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Voltammetric behaviour of drotaverine hydrochloride in surfactant media and its enhancement determination in Tween-20

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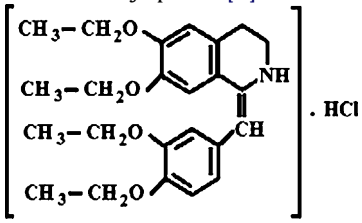
ABSTRACT

Simple, sensitive and rapid adsorptive voltammetric behaviour of drotaverine hydrochloride onto the HMDE has been explored and validated in surfactant media by using cyclic, differential pulse and square-wave voltammetry. Addition of Tween-20 to the drotaverine hydrochloride containing electrolyte enhances the reduction current signal. The voltammograms of the drug with Tween-20 in phosphate buffers of pH 2.5–11.0 exhibit a single well defined reduction peak which may be due to the reduction of –C=C– group. The cyclic voltammetric studies indicated the reduction of drotaverine hydrochloride at the electrode surface through two electron irreversible step and diffusion-controlled. The peak current showed a linear dependence with the drug concentration over the range 0.8–7.2 μg mL^{-1}. The calculated LOD and LOQ are 1.8 and 6.0 ng mL^{-1} by SWCAdSV and 8.1 and 27.2 ng mL^{-1} by DPCAdSV, respectively. The procedure was applied to the assay of the drug in tablet form with mean percentage recoveries of 100.2% with SWCAdSV and 99.7% with DPCAdSV. The validity of the proposed methods was further assessed by applying a standard addition technique.

1. Introduction

Drotaverine [A] is widely used in medicine as an effective spasmolytic agent [1–3]. This drug is capable of relieving spasms of various organs, regardless of their function and innervation. Drotaverine hydrochloride has been proved to be superior in its efficiency to papaverine hydrochloride and its absorption after oral administration is more reliable [4]. It is used as an antispasmodic in the treatment of various conditions, e.g., gastrointestinal diseases, biliary dyskinesia, nephrolithiasis, gynaecological diseases and vasomotor diseases associated with smooth muscle spasms [5,6]. It can also be used as an adjuvant to hypotensive agents in acute disturbances of blood pressure in hypertensive disease, angina pectoris and coronary spasms [7].



[A]

There are few reports in the literature for the determination of drotaverine by, spectrophotometry [8–11], high performance liquid chromatography [12–15], differential spectrophotometry [16,17], computer-aided spectrophotometry [18], potentiometric flow injection analysis [19], spectrofluorometric [20], ion selective electrode [21–23] and voltammetry [24–26].

Surfactants influence the electrochemical processes of electroactive species [27–29] and thus are widely used in electroanalytical chemistry to improve the sensitivity and selectivity [30–33]. Contrary to the extensive applications of surfactants in the electroanalytical chemistry, little work has been carried out to explore the nature of surfactant adsorption on electrode surfaces. Adsorption of surfactant aggregates on the electrode surface might significantly facilitate the electron transfer, change the redox potentials or charge transfer coefficients or diffusion coefficients and alter the stability of electrogenerated intermediates or electrochemical products [34–38]. The main objective of the present work is to develop an electrochemical method for the determination of drotaverine hydrochloride utilizing enhancement effect of surfactant.

2. Experimental

2.1. Instrumentation

Electrochemical measurements were performed with Metrohm Computrace Voltammetric Analyzer μ-AUTOLAB TYPE III Poten-

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tiostat Ecochemie (Utrecht, The Netherlands) Model 757 VA computrace software. A conventional three-electrode system was used consisting of an Ag/AgCl (3.0 M KCl) as a reference electrode, hanging mercury drop electrode (HMDE) as a working electrode and a graphite rod as auxillary electrode. The whole measurements were automated and controlled through the programming capacity of the apparatus. The data were treated through a PC connected to the Electrochemical Analyzer version-757 VA computrace. Controlled potential coulometric experiments were performed using an Autolab Potentiostat/Galvanostat PGSTAT Metrohm 663 VA stand as electrochemical cell, fitted with a PC provided the appropriate GPES 4.2 (General Purpose Electrochemical Software). All pH-metric measurements were made on Decible DB-1011 digital pH meter fitted with a glass electrode and saturated calomel electrode as reference, which was previously standardized with buffers of known pH.

2.2. Reagents and materials

Drotaverine hydrochloride was generously provided by Mapra Laboratories Pvt. Ltd., Mumbai. Tablets containing drotaverine hydrochloride (*Drotin*) labeled 40 mg were obtained from commercial sources. Phosphate buffers in the pH range 2.5–11.0 were prepared in distilled water by adding suitable amounts of 85% H_3PO_4, KH_2PO_4, Na_2HPO_4 and Na_3PO_4 to obtain a final pH 2.5–11.0. The final volume of all buffer solutions is 200 mL^{-1}; the ionic strength is 0.2 M and is used as supporting electrolyte. The ionic strength was kept constant by adjusting with 1.0 M KCl. All chemicals used for preparation of buffers and supporting electrolytes were of analytical reagent grade (Merck and Sigma) quality and were employed without further purification.

2.3. Procedure

Ten tablets were weighted accurately and crushed to a fine powder. For preparation of stock solution of 1.6 mg mL^{-1}, 40 mg drotaverine hydrochloride powder was accurately weighed and transferred into 25 mL of two volumetric flasks separately and completed to volume with methanol and Tween-20. The contents of flask were stirred magnetically for 30 min and then diluted to volume with same solvent. After dilution the solution was centrifuged. An aliquot of the sample was then transferred into a calibrated flask and a series of dilutions were prepared with 1.0 M KCl and then transferred to a volumetric cell and desired waveform was recorded in the range (−0.8 to −1.4 V). The drug contents per tablet were determined referring to the related regression equations.

2.4. Operational conditions and electrochemical measurements

All the solutions examined by electrochemical technique were purged for 10 min with purified nitrogen gas after which a continuous stream of nitrogen was passed over the solutions during the measurements. For cathodic adsorptive stripping voltammetric measurements, a known volume of drotaverine hydrochloride was pipetted into a 10 mL volume calibrated flask and then completed to the volume with phosphate buffer (pH 2.5), Tween-20 and KCl. Then nitrogen was passed for 5 min to remove the dissolved oxygen under stirred conditions. The selected accumulation potential was applied at the working electrode for a selected time by keeping the constant pulse amplitude while the solution was stirred. At the end of the accumulation time period the stirrer was stopped and 10 s was allowed for the solution to become quiescent. Then the voltammograms were recorded by scanning the potential towards the negative direction over the range −0.8 to −1.4 V vs. Ag/AgCl reference electrode by applying the square-wave waveform and peak current was measured at −1.0 V. The electrode cleaning procedures were carried out for each and every experiment and this required only 5 min. Electrochemical pretreatment was always performed in the same solution in which the measurement was subsequently carried out.

Table 1
Electrochemical data for the reduction of drotaverine hydrochloride in presence of different solvents.

Electrolyte (phosphate buffer pH 3.51)	i_p (μA)	Potential (V)
Drotaverine hydrochloride (8.0 μg mL^{-1}) + Methanol	1.53	0.97
Drotaverine hydrochloride (8.0 μg mL^{-1}) + CTAB (1.0%)	1.05	0.98
Drotaverine hydrochloride (8.0 μg mL^{-1}) + SLS (1.0%)	0.98	1.12
Drotaverine hydrochloride (8.0 μg mL^{-1}) + Tween-20 (1.0%)	2.08	1.02

3. Results and discussion

The electrochemical behaviour of drotaverine hydrochloride on HMDE was studied by using cyclic voltammetry (CV), differential pulse cathodic adsorptive stripping voltammetry (DPCAdSV) and square-wave cathodic adsorptive stripping voltammetry (SWCAdSV). In all electrochemical methods drotaverine hydrochloride gave one well defined reduction peak in methanol and surfactant, which is attributed to the reduction of –C=C– bond.

3.1. Effect of surfactant

The square-wave voltammetric response of drotaverine hydrochloride was compared in methanol and in presence of surfactants. The influence of different kinds of surfactants including cetyltrimethylammonium bromide (CTAB), sodium lauryl sulphate (SLS) and Tween-20 were investigated. It is observed that the addition of Tween-20 to the drotaverine hydrochloride containing electrolyte enhanced the peak current and the limit of detection is found to be lower while CTAB and SLS showed an opposite effect (Table 1).

The enhancement in reduction peak is related to the concentration of Tween-20. The relationship between the reduction peak current and Tween-20 concentration is illustrated in Fig. 1. Gradual increment in the peak current is observed as the concentration of Tween-20 is increased from 0.001 to 1.0%. However the reduction current of drotaverine hydrochloride decreases as the concentration of Tween-20 is higher than 2.0%. The decrease in peak current with increased concentration of Tween-20 is due to micelle formation, resulting in partition of the drug between the aqueous phase and micelle, i.e. it gets entrapped in the insulated hydrophobic environment of the micelle and then diffuse along with the micelle, which leads to drop in peak current [39]. Therefore 1.0% concentration of Tween-20 is chosen as optimum one.

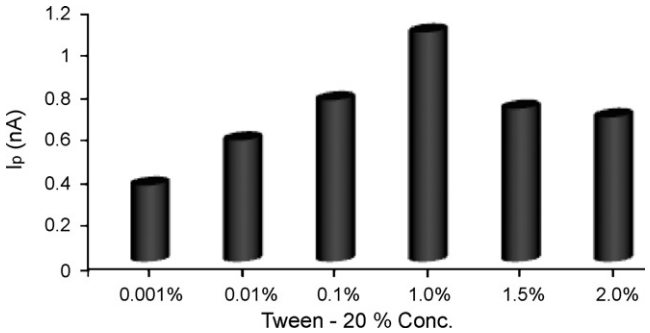

Fig. 1. Plot of i_p (μA) vs. concentration of Tween-20 in phosphate buffer, pH 4.51.

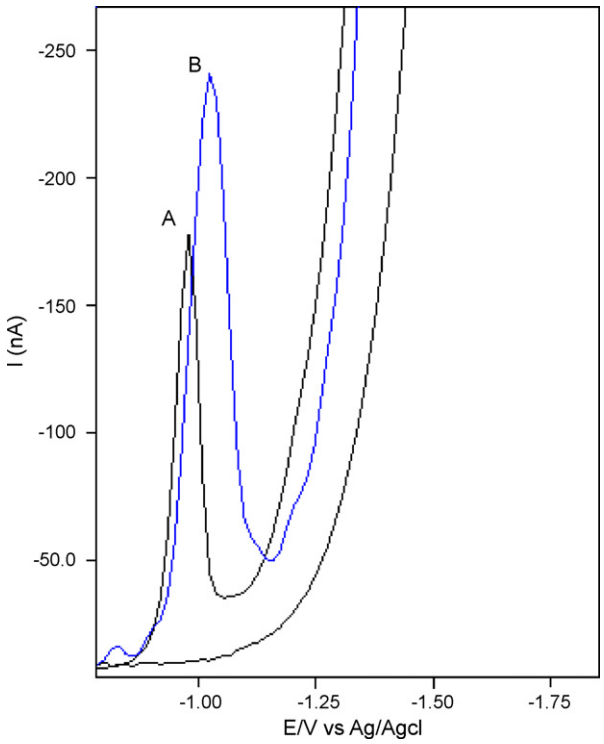

Fig. 2. Square-wave voltammograms of 8.0 μg mL^{-1} drotaverine hydrochloride (B) in presence of Tween-20 and (A) in methanol.

3.2. Comparison of square-wave cathodic adsorptive stripping voltammetric behaviour of drotaverine hydrochloride in the presence and absence of surfactant

On comparing the voltammetric behaviour of drotaverine hydrochloride in methanol and in the presence of Tween-20, it is observed that drotaverine hydrochloride shows substantial increase in peak current and the limit of detection is also found to be lower in Tween-20 (Fig. 2).

The reason for the increase in peak current may due to the occurrence of lateral interaction in the adsorbing species. These workers concluded that once the adsorbed ions reach a certain critical concentration at the interface; they begin to associate into two dimensional patches of ions, which Fuerstenau et al. termed as "hemi micelles" [40–42]. The hemi micelle concentration of Tween-20 is 8.14×10^{-3} mol L^{-1}. The drotaverine hydrochloride molecules which are essentially nonpolar, as is observed by its low solubility in water are attracted to nonpolar region of these hemi micelles which are oriented towards the electrode surface. Thus more drotaverine hydrochloride molecules reach to the electrode surface as a consequence of which there is a rise in peak height. There is no possibility of hemi micelle formation of cationic (CTAB) and anionic (SLS) surfactants. This is because of micelle formation with both surfactants; the sparingly water soluble drotaverine hydrochloride drug gets entrapped in the insulated hydrophobic environment of the micelle and then diffuses along with the micelle, which leads to drop in the peak current. More energy is thus required for the reduction process to occur. Similar observations were reported by Kirchoff et al. in their studies on rhenium and technetium complexes [43].

3.3. Effect of pH

Various electrolytes such as Britton Robinson, acetate, borate, citrate and phosphate buffers were used. The best results with respect to sensitivity accompanied with sharper response were obtained with phosphate buffer (0.2 M). Therefore studies were made in the pH range 2.5–11.0 is phosphate buffer at a target concentration of 9.6 μg mL^{-1} aqueous drotaverine solution. With the rise in pH the peak potential shifted towards more negative potential which indicated the existence of a protonation reaction coupled with the drotaverine hydrochloride reduction process.

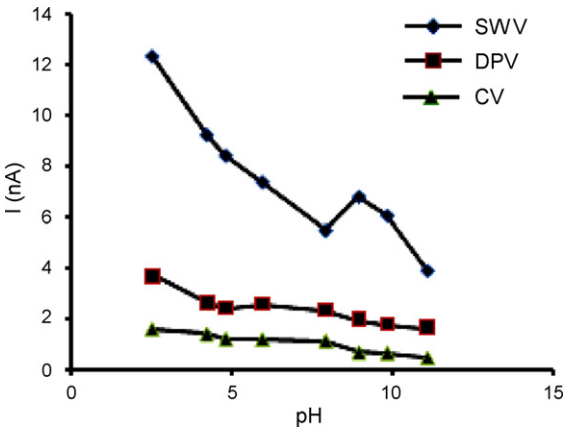

Fig. 3. Effect of pH on the cathodic adsorptive peak current response for 9.6 μg mL^{-1} drotaverine in phosphate buffer (pH 2.5–11.0) after 10 s preconcentration time; frequency (f) = 50 Hz, Δs = 15 mV and pulse amplitude = 50 mV at E_{acc} = −0.1 V.

The relation between E_p of the wave and pH of the medium over the range 2.5–11.0 is expressed by the following equations:

SWCAdSV; pH 2.5–11.0 : $E_p(V) = 0.012 + 1.024$ pH : $r^2 = 0.994$

DPCAdSV; pH 2.5–11.0 : $E_p(V) = 0.014 + 0.978$ pH : $r^2 = 0.914$

CV; pH 2.5–11.0 : $E_p(V) = 0.015 + 0.987$ pH : $r^2 = 0.994$

Linear pH dependence of the peak potential for reduction wave in the entire pH range shows that protons participate directly in the reduction process. The study of the influence of pH on peak current (Fig. 3) was also carried out to determine whether the electroactive species participate in equilibria involving protons directly and to obtain the pH for maximum signal. The height of the peak is maximum at pH 2.5 and after that it decreases. Therefore, pH 2.5 was chosen as the optimum one for the determination of drotaverine hydrochloride.

3.4. Cyclic voltammetric behaviour

The reversibility of the reduction process was investigated by using cyclic voltammetry. The cyclic voltammogram of drotaverine hydrochloride (20 μg mL^{-1}) in 1.0 M KCl containing 1% Tween-20 HMDE exhibits a single well defined peak in the potential range −0.8 to −1.4 V, at all concentrations due to the reduction of the –C=C– group. No peak could be observed in anodic direction of the reverse scan suggesting the irreversible nature of the electrode process [44].

The peak potential shifted towards more negative values with increased scan rate, confirming the irreversible nature of the reduction process. For a totally irreversible electrode process, the relationship between the peak potential (E_p) and scan rate (υ) is expressed as [45]:

$$E_p = \left(2.303RT\alpha_n F \log\left(\frac{RTK_f}{\alpha_n F}\right)\right) - (2.303RT\alpha_n F) \log \upsilon$$

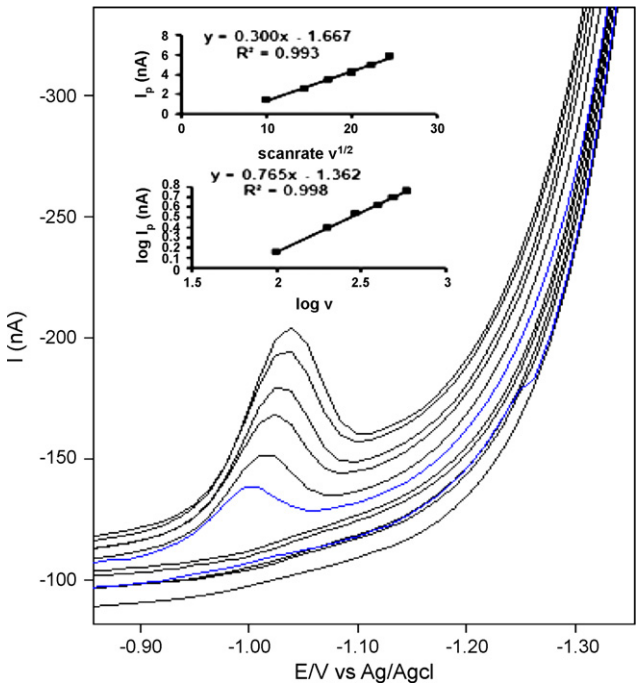

Fig. 4. Cyclic voltammograms of 20 μg mL^{-1} drotaverine hydrochloride in 1.0% Tween-20 at different scan rates; 100, 200, 300, 400, 500 and 600 mV s^{-1}.

A straight line was observed when E_p was plotted against log υ at a particular concentration at pH 2.5 and can be expressed as

$E_p = 0.102(\log \upsilon) + 0.7644$; $r^2 = 0.998$

From the slope of the straight line ($\Delta E/\log \upsilon$), the value was calculated by the expression $\Delta E/\log \upsilon = 30/\alpha_n$. The α_n value is found to be 0.21 and is taken for further calculation for the number of electrons transferred. Fractional α_n values further confirmed the irreversible reduction of drotaverine hydrochloride.

The effect of scan rate ($\upsilon^{1/2}$) on stripping peak current (i_p) was examined under the above experimental conditions. As the sweep rate was increased from 100 to 600 mV/s at a fixed concentration of drotaverine hydrochloride, (i) the peak potential shifted cathodically, (ii) the peak current increased steadily, and (iii) the peak current function, $i_p/AC\upsilon^{1/2}$, exhibited near-constancy (Fig. 4). A linear Randles–Seveik plot (plot of i_p against $\upsilon^{1/2}$) was obtained; a straight line is obtained with linear regression equation; $y(i_p) = 0.3002\upsilon^{1/2}$ (mV/s) − 1.6675 (nA), $r^2 = 0.9937$ indicating that diffusion-controlled nature of the electrode process.

For finding the adsorptive character of the drug at HMDE a cyclic voltammogram was recorded after 10 s preconcentration at −1.0 V and second cyclic at same mercury drop. Furthermore a substantial decrease in the peak current value in subsequent scans was observed, which reached a steady state, indicating that drotaverine hydrochloride also shows adsorptive characteristics at mercury electrode.

This finding is confirmed by plotting log i_p against log υ; a straight line is obtained which can be expressed by the equation: $\log i_p = 0.765 \log \upsilon$ (V s^{-1}) − 1.3627; $r^2 = 0.998$; $n = 6$ with slope value 0.76, which is less than the theoretical value of 1.0 that is expected for an ideal reaction of surface species. The lower experimental slope (0.76) than the theoretical one may be attributed to the partial involvement of the diffusive drug molecules in the electrode reaction of the adsorbed ones. The overall electrode process is mainly diffusion-controlled with adsorption of the drug molecules at the electrode surface.

3.5. Optimization of operational parameters

Variation of the stripping voltammetric peak current of drotaverine hydrochloride in Tween-20 at HMDE was investigated using square-wave and differential pulse modes. Both the techniques gave comparable results but square-wave cathodic adsorptive stripping voltammetry has been chosen for optimizing the operational parameters. The SWV technique is more sensitive than DPV and CV, because in SWV both forward and reverse current are measured while only forward current are measured in DPV and also the scan rate determined by the SW frequency (5–500 Hz) is much faster than DPV [46]. The peak current obtained in SWV are about four times higher than differential pulse response. The important instrumental variables in SWV are accumulation time (t_{acc}), accumulation potential (E_{acc}), pulse amplitude (ΔE_{sw}), scan increment (Δs) and frequency (f) were examined.

3.5.1. Influence of preconcentration time

The effect of preconcentration time for 9.6 μg mL^{-1} drotaverine hydrochloride was investigated from 0 to 100 s. A linear relationship is observed in preconcentration time range from 0 to 100 s. Above 10 s, saturation coverage of the electrode occurs. Thus for this work preconcentration time of 10 s was chosen for adsorptive stripping voltammetric determination of drotaverine hydrochloride.

3.5.2. Influence of preconcentration potential

The influence of preconcentration potential (E_{acc}) on the cathodic peak current (i_p) of drotaverine hydrochloride was also examined over the potential range −0.1 to −1.2 V and the maximum peak current was achieved at −0.1 V. Hence, preconcentration potential of −0.1 V was used throughout the present study. At more cathodic values a decrease in peak current was observed.

3.5.3. Influence of frequency

Frequency was varied from 10 to 140 Hz using a scan increment of 100 mV, pulse amplitude of 50 mV and 10 s preconcentration time. A linear relationship was obtained between the peak current and frequency of the signal up to 50 Hz. Hence the frequency of 50 Hz was chosen for entire analysis.

3.5.4. Influence of scan increment and pulse amplitude

The effect of scan increment on adsorptive cathodic peak current of the drug in Tween-20 at pH 2.5 revealed that the peak current increases upon the increase of scan increment (100–1000 mV). A scan increment of 100 mV was used in the present study. At pulse amplitude of 50 mV, the peak current was found to be much more sharp and defined.

Several instrumental parameters, those directly affect voltammetric response, were also optimized for e.g., mercury drop size, stirring rate and the rest period. The working conditions decided upon were: drop size 4 cm^2 and 2000 rpm. The stripping was not significantly affected when varying the rest period, since it was observed that 10 s was sufficient for the formation of a uniform concentration of the reactant onto the mercury drop.

3.6. Validation of the proposed method

3.6.1. Linearity

The applicability of the proposed square-wave cathodic adsorptive stripping voltammetric (SWCAdSV) and differential pulse cathodic adsorptive stripping voltammetric (DPCAdSV) procedures as an analytical method for the determination of drotaverine hydrochloride was examined by measuring the stripping peak current as function of concentration of the bulk drug for at least three times under the optimized operational parameters. The calibration

Table 2
Analytical parameters for voltammetric determination of drotaverine hydrochloride using SWCAdSV and DPCAdSV modes.

Parameter	SWCAdSV	DPCAdSV
Measured potential (V)	1.01	0.97
Linear range ($\mu g\,mL^{-1}$)	0.8–8.0	0.8–8.0
Slope ($\mu A/(\mu g\,mL^{-1})$)	7.0	2.0
Intercept (nA)	2.674	0.237
Correlation coefficient (r^2)	0.997	0.993
S_a	0.0042	0.0054
LOD ($ng\,mL^{-1}$)	1.8	8.1
LOQ ($ng\,mL^{-1}$)	6.0	27.2
Application	Tablet	Tablet

plot of the peak current vs. the concentration was found to be linear over the range 0.8–7.2 $\mu g\,mL^{-1}$ in the square-wave and differential pulse voltammetric method and the linear regression equation is expressed as:

$$\text{SWCAdSV}: \quad [i_p \ \ (\text{nA}) = (7.0 \times 10^6)\text{DRO} \ \ (\mu g\,mL^{-1}) - 2.674],$$

$$r^2 = 0.996$$

$$\text{DPCAdSV}: \quad [i_p \ \ (\text{nA}) = (2.0 \times 10^6)\text{DRO} \ \ (\mu g\,mL^{-1}) - 0.237],$$

$$r^2 = 0.993$$

The regression plots showed that there is a linear dependence of the current intensity on the concentration in both SWCAdSV and DPCAdSV modes over the range as given in Table 2. The table also shows the detection limits and the results of the statistical analysis of the experimental data such as slopes, intercept, the correlation coefficients obtained by the linear least squares treatment of the results along with standard deviation (S.D.) of intercept (S_a) on the ordinate. The good linearity of the calibration graphs and the negligible scatter of the experimental points are clearly evident by the values of the correlation coefficient and S.D. The specificity of the method was investigated by observing any interference encountered from the excipients of the tablets mass. It is shown that in the proposed method co-administered drugs did not interfere.

3.6.2. Sensitivity/detection limits

The limit of detection was calculated by the equation:

$$\text{LOD} = \frac{3S_a}{b}$$

where S_a is the standard deviation of intercept and b is the slope of the regression line [47]. The calculated detection limit for the standard solution for SWCAdSV was 1.8 $ng\,mL^{-1}$ and for DPCAdSV was 8.1 $ng\,mL^{-1}$. The peak is not resolved from the noise at concentration lower than LOD.

3.6.3. Quantitation limits

The quantitation limits were estimated by equation:

$$\text{LOQ} = \frac{10S_a}{b}$$

where S_a is the standard deviation of intercept and b is the slope of the regression line [48]. The lower limit of quantitation for the standard solution for SWCAdSV was 6.0 $ng\,mL^{-1}$ and for DPCAdSV was 27.2 $ng\,mL^{-1}$.

3.6.4. Specificity

Specificity is the ability of method to measure analytical response in presence of all potential impurities. For specificity test, voltammograms of standard solutions of tablet excipients (starch, gelatin, lactose, and magnesium stearate) were recorded under selected conditions. Response of analyte in this mixture was compared with the response of pure drotaverine hydrochloride. It is found that assay results are not changed.

3.6.5. Accuracy

The accuracy of developed method was carried out by spiking with accurately weighed amounts of drotaverine at concentration of the drotaverine tablets (40 mg). The accuracy is expressed as a mean relative error (measured conc. – nominal conc./nominal conc. × 100). The mean recoveries in tablets were found to be 100.2 (SWCAdSV) and 99.6% (DPCAdSV), respectively and the values of mean relative error are acceptable (Table 3); this shows the best accuracy obtained by using these methods.

3.6.6. Precision/reproducibility

The precision and reproducibility of these developed methods (SWCAdSV, DPCAdSV) for drotaverine were determined in three replicate analyses (Table 3). The precision of the proposed procedure was estimated by analyzing drotaverine in tablets assay solutions for three times in four successive days using SWCAdSV and DPCAdSV. The percentage recoveries based on the average of three separate determinations are given in Table 3. The results confirmed both the good precision of the proposed procedure and stability of the drug's solution. The mean variation coefficients are 1.24 and 1.23% for SWCAdSV and DPCAdSV methods, respectively. The variation coefficients are less than 2.0% indicating that two methods are precise and confidence.

3.6.7. Stability

In this study, drotaverine stock solutions for controlling the stability were kept in the dark at +4 °C during 1 month and were analyzed at different times (every day). It has been seen that repeatable peak currents of drotaverine stock solution occurred up to 20 days and after that the peak current decreases significantly. So the solutions were found to be stable during 20 days.

3.6.8. Robustness

The robustness was examined by evaluating the influence of small variation of some of the most important procedure variables including preconcentration potential (E_{acc}) and preconcentration time (t_{acc}). The obtained result provided an indication of the reliability of the proposed procedure for the assay of drotaverine hydrochloride and hence it can be considered robust. The obtained mean percentage recoveries based on the average of five replicate measurements were not significantly affected within the studied range of variations of some operational parameters, and consequently the proposed procedure can be considered robust.

Table 3
Precision and accuracy for assay of drotaverine hydrochloride in tablet samples by the proposed procedure.

SWCAdSV					DPCAdSV			
Added ($\mu g\,mL^{-1}$)	Found ($\mu g\,mL^{-1}$)	%R	Precision (%R.S.D.)	Accuracy (%bias)	Found ($\mu g\,mL^{-1}$)	%R	Precision (%R.S.D.)	Accuracy (%bias)
4.0	4.02	100.5	1.80	0.49	3.95	98.75	1.56	−1.26
5.6	5.58	99.6	0.90	0.35	5.62	100.30	1.28	0.35
7.2	7.23	100.4	1.02	0.41	7.15	99.30	0.85	−0.69

Average of five replicate measurements.

Table 4
Comparison of the detection limit of the proposed method with the other reported method.

Method	Detection limit	Reference no.
High performance liquid chromatography	4.80 ng mL^{-1}	[14]
Spectrofluorometric	0.03 μg mL^{-1}	[20]
Voltammetry	3.15 ng mL^{-1}	[24,26]
Square-wave voltammetry in solubilized system	1.8 ng mL^{-1}	This work

3.6.9. Ruggedness

Two analysts analyzed the same standard with SWCAdSV and DPCAdSV methods using the same instrument. The methods were found to be rugged with the results of variation coefficients 1.3 and 1.6% for SWCAdSV, 1.4 and 1.8% for DPCAdSV methods for first and second analysts, respectively. The results show no statistical differences between different analysts.

4. Comparison of the sensitivity of the method with previously reported methods

Table 4 compares the detection limit of the proposed method with the other reported methods [14,20,24,26]. Its obvious sensitivity of the method is superior to all previously reported methods. The data in Table 4 reveal that the detection limit of the method is lower than all previous reported methods.

5. Application of method to the pharmaceutical dosage forms

The optimized procedure was successfully applied for determination of drotaverine hydrochloride drug in tablets (*Drotin* 40 mg). No need for filtration of tablet extracts from un-dissolved excipients; just dilution of an aliquot from the supernatant layer with the supporting electrolyte is required before measurement. Voltammograms of drotaverine in phosphate buffer exhibit well defined cathodic peak. The current is mainly adsorption-controlled and proportional to the concentration. The analytical performance data of the proposed method are compiled in the Table 2. The good linearity of the calibration graph and the negligible scatter of the experimental points are clearly evident by the correlation coefficients. The precision was estimated using the calibration graph and standard addition method. Representative voltammograms are shown in (Fig. 5).

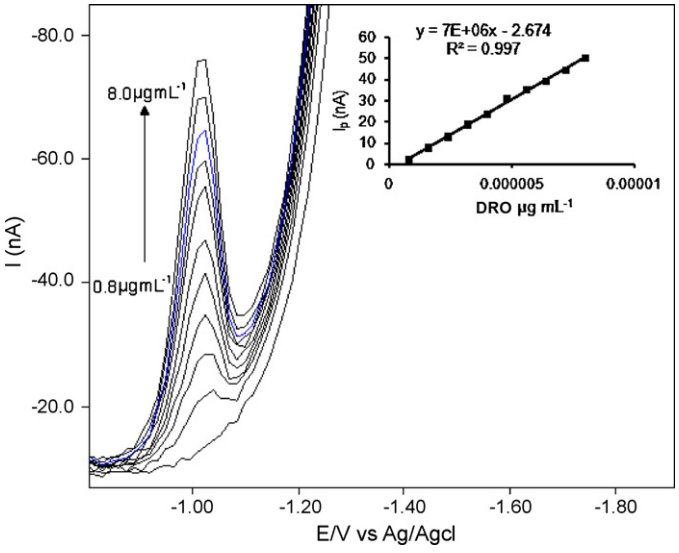

Fig. 5. The dependence of the SWCAdS voltammetric current for drotaverine at different concentrations; phosphate buffer pH 2.5, $E_{acc} = -0.1$ V, $t_{acc} = 10$ s, frequency (f) = 50 Hz, pulse amplitude $\Delta E_{sw} = 50$ mV and scan increment $\Delta s = 10$ mV, (i) Blank, (ii) 0.8 μg mL^{-1}, (iii) 1.6 μg mL^{-1}, (iv) 2.4 μg mL^{-1}, (v) 3.2 μg mL^{-1}, (vi) 4.0 μg mL^{-1}, (vii) 4.8 μg mL^{-1}, (viii) 5.6 μg mL^{-1}, (xi) 6.4 μg mL^{-1}, (x) 7.2 μg mL^{-1}, (xi) 8.0 μg mL^{-1}.

The percentage recovery of drotaverine based on the average of five replicate measurements is 100.2 and 99.6% for SWCAdSV and DPCAdSV, respectively (Table 3). The accuracy of the proposed procedure was also judged by applying the standard addition method as excellent percentage recovery of added drotaverine could be achieved. Therefore, the proposed procedure can be applicable to the analysis of this and other similar formulation products containing drotaverine.

6. Conclusion

The determination of drug in presence of surfactants provides new medium for study of interaction of drugs with surfactants. The above stripping methods show high percentage of recovery i.e. compounds are almost completely extracted from tablet formulation and thus above method can be used to quantify the drotaverine hydrochloride without interference from other ingredients. The reduction peak potential and current values are functions of pH of electrolyte. The developed method with detection limit of 1.8 ng mL^{-1} is more sensitive to already reported method for determination in pharmaceutical dosage form (Table 4). The proposed method has been successfully applied for the determination of the studied drugs in pure and in pharmaceutical formulations applying the standard additions technique and the results obtained are in good agreement with those obtained by the official method. The accuracy and precision of the methods are determined and validated statistically. Consequently, the proposed methods have the potential of a good analytical alternative for determining drotaverine hydrochloride in pharmaceutical formulation.

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