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Adsorptive stripping voltammetric determination of the antidepressant drug sulpiride

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Abstract

The electrochemical behaviour of the antidepressant drug sulpiride (SP) at a hanging mercury drop electrode (HMDE) is investigated. Linear sweep cathodic stripping voltammetry (LSCSV) was used to determine sulpiride in the presence of 0.01 M sodium acetate medium pH 10.5 and 25 ± 1°C. Different parameters such as, supporting electrolyte, pH, accumulation potential, scan rate, accumulation time and ionic strength, were tested to optimize the conditions for the determination of SP. The adsorbed form is reduced irreversibly. The linear concentration range is from 2×10^{-9} to 5×10^{-8} M SP. Experimentally, 2×10^{-9} M (0.68 ppb) with accumulation time 60 s can be determined successfully. Furthermore, a theoretical detection limit of 2×10^{-10} M (0.068 ppb) Sp was calculated. The interferences of some metal ions, ascorbic acid and some amino acids were studied. The method was applied to the analysis of tablets and spiked urine, with recoveries of 104 ± 3 and 101 ± 3, and the relative standard deviation of 3.3 and 3.4%, respectively.

Keywords: Cathodic stripping voltammetric determination of sulpiride; Dogmatil fort tablets; Urine

1. Introduction

Depression is one of the most common psychiatric disorders at any given moment, about 5–6% of the population is depressed (point prevalence), and an estimated 10% of people may become depressed during their life (life time prevalence) [1].

Antidepressant drugs are apt to be most successful in patients with clearly (vegetative) characteristics, including psychomotor retardation, sleep disturbance, poor appetite and weight loss, and loss of libido. However, a variety of different chemical structures have been found to have antidepressant activity. Their number is constantly growing, but as yet no group has been found to have a clear therapeutic advantage over the others [1]. Sulpiride as a crystalline solid is very stable, after 60 months of storage no variation was observed in a batch analyzed by HPLC. Similar results have been obtained when sulpiride was maintained for 30 days at 55, 75 and 100°C. Also daylight and UV light did not affect sulpiride even after a month of exposure [2]. However, direct

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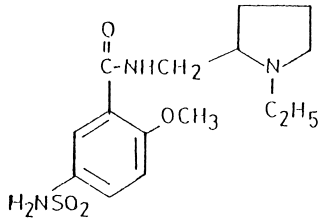
determination of SP can be done spectrophotometrically after extraction with chloroform of an aqueous solution at pH ~ 10 [3]. Moreover, sulpiride was stable in solution and during the determination until pH ≥ 10.5 which in a good agreement with the p*K*a value of the drug [4,5], as well as a stock solution of the drug was prepared daily during the procedure. The structure of sulpiride is drawn as below:



Different amounts of sulpiride were recovered from body fluids and tissues depending on the conditions and solvents used by the different methods viz: spectrophotometry [3], spectrofluorimetry [6], high performance liquid chromotography [7–12], GLC-mass spectrometry [13] and ion-pair HPLC with fluorescence [14]. However, the study of interamuscular administration [8] at the dose levels of 50, 100 and 200 mg to nine healthy male subjects indicated that sulpiride is excreted in urine. Furthermore, rapid determination of sulpiride and other drugs has been performed in pharmaceutical preparations using different analytical techniques viz: liquid chromatography [15], ion-pair reversed-phase high performance liquid chromatography [16], fluorimetry [17], Thin layer chromatography [18], mass spectrometry [19], simultaneous HPLC [20], computer-assisted HPLC system [21] and absorption spectra [22]. Also, sulpiride has been determined using an osillopolarographic method [23] in the presence of acetic acid/sodium acetate buffer of pH 5. This method was applied to the analysis of tablets, as well as it suffer from lack in sensitivity (0.1 mM). But, all techniques maintained previously are not sufficiently sensitive for the direct determination of sulpiride in biological fluids, so that a preconcentration stage is necessary. Cathodic adsorptive stripping voltammetry is a technique in which the analyte is preconcentrated first by adsorption onto a working electrode surface followed by the voltammetric reduction of the electroactive species. Furthermore, stripping voltammetry is an important technique for trace determination of many inorganic and organic substances [24]. The cathodic stripping technique has been used successfully for the determination of subnanogram level of several drugs [25–30]. This technique eliminates both time-consuming solvent extraction steps and calculations of recovery common to photometric and chromatographic methods while the resulting accuracy and precision are at least comparable if not better than the above mentioned methods [31].

The present study deals with the quantitative determination of sulpiride using direct current and differential pulse cathodic stripping voltammetric methods. This technique is simple, rapid, sensitive, reproducible and easy to apply in routine analysis.

2. Experimental

2.1. Instrumentation

For the voltammetric measurements, an EG & G PAR Model 263A polarographic analyzer with 250/270 research electrochemistry software version 4.0 was used with a PAR 303 static mercury drop electrode (SMDE). Silver/silver chloride (saturated KCl) was used as a reference electrode and a platinum wire as an auxiliary electrode.

All the pH measurements were made with an Orion Model 601 A digital ionalyzer.

2.2. Chemicals

A stock solution of 1×10^{-3} M sulpiride (Aldrich Chemical Company, Inc.) was prepared daily by dissolution of the appropriate amount in doubly distilled water. Sodium acetate–acetic acid mixture was prepared and adjusted to the desired pH value with sodium hydroxide. Urine samples from healthy donors and sulpiride Dogmatil fort tablets (Memphis CO. for Pharm.

& Chem. Ind., Cairo, Egypt) were used in the analysis. All other reagents were of analytical grade.

2.3. Procedure

After deaeration with nitrogen for 16 min, a hanging mercury drop (medium size) was formed and the selected accumulation potential was applied with stirring for a given time interval while accumulation of the analyte at the electrode proceeded. After a selected accumulation time and a rest period of 15 s, the potential was scanned from positive to negative direction. Preliminary experiments indicated that the optimal pH should be adjusted to 10.5.

The urine sample was diluted (1:10) with supporting electrolyte (0.01 M sodium acetate–acetic acid buffer), the pH was raised to 10.5 by addition of sodium hydroxide before the voltammograms were recorded and increasing drug concentration. Furthermore, tin Dogmatil fort tablets (each one contains 200 mg SP) were dissolved in bidisttiled water, and the insoluble components were separated by filtration. The filtrate and washings were collected quantitatively in a 250 ml measuring flask.

3. Results and discussion

3.1. Cyclic voltammetry

Cyclic voltammetry of 1×10^{-7} M sulpiride (SP) preceded by quiescent period of 15 s, at accumulation potential $+0.05$ V, 60 s preconcentration time and scan rate 100 mV s^{-1}, in the presence of 0.01 M sodium acetate medium (pH 10.5) was investigated. The cathodic reduction peak is located at -0.125 V and there is a slightly current signal in the reverse direction, within the potential range selected as in Fig. 1. Repetitive cyclic voltammograms suggest rapid desorption of the adsorbed Hg–SP complex and the peak current decreases in the second and third cycles. However, a signal appears on reversing the scan, lower than the reduction one but probably due to the desorption of the reduced compound. Its decrease during the second scan is smaller than that of the reduction peak. This may indicate that the reduction process of the adsorbed form, investigated by cyclic voltammetry is irreversible, through the formation of mercury complex with compounds containing sulfonyl group in general [32,33].

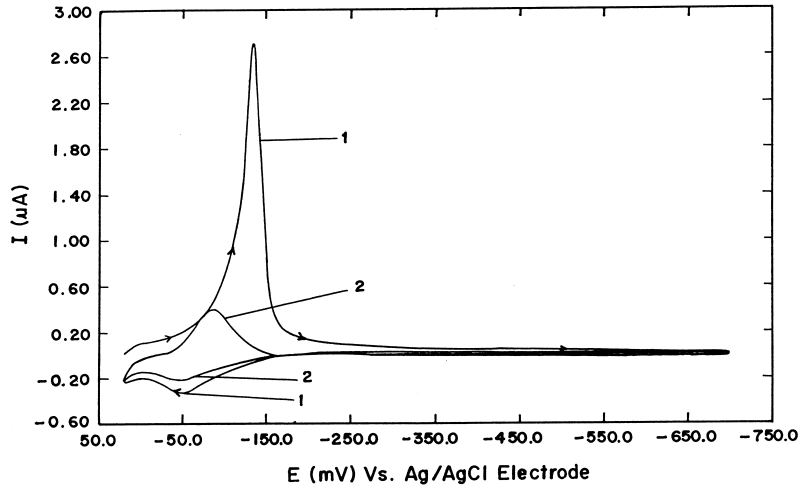


Fig. 1. Cyclic voltammograms of 1×10^{-7} M SP, 0.01 M sodium acetate (pH 10.5) at 60 s accumulation time and 100 mV s^{-1} scan rate.

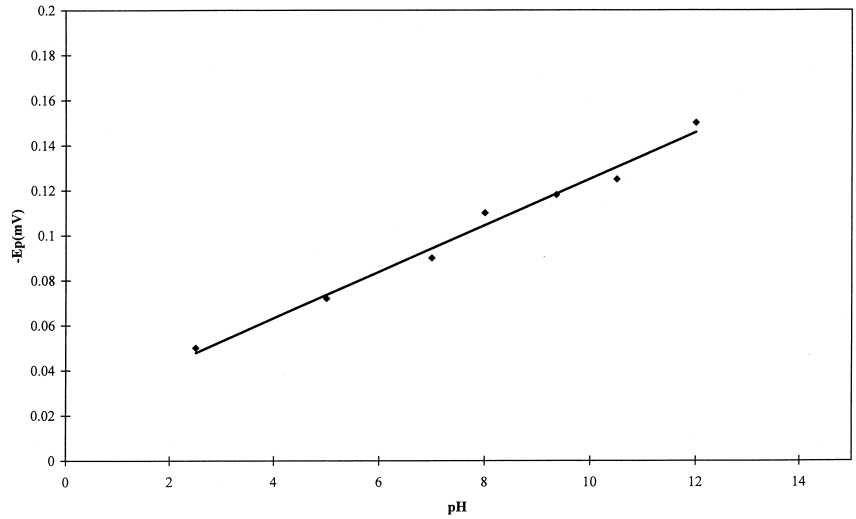


Fig. 2. Plot of pH versus peak potential for 2×10^{-6} M SP, in presence of 0.01 M sodium acetate (pH 10.5) and 60 s accumulation time.

3.2. Effect of supporting electrolyte and pH

A series of supporting electrolytes (borax, disodium hydrogen phosphate, potassium nitrate, sodium hydroxide, trisodium phosphate, citrate and sodium acetate–acetic acid buffer) were tested in the presence of 2×10^{-6} mol dm^{-3} Sp and 60 s accumulation time. Both the peak height and the peak shape were taken in consideration during choosing the supporting electrolyte. The results showed that sodium acetate–acetic acid mixture (pH ~ 10.5) gave the best background and signal response. The solution condition such as the pH and the concentration of sulpiride, affect the peak potential and peak current significantly. The supporting electrolyte concentrations (0.01, 0.03, 0.05 and 0.07 M) have no observable effect on the peak current. The effect of pH was investigated. A small current was observed at pH < 5, which increases gradually up to pH 9 and then increased sharply with a maximum at pH 10.5.At higher pH, the decrease in current and broadening of the peak were observed. Also, the peak potential is shifted to more negative values with increasing pH, as can be seen in Fig. 2. This behaviour indicate that hydrogen ion is participating in the electrode process [34].

3.3. Effect of accumulation potential and scan rate

The effect of the potential on the stripping peak current was examined over the range + 0.2 to − 0.03 V. The results showed that on going in the positive direction from − 0.03 to 0.2 V, the peak height increases. + 0.1 V was chosen to avoid the obscured the required peak at more positive potential. Cathodic stripping voltammetry carried for increasing values of the scan rate, v, under the above optimised conditions gave rise to reduction peaks with intensities that showed a linear increase with the scan rate between 20 to 250 mVs^{-1}, according to the following relationship: $Ip\ (nA) = 1.11(v/V\ s^{-1}) + 0.4$; $r = 0.9996$, $n = 7$ where r is the correlation coefficient and n is the number of cycles. It was found that the peak current increases and the peak potential shifts to more negative values with increasing scan rate (Fig. 3). For subsequent work, 100 mV s^{-1} was selected. The plot of peak current against scan rate (v) gave a straight line with a slope of 1.11. A

slope of 1.0 is expected for ideal reaction of surface species [35].

3.4. Effect of preconcentration time, reproducibility and repeatability

Fig. 4 shows the effect of preconcentration time in the presence of different concentrations of sulpiride. The peak current increased linearly with preconcentration time up to 420 s for 2×10^{-9} M SP. A deviation from the linearity was observed at accumulation times longer than 300 s for both 1 and 3×10^{-8} M sulpiride, respectively. Table 1 illustrates the data collected. In some cases, the linear increasing leads to a large intercept. This is due to that during the rest period, electrodeposition, which facilitated by the diffusion transport, is continued. However, this is no longer affect the

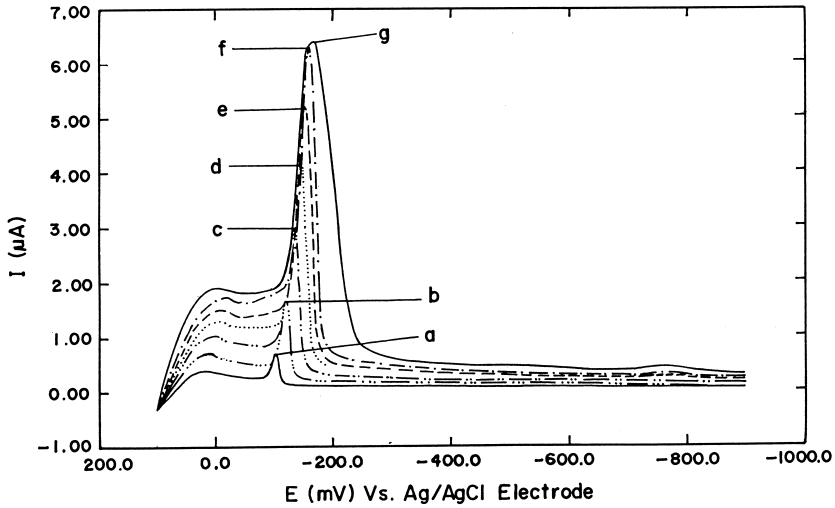


Fig. 3. DC Voltammograms of 1×10^{-7} M SP, with 0.01 M sodium acetate (pH 10.5) and 60 s accumulation time, at differentscan rates: (a) 10; (b) 20; (c) 50; (d) 75; (e) 100; (f) 150 and (g) 250 mV s^{-1}.

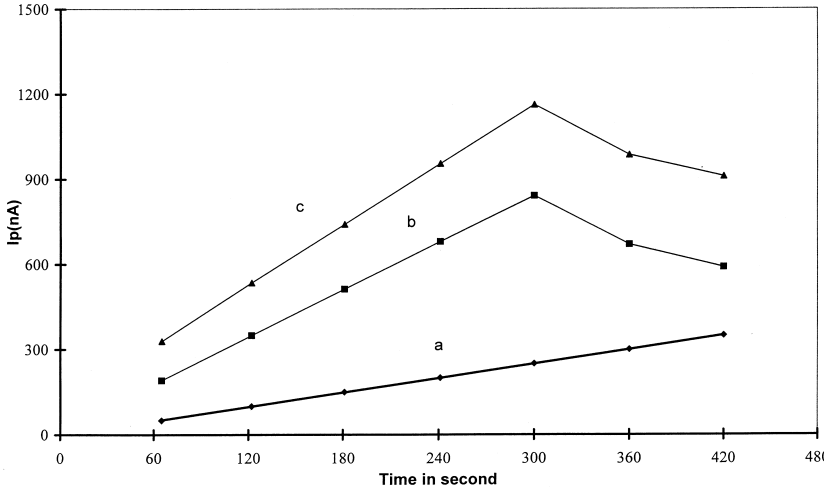


Fig. 4. Plot of current against current in presence of 0.01 M acetate buffer (pH 10.5) for: (a) 2×10^{-9}; (b) 1×10^{-8} and (c) 3×10^{-8} M SP.

Table 1
Characteristic of current-time curves established using different sulpiride concentrations with 0.01 M sodium acetate (pH 10.5)

SP (M)	Equation[a]	Linearity range (s)	RSD for slope	RSD for intercept	Correlation coefficient
2×10^{-9}	$Y=0.834X+3.8$	60–420	0.15	0.17	0.9969
1×10^{-8}	$Y=2.829X+11.17$	60–300	0.25	0.19	0.9978
3×10^{-8}	$Y=2.738X+100.5$	60–300	0.18	0.25	0.9958

[a] Peak height (Y) in nA, concentration (X) in molar.

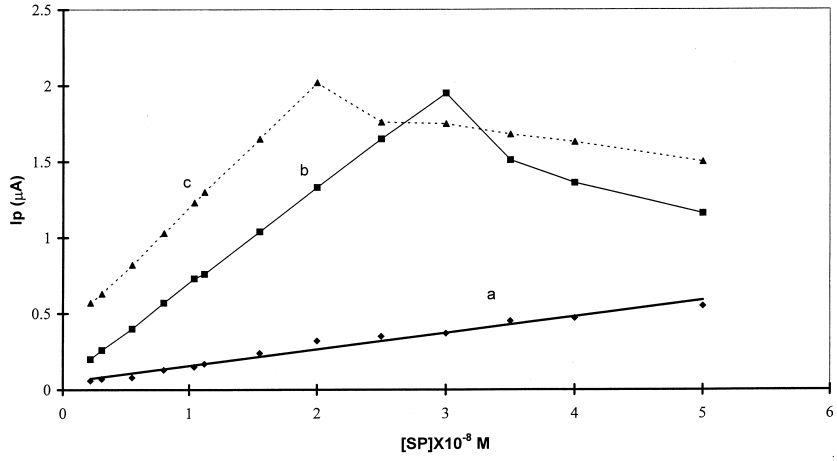


Fig. 5. Plot of I_p versus concentrations of SP in the presence of 0.01 M acetate medium (pH 10.5) at different accumulation times: (a) 60; (b) 90 and (c) 120 s.

precision of the method. On plotting the peak current against the square root of time for 1×10^{-6} M SP (without stirring), a straight line was obtained with a correlation coefficient of 0.9981 and a slope of 0.971. This behaviour is expected for mass transport controlled by adsorption [36].

The reproducibility of the results can be attributed to the reproducible area and self-cleaning control provided by the instrument used. Also, the repeatability of the data can be achieved by seven successive measurements of 2×10^{-9} M SP with 2% relative standard deviation.

3.5. Calibration plot

A well defined stripping peak was observed over the concentration range 2×10^{-9}–5×10^{-8} M at 60, 90 and 120 s, respectively, with stirring at $+0.1$ V. The resulting calibration plots for these concentrations are shown in Fig. 5. The graph show deviations from linearity at concentrations higher than 3 and 2×10^{-8} M SP at 90 and 120 s, respectively. The data obtained from the least-square analysis are given in Table 2.

3.6. Quantitation limit

As low as 2×10^{-9} M (0.68 ppb) at 60 s, in the presence of 0.01 M sodium acetate pH 10.5, using LSCSV technique, has been experimentally determined successfully. Furthermore, a theoretical detection limit of 2×10^{-10} M SP was calculated from 2×10^{-9} M SP based either on a signal-to-noise ratio of 3 [37] or the IUPAC definition[38], by measuring seven blank samples and using as the criterion the equation: (A) $X_L=X_b+3S_b$, where X_L is the smallest measure of response, X_b is the mean of the blank measure, and (B) $LOD=3S_b/S$, where S is the slope of the calibration curve. The relative standard deviation was

2% (seven replicates), with 0.9968 correlation coefficient. The accuracy of the method was investigated by determining the recovery (100 ± 3%) of a definite concentration 0.68 ppb (2×10^{-9} M) sulpiride ($n = 7$), as shown in Table 3. This is a significant improvement over the literature data (1×10^{-4} M) [23].

3.7. Interferences

The influence of ascorbic acid, aspartic acid, *L*-valine, *L*-leucine and glycine, which are potent interfering compounds present in biological samples, were investigated. It was found that an equimolar concentration of each compound (individually and in one mixture) had no effect on the peak response of SP. However, at a higher molar excess (10:1) of these compounds, a depression of the peak response by about 25% were observed.

Furthermore, when some co-existing ions such as Ca(II) [23], Sr(II), Mn(II), Pb(II), Cu(II), Zn(II), were added as an equimolar concentration (individually and in one mixture) to the sample solution, a slight decrease in the peak current has been observed. However, Y. Zeng and Q. Song have been reported that, none of the co-existing ions such as Ca(II) and co-administrable drugs, e.g. chlorpromazine hydrochloride and doxepin, interfered [23].

3.8. Application

3.8.1. In urine

The method was applied to the determination of sulpiride in spiked urine samples without any treatment. A linear dependence on the SP concentration was observed between 1×10^{-8} and 3×10^{-7} M ($r = 0.9978$). From the standard addition plot (Figure not shown), the quantitation limit is

Table 2
Characteristic of the calibration curves established using different deposition times with 0.01 M sodium acetate (pH 10.5)

Deposition time (s)	Equation[a]	Linearity range (M)	RSD for slope	RSD for intercept	Correlation coefficient
60	$Y = 0.108X + 0.049$	$(0.2–5) \times 10^{-8}$	0.12	0.13	0.9969
90	$Y = 0.222X + 0.061$	$(0.2–3) \times 10^{-8}$	0.17	0.15	0.9948
120	$Y = 0.276X + 0.378$	$(0.2–2) \times 10^{-8}$	0.18	0.17	0.9979

[a] Peak height (Y) in μA, concentration (X) in molar.

Table 3
Statistical analysis of the results obtained by the LSCSV for the pure drug, tablet and for urine

Value	Pure drug	Tablet	Urine
n (replicates)	7	7	7
Av. dev for estimation (%)	2.1	2.8211	19.84
Mean recovery (%)			
This work	100 ± 3	104 ± 3	101 ± 3
Literature	96.1–104 [18]	98.8–100.92 [17]	93.1 ± 6.6 [9]
Correl. coefficient	0.9958	0.9868	0.9873
Slope (μA/10^{-8} M)	0.108	0.165	0.0519
Intercept (μA)	0.049	0.655	0.2594
Standard deviation (%)	2	3.32	3.4
Confidence at 95% significant level	0.5013	0.9700	0.4011
F-test	0.5342	0.00232	0.1325

9×10^{-7} M in the original sample, could be determined after 30 s accumulation time using LSCSV technique with good recoveries ($101 \pm 3\%$; $n = 7$), compared with the reported values (93.1 ± 6.6) [8], as observed from Table 3.

The repeatability and reproducibility of the results was tested and the relative standard deviation was found to be 3.4% ($n = 7$).

3.8.2. In tablets

The contents of tin Dogmatil Fort tablets (each contains 200 mg of sulpiride) can be determined using the method described above. The LSV voltammogram was recorded after preconcentration for 30 s, in the presence of 0.01 M sodium acetate medium pH 10.5. The content of the tablet in the cell was determined by the standard addition method. One peak was observed on addition of pure drug to the sample at -0.135 V. On increasing the SP concentration, the peak current was increased linearly according to this equation: $Y = 0.165X + 0.655$, where Y is the peak current in μA and X is the concentration in 10 nM. From the standard addition plots, 204 mg sulpiride in the tablet could be determined. The average percentage recovery was $104 \pm 3\%$, with 2.3% RSD and 0.9968 correlation coefficient, which in a good agreement with the reported value [16]. The statistical parameters of pure drug, urine and tablets were summarized in Table 3.

4. Conclusion

The LSCSV method for the quantitative determination of sulpiride was found to be simple and highly sensitive. A detection limit of 2×10^{-9} M (0.68 ppb or 0.002 mM) was experimentally obtained in pure solution, compared with reported value of 0.1 mM [23]. The method can be used successfully to assay the drug in dosage form as well as in spiked urine.

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