), where c is procaine in M at low and high concentrations. LOQ: Limit of quantification

formulation (injection). The applicability of the proposed procedure for the analysis of procaine HCl in pharmaceutical formulations was examined by investigating two pharmaceutical injections (PenG, 300000 IU, 295 mg) and (Deva, 600000 IU, 590 mg) at three different concentrations $(0.1999, 0.9999, 4.997) \times 10^{-7}$ M (SWV) and $(0.1999, 1.999, 4.997) \times 10^{-7}$ M (DPP) of procaine hydrochloride. The results are shown in Table IV.

The performance of the proposed procedure was referred by calculating the experimental t-values. At a95% confidence

level, the calculated t-values did not overstep the theoretical values as noticeable from Table IV. Consequently, it was concluded that there is no significant difference between the proposed methods and the standard method. Moreover, the electrochemical methods for the determination of procaine HCl in pharmaceutical injection addressed in this work are simple, fast, inexpensive, precise, and accurate and they may be suitable for routine analysis and quality control laboratories.

Evolution of the proposed methods

The standard addition method was applied for the estimation of procaine hydrochloride in pharmaceutical products. In SWV two different concentrations 0.999×10^{-7} and 1.999×10^{-7} M of the pharmaceutical form (injection) of procaine hydrochloride were added to the voltammetric cell that contained BRB, 1 mL HCl, 2 mL NaNO_2 , while for DPP 0.1999×10^{-7} and 0.2999×10^{-7} M of the pharmaceutical form (injection) of procaine hydrochloride were added to the voltammetric cell that contained BRB and lead acetate. In each case, a varying amount of standard procaine hydrochloride with a range of 0–5 μL of 1×10^{-4} M was added and measured under the optimum instrument conditions that mentioned before. The results listed in Table V and shown in Fig. 10.

At present, unstable power grid accidents happen frequently; out of these, accidents caused by voltage

instability take up a great part, so research on voltage stability is imperative. Voltage instability may occur when the system voltage is either normal or abnormal, and it is more likely to occur after suffering disturbances in the system (Meng and Pian, 2016). The exact preparation of the pharmaceutical sample might have effect on recovery, these involved minor difference between the amount taken and found from the proposed methods. During the experimental procedure, the slight difference had no impact on the peak current strength, signifying the reliability of the applied method during the regular procedure. The good recovery implied the high selectivity, and efficiency of the method. Indicate that there is a high agreement between the standard addition method and the proposed methods (SWV and DPP) for the determination of procaine hydrochloride in its pharmaceutical preparations (injection).

G. Comparison of the Proposed Methods with other Electrochemical Methods

In the literature, procaine hydrochloride was quantified using different electrochemical techniques and working electrodes whether modified or unmodified. A number of analytical variables of the proposed methods were compared with the same variables of two other electrochemical methods and shown in Table VI.

TABLE IV
ANALYSIS OF PROCAINE HCL IN PHARMACEUTICALS PREPARATIONS FOR METHODS SWV AND DPP

Drug	Certified Value (mg)	Method (A) SWV			Method (B) DPP		
		Found ($\times 10^{-7}$ M)	Rec. (%) \pm RSD* t_{exp}	Measured value (mg)	Found $\times 10^{-7}$ (M)	Rec. (%) \pm RSD* t_{exp}	Measured value (mg)
PenG injection (Iran)	295	0.1949	97.49 \pm 0.526 $t_{\text{exp}} = 1.972$	287.59	0.1991	99.59 \pm 0.708 $t_{\text{exp}} = 1.995$	293.79
	295	0.9974	99.74 \pm 0.760 $t_{\text{exp}} = 0.219$	294.23	1.979	98.99 \pm 0.523 $t_{\text{exp}} = 2.171$	292.02
	295	4.979	99.63 \pm 0.865 $t_{\text{exp}} = 0.426$	293.91	4.989	99.84 \pm 0.764 $t_{\text{exp}} = 0.314$	294.52
Deva injection (Turkey)	590	0.1988	99.44 \pm 0.913 $t_{\text{exp}} = 0.329$	586.69	0.1976	98.85 \pm 0.872 $t_{\text{exp}} = 1.182$	583.21
	590	0.9866	98.66 \pm 0.413 $t_{\text{exp}} = 1.923$	582588.09	1.992	99.65 \pm 0.951 $t_{\text{exp}} = 0.438$	587.93
	590	4.984	99.74 \pm 0.612 $t_{\text{exp}} = 1.224$	46	4.960	99.26 \pm 0.743 $t_{\text{exp}} = 2.645$	585.63

*Average of three determinations, **Theoretical calculation of t at 95% confidence level (n=5) was 3.18, ***The values after the sign \pm are the relative standard deviation of the three replications of each sample

TABLE V
THE RESULTS OF STANDARD ADDITION METHODS FOR ANALYSIS OF PROCAINE HYDROCHLORIDE IN ITS DRUGS

Drug	Certified value (mg)	Amount taken ($\times 10^{-7}$ M)	Amount measured ($\times 10^{-7}$ M)	Average of recovery (%)	Average of measured value (mg)
SWV					
PenG injection (Iran)	295	0.999	1.030	101.79	300.28
		1.999	2.004		
Deva injection (Turkey)	590	0.999	1.020	99.99	589.94
		1.999	1.957		
DPP					
PenG injection (Iran)	295	0.1999	0.2007	98.24	289.81
		0.2999	0.2882		
Deva injection (Turkey)	590	0.1999	0.1982	99.67	588.05
		0.2999	0.3005		

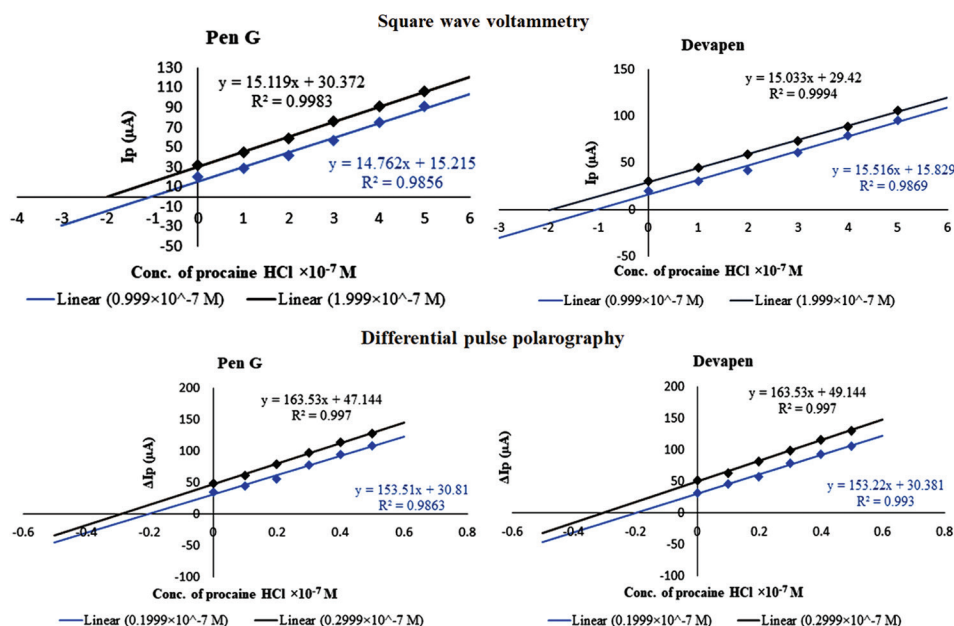


Fig. 10. Plot of standard addition method for determination of procaine HCl in pharmaceutical preparations using proposed methods SWV and DPP.

TABLE VI
 COMPARING A NUMBER OF VARIABLES OF THE PROPOSED METHOD WITH OTHER ELECTROCHEMICAL METHODS

Literature method	Literature method	Proposed method 2	Proposed method 1	Parameter
(Zhu, Xu and Liu, 2021)	(Silva, Salles and Paixão, 2015)			
Differential pulse voltammetry	Square wave voltammetry	Differential pulse polarography	Square wave voltammetry	Used technique
Molecular imprinting membrane/ diamond graphite surface	GCE/RuOHCF	Silver	Silver	Electrode
Phosphate Buffer/pH 7	NaNO ₃ and HCl in deionized water	BRB/pH 2	BRB/pH 2	Supporting media
0.9	0	-0.4	-0.05	Ep (V)
4×10^{-8} – 2.5×10^{-5}	$(5-100) \times 10^{-6}$	$(0.1999-5.996) \times 10^{-7}$	$(0.0999-5.996) \times 10^{-7}$	Linearity (M)
1.5×10^{-8}	11×10^{-9}	3.5192×10^{-9}	1.9843×10^{-9}	LOD (M)
2.22–3.12	2.2–3.0	0.413–0.913	0.523–0.951	RSD %

LOD: Limit of detection

Based on the data shown in the Table above, the proposed methods are more sensitive than the other literature methods, have a better RSD% range compared to other methods, and can be applied for the determination of PROC-HCl at low concentrations. Despite that, some analytical methods have lower LOD values and wider linear range, but the proposed methods do not need pre-treatment of the sample besides the easy and short time of the analysis.

IV. CONCLUSION

The electrochemical estimation of procaine hydrochloride by SWV and DPP on the basis of reduction of diazotized procaine hydrochloride and interaction of procaine with lead ion, respectively, signifies a substantial and reliable analytical process. The proposed method has the expediency of simplicity and rapidity for the determination of procaine in both bulk and dosage forms (injection). The proposed methods offer high sensitivity, precision and accuracy for the quantification of procaine hydrochloride in pharmaceutical samples (injection). The sensitivity of method 1 (SWV) was

found to be greater than method 2 (DPP) with LOD value 1.9843×10^{-9} M, and RSD% of method 1 was in a good range of 0.413–0.913%. The simplicity of the approach, linked with its cost-effectiveness and potential for automation, positions it as a critical tool for routine quality control analysis in the pharmaceutical sector.

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