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Electrochemical behavior and determination of amiloride drug in bulk form and pharmaceutical formulation at mercury electrodes

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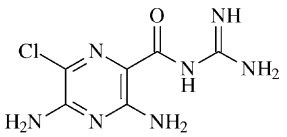
Abstract

The polarographic behavior of amiloride hydrochloride has been studied in Britton–Robinson buffers of pH 1.9–11. In acidic medium at pH $\leq$ 2, the dc-polarograms exhibited a single 4-electron cathodic irreversible wave, while at pH values >2, a second two-electron irreversible cathodic wave appeared at a more negative potential. The single or first wave may be attributed to the cleavage of the double bond of the –CH=NH of the imidino amide group with the release of NH_3. While the second wave may be due to the saturation of the C=O of the carboxamide moiety. A polarographic procedure of suffocate sensitivity for the determination of bulk amiloride drug in Britton–Robinson buffer at pH 2 is described. The calibration graph was obtained over the concentration range 2.5×10^{-5} to 2.5×10^{-4} M amiloride. The limits of detection (LOD) and quantitation (LOQ) of the procedure were 1×10^{-5} and 3.3×10^{-4} M bulk amiloride, respectively. Moreover, a differential-pulse adsorptive cathodic stripping voltammetric procedure has been described to assay of the drug at lower concentration levels. The optimal conditions were: $E_{acc} = -0.9$ V, $t_{acc} = 30$ s, scan rate = 20 mV, pulse-height = 90 mV and Britton–Robinson buffer of pH 8. The calibration graph was obtained over the concentration range 2×10^{-8} to 1×10^{-6} M for bulk amiloride. Both procedures were successfully applied to the determination of amiloride in tablets without the necessity for sample pretreatment or any time-consuming extraction or evaporation steps prior to the drug analysis.

Keywords: Amiloride hydrochloride; Yostriretic® tablets; Determination; Differential-pulse stripping voltammetry

1. Introduction

Amiloride (I): [*N*-amidino-3,5-diamino-6-chloropyrazine-2-carboxamide] is a pyrazinecarbonyl-guanidine-derivative, actiny as a potassium—sparing diuretic [1].



(I)

Amiloride acts directly on the distal renal tubule of the nephron to inhibit sodium–potassium ion

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exchange. Administration of amiloride increases urinary excretion of sodium, bicarbonate, and calcium with little, if any, increase in chloride excretion. Amiloride is used for its potassium-sparing effect in the treatment or prevention of hypokalemia induced by thiazide or other kaliuretics in patients with congestive heart failure or hypertension [1]. Use of amiloride alone or in combination with hydrochlorothiazide has been effective in reducing systolic and diastolic blood pressure.

The drug has been determined in pharmaceutical preparations and biological fluids using several methods including, spectrophotometry [2–10], high performance liquid chromatography [5,11,12], fluorimetry [13–15], capillary isotachophoresis [16], chemiluminescence oxidation [17] and differential-pulse polarography [18]. No adsorptive stripping voltammetric procedures have been reported to date for the determination of amiloride.

In this paper, we demonstrate the electrochemical behavior of amiloride at the dropping mercury and hanging mercury drop electrodes. Moreover, new polarographic and differential-pulse adsorptive cathodic stripping voltammetric procedures are also described to the direct estimation of amiloride drug in bulk form and a pharmaceutical formulation.

2. Experimental

2.1. Materials

Bulk amiloride hydrochloride was obtained from Sigma (St. Louis, MO, USA) The drug tablets, Yostriretic® (Amoun Co., Cairo, Egypt) labeled to contain 5 mg amiloride co-formulated with 50 mg hydrochlorothiazide per tablet. The latter was found to be electro-inactive at the mercury electrode, therefore, it did not interfere in the electroanalytical assay of amiloride drug.

2.2. Reagents and solutions

2.2.1. Bulk drug solutions

A stock solution of 1×10^{-3} M bulk amiloride hydrochloride was prepared by dissolving an accurate mass in a specific volume of ethanol, kept in a dark glass bottle and then stored at 4 °C. More dilute solutions (10^{-4}–10^{-6} M) of bulk amiloride hydrochloride were prepared by accurate dilution with ethanol. The drug solutions were stable and their concentrations did not change with time. The bulk drug solutions were analyzed by means of both the proposed polarographic and differential-pulse adsorptive stripping procedures.

2.2.2. Tablets solution

Ten tablets (Yostriretic®) were weighed and the average mass per tablet was determined. A mass of finely ground material, equivalent to 25 of amiloride, was accurately weighed, and transferred into a 100 ml calibrated flask containing 70 ml ethanol. The contents of the flask were shaken for 15 min and then made up to the volume with ethanol. The solution was next filtered through a 0.45 μm milli-pore filter (Gelman, Germany). Aliquots of this solution were diluted with ethanol to produce 10^{-4}–10^{-6} M amiloride solutions. The tablet solutions were analyzed by means of both of the proposed polarographic and differential-pulse adsorptive stripping procedures.

2.2.3. Britton–Robinson buffer

A series of Britton–Robinson buffers of pH 1.9–11 were prepared [19]. The pH of the buffer was checked using a pH-meter (Knick) of sensitivity ±0.02 pH units. All the chemicals (Sigma) used were of analytical grade and were used without further purification.

2.2.4. Nessler's reagent

Nessler's reagent, $\{K_2(HgI_4)$ in dilute sodium hydroxide$\}$, was used in the present study for testing the formation of ammonia during complete electrolysis of the drug solution at a controlled-potential by mixing the electrolyzed drug solution with Nessler's reagent while warming to about 40 °C. The presence of ammonia gives a reddish brown coloration to a yellow or orange-red to a brown precipitate of basic mercury(II) amido-iodine $\{HgO{\cdot}Hg(NH_2)I\}$, depending on the amount of ammonia [20]. This indicates the release of ammonia on electrolysis of the drug solution at a controlled potential.

2.3. Instrumentation

A pen-recording polarograph Model 4001 Sargent Welch (Skokie, IL, USA) was used for study of the polarographic behavior of amiloride. The cell described by Meites [21] was used for the polarographic studies.

The characteristics of the dropping mercury electrode were $m = 1.03\,mg\,s^{-1}$ and $t = 3.3\,s$, at 60 cm of mercury height. A saturated calomel electrode (SCE) was used as a reference electrode.

The voltammograms were recorded using an Electrochemical Trace Analyzers models 394 and 263A-PAR (Princeton, NJ, USA). The 303A-PAR electrode assembly of a hanging mercury drop electrode (area $= 2.6 \times 10^{-2}\,cm^2$) as a working electrode, a Pt wire as a counter electrode and an $Ag/AgCl/KCl_s$ as a reference electrode was used for the voltammetry measurements. Stirring of the solution in the micro-electrolysis cell at 400 rpm was performed using a magnetic stirrer (Model 305-PAR) with a star-shaped magnet to provide the convective transport during the preconcentration step. The measurements were automated and controlled through the programming capacity of the apparatus. The data were treated through a personal computer connected to the electrochemical analyzer and loaded with the 394 Analytical voltammetry software version—2.01 (copyright 1994).

The potentiostat/galvanostat model 173-PAR incorporated with a digital coulometer model 179-PAR was used for the controlled-potential electrolysis of the drug. A dark coulometric cell of a mercury pool as a working electrode, a saturated calomel electrode as a reference electrode and a platinum gauze immersed in a bridge tube as a counter electrode was used. The potential of the working electrode was maintained constant with respect to that of the reference electrode (potentiostatic control). The potential selected was adjusted to a value equal to the $E_{1/2}$ of the polarographic wave of reactant plus 0.1 V or at the beginning of the limiting current of the polarographic wave. The charge Q (Coulombs) passed during the exhaustive electrolysis was obtained by integrating the current electronically. The number of electrons (n) transferred per reactant molecule via each of the two reduction step was determined using Faraday's relation $N = Q/nF$, where N is the number of moles of substance being electrolyzed, and F is Faraday's constant (96,485 C/g eq.).

A Mettler balance model Toledo-AB104 (Switzerland) was used for weighing the solid materials. Deionized water was obtained from a Purite Still Plus HP deionizer connected to a Hamilton AquaMatic bidistillation water system (UK).

2.4. Procedures

(i) For polarographic and cyclic voltammetric measurements, a known volume of amiloride solution was pipetted into a 10 ml volume calibrated flask and then completed to the volume with Britton–Robinson buffer. The solution was transferred into the electrolysis cell and deoxygenated with pure nitrogen for 10 min, then the polarograms/voltammograms were recorded.

(ii) For stripping voltammetry measurements, a known volume of amiloride solution was pipetted into a 10 ml volume calibrated flask and then completed to the volume with Britton–Robinson buffer at pH 8. The solution was introduced into a dark micro-electrolysis cell, then deoxygenated with pure nitrogen for 10 min. A selected accumulation potential was applied to the working electrode for a selected time while the solution was stirred at 400 rpm. 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 toward the negative direction applying the differential-pulse waveform. All data were obtained at room temperature.

3. Results and discussion

3.1. dc-Polarographic and cyclic voltammetric studies

The polarographic behavior of amiloride hydrochloride was studied in the Britton–Robinson buffers of pH 1.9–11. In buffers of pH $\leq$ 2, the dc-polarograms exhibited a single irreversible cathodic wave, while at pH values >2, two irreversible cathodic waves of unequal heights were observed. The height of the first wave was practically double that of the second one. The total limiting current and that of each of the two waves were practically pH-independent (Fig. 1). Controlled-potential electrolysis of the drug in B–R buffers of pH 3–11 revealed that four and two electrons were consumed in the reduction processes via the 1st and 2nd waves, respectively. At pH $\leq$ 2, four electrons were consumed via the single wave. The single or first wave may be attributed to the cleavage of the double

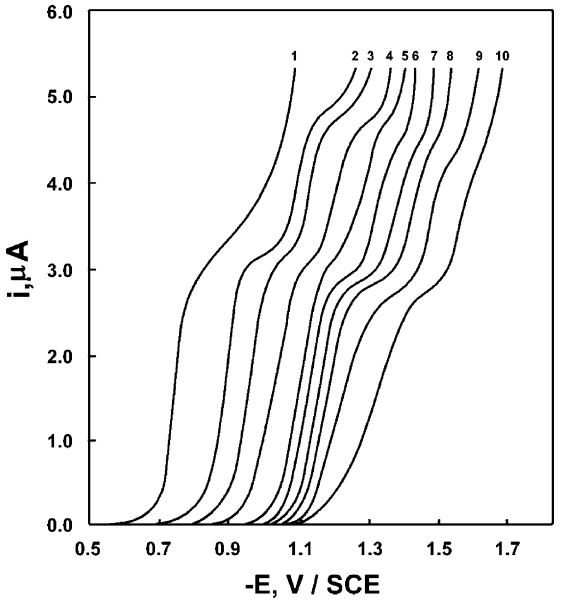

Fig. 1. dc-Polarograms for 2.5×10^{-4} M bulk amilorid in B–R buffers of different pH values: (1) 1.9, (2) 2.9, (3) 3.9, (4) 4.9, (5) 6.0, (6) 7.0, (7) 7.9, (8) 8.9, (9) 9.8, and (10) 10.9.

bond –CH=NH of the *N*-imidino amide group with the release of NH_3. The latter was confirmed by adding the Nessler's reagent to the completely electrolyzed amiloride solution where a reddish brown precipitate was formed [20]. While the second wave may be due to the saturation of the C=O of the carboxamide moiety [22]. In solutions of pH $\leq$ 2 the wave due to the saturation of the C=O of carboxamide moiety did not appear which may be due to its overlap with that of the hydrogen evolution.

The plots of $E_{de} - \log(i/i_d - i)$ [21] for the 1st and 2nd waves of amiloride at different pH values were straight lines with slope values S_1 ($S_1 = 0.0591/\alpha n_a$) reported in Table 1. Values of αn_a at different pH values were estimated from the slope values $S_1$and were found to equal 1.02–1.23 and 1.08–1.33 for the two waves, respectively. The number of electrons (n_a) involved in the rate-determining step was found to equal 2. Consequently, values of the transfer coefficient α at different pH values were found to equal 0.51–0.67.

The half-wave potentials of the two reduction waves were pH-dependent, being shifted to more negative values with increase of the pH indicated the participation of the H^+ ions in the electrode reaction and

Table 1
Values of αn_a and α as calculated from the slope (S_2) of the $E_{1/2}$–pH plots and number of protons ($Z_H{}^+$) as calculated from the slopes (S_2) and (S_1) for amiloride in B–R buffers of different pH values at 25 °C

pH	$-E_{1/2}$ (V)	S_1 (mV)	S_2 (mV)	αn_a	α ($n_a = 2$)	$Z_H{}^+$ (S_2/S_1)
1st wave						
2.9	0.91	60.39	62.00[a]	1.02	0.51	1.02
4.9	1.04	62.10		1.05	0.52	1.00
6.0	1.10	61.22		1.04	0.52	1.01
7.0	1.13	47.92	37.60[b]	1.23	0.62	0.77
8.9	1.18	56.37		1.04	0.52	0.67
2nd wave						
2.9	1.12	46.43	53.40	1.27	0.64	1.15
4.9	1.20	46.34		1.27	0.64	1.15
6.0	1.28	46.75		1.26	0.63	1.14
7.0	1.32	44.61		1.33	0.67	1.20
8.9	1.42	43.13		1.36	0.68	1.24

[a] 1st segment (pH $\leq$ 6.0) of $E_{1/2}$–pH plot.
[b] 2nd segment (pH > 6.0) of $E_{1/2}$–pH plot.

that the proton-transfer reaction precedes the electrode process proper [23]. The $E_{1/2}$–pH plot for the 1st wave was a broken line of two segments where it was a straight line for the 2nd wave. From the slope values S_1 ($S_1 = 0.0591/\alpha n_a$) and S_2 [$S_2 = (0.0591/\alpha n_a) \cdot Z_H^+$] of both the $E_{de} - \log(i/i_d - i)$ and $E_{1/2}$–pH plots, respectively (Table 1), the number of protons ($Z_H{}^+$) participated in the rate-determining step at the different pH values was estimated from the following relation [21,24]:

$$\frac{\partial E_{1/2}}{\partial \mathrm{pH}} = (0.0951/\alpha n_a) \cdot Z_H{}^+$$

i.e.

$$S_2 = S_1 \cdot Z_H{}^+$$

$$Z_H{}^+ = \frac{S_2}{S_1}$$

Value of $Z_H{}^+$ was found to equal one over the entire pH range (Table 1). The polarograms for different concentrations of bulk amiloride were recorded in B–R. buffer at pH 2. The linear variation of the polarographic limiting current (i_l) of the 1st wave with amiloride concentration (C) in B–R buffer of pH 2 (Fig. 2) was represented by a straight-line equation: i_l (μA) $= 0.119 \times 10^2 C$ (mM) + 0.25 ($r = 0.995$ and

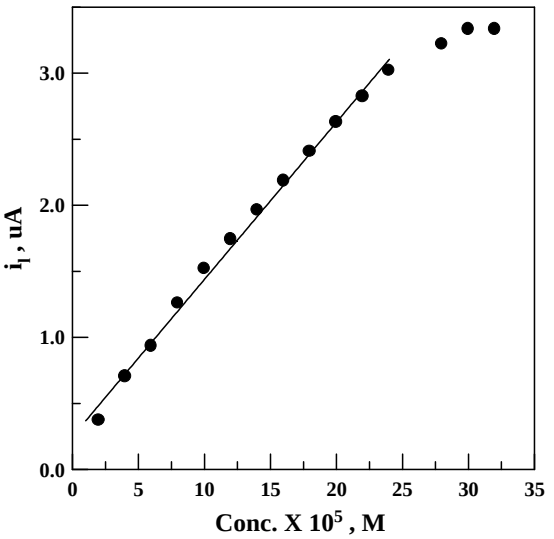

Fig. 2. The plot of polarographic limiting current (i_l) of the 1st wave vs. the concentration (C) of the drug in B–R buffer at pH 2.

$n = 12$). Three replicate calibration curves were obtained over the concentration range 2.5×10^{-5} to 2.5×10^{-4} M amiloride. A mean percentage recovery (for 5×10^{-4} M amiloride), based on the average of three determinations, of 99.37 ± 0.64 was achieved. The limits of detection (LOD) and quantitation (LOQ) were estimated using the following relations [25]

$$\text{LOD} = 3\text{S.D.}/b \quad (1)$$

and

$$\text{LOQ} = 10\text{S.D.}/b \quad (2)$$

where S.D. is the standard deviation of the intercept and b is the slope of the calibration curve. The LOD and LOQ of 1×10^{-5} and 3.3×10^{-4} M amiloride were achieved, respectively.

The cyclic voltammograms of amiloride at the hanging mercury drop electrode (HMDE) in B–R buffers of pH ≤ 2 exhibited a single cathodic irreversible peak, while in solution of higher pH values two cathodic irreversible peaks were observed. No anodic peak was observed on the reverse scan, which indicated the irreversible nature of the electrode reaction.

The peak potentials (E_p) shifted to a more negative value with rising pH. The irreversible nature of the reduction process was confirmed by the shift of the peak potentials (E_p) to more negative values on the increase of the scan rate, ν. The plots of E_p versus $\ln(\nu)$ at different pH values gave linear correlations, with slope values proportional to αn_a. The number of electrons (n_a) transferred in the rate-determining step was found to equal two.

3.2. Stripping voltammetric studies

The differential-pulse adsorptive cathodic stripping (DPAdCS) voltammograms for 5×10^{-7} M amiloride following preconcentration for 30 s at $E_{acc} = -0.5$ V versus $Ag/AgCl/KCl_s$ (scan rate = 10 mV/s and pulse-height = 50 mV) exhibited a single cathodic peak in B–R buffers of pH < 5, while two well-defined peaks were observed over the pH range 5–9 (Fig. 3). The i_p–pH plot (Fig. 4) showed that the 1st peak current intensity was much more developed over the pH values 7–8. Therefore, the first peak observed in B–R buffer at pH 8 was considered for the present analytical study owing to its high signal relative to that of the second one. The differential-pulse adsorptive cathodic stripping peak current intensity of amiloride in B–R buffer of pH 8 was found to be dependant on the preconcentration time period ($t_{acc.}$). At $t_{acc} = 30$ s an equilibrium surface concentration was reached.

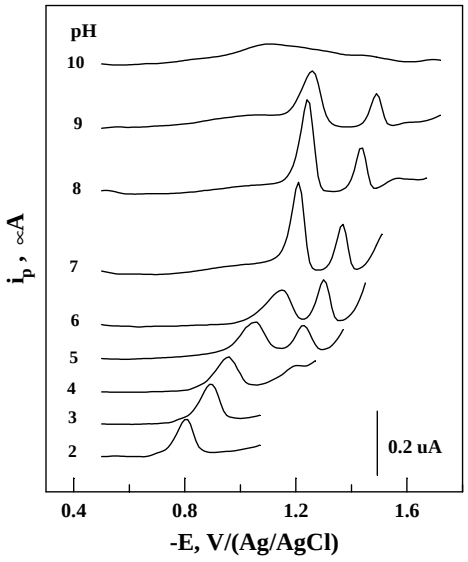

Fig. 3. DPAdCS voltammograms for 6.5×10^{-7} M amiloride in B–R buffers of different pH values, $t_{acc} = 30$ s, $E_{acc} = -0.5$ V, pulse-height = 50 mV and scan rate = 10 mV/s.

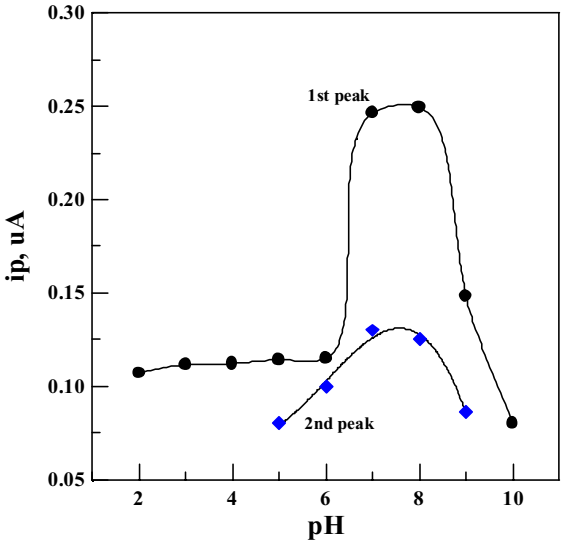

Fig. 4. The DPAdCS peak current (i_p)–pH plot for 6.5×10^{-7} M amiloride. Operational conditions are as those indicated in Fig. 3.

At shorter or longer time periods the DPAdCS peak current intensity was much less developed (Fig. 5). Therefore, a preconcentration period of 30 s was adopted in the present work for the adsorptive stripping analysis of amiloride.

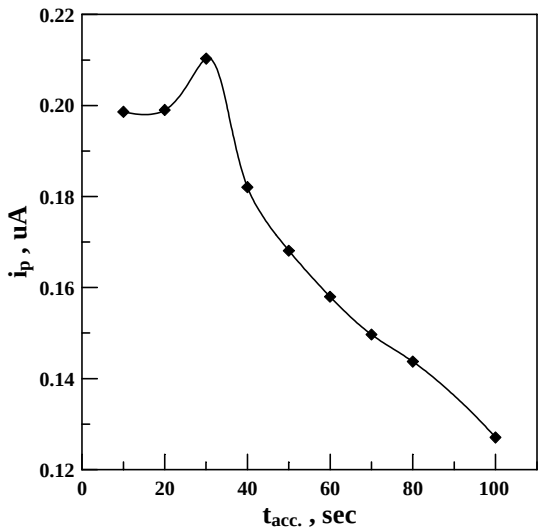

Fig. 5. Effect of accumulation time (t_{acc}) on the 1st peak current intensity for 5×10^{-7} M amiloride in B–R buffer at pH 8; $E_{acc.} = -0.9$ V, scan rate = 10 mV and pulse-height = 50 mV.

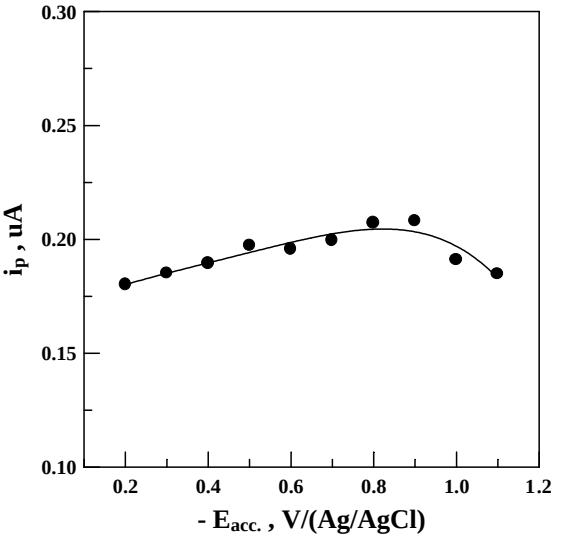

Fig. 6. Effect of accumulation potential (E_{acc}) on the 1st peak current intensity for 5×10^{-7} M amiloride in B–R buffer at pH 8; $t_{acc} = 30$ s. Other operational conditions are as those indicated in Fig. 5.

On the other hand, the DPAdCS peak current intensity as a function of the accumulation potential in B–R. buffer at pH 8 was studied (Fig. 6). The voltammograms showed that at $E_{acc} = -0.9$ V the 1st peak was much more developed and sharp. Accordingly, the accumulation potential ($E_{acc.}$) of −0.9 V versus $Ag/AgCl/KCl_s$ was chosen for preconcentration of the drug onto the hanging mercury drop electrode.

The variation of the DPAdCS 1st peak current intensity of amiloride in pH 8 B–R buffer with the scan rate was maximum over the range 10–20 mV/s (Fig. 7) and thus a scan rate of 10–20 mV/s was chosen for the present stripping analytical study. The peak current intensity of the DPAdCS voltammogram of amiloride in pH 8 B–R buffer was directly proportional to the pulse-height up to 90 mV; therefore, the present analytical determination was performed at pulse-height = 90 mV.

The influence of the surface area of the working mercury electrode on the peak current was also studied. As expected, an increase of the electrode surface area generated a higher peak current, so a mercury drop of a large area (0.026 cm^2) was considered in the present study. The influence of the rest time was also considered and a time period of 10 s was chosen.

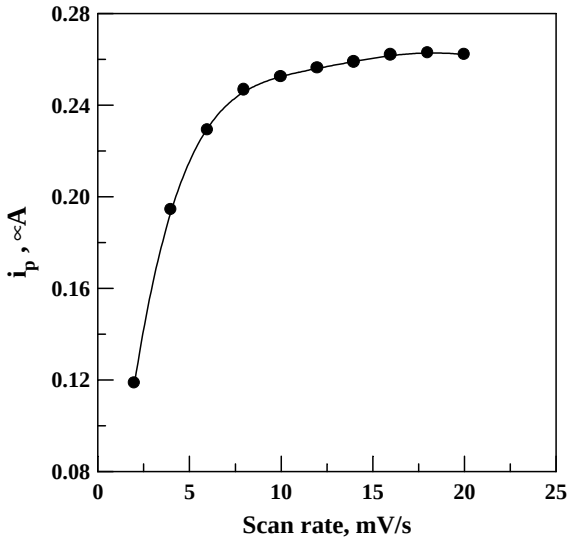

Fig. 7. Effect of scan rate on the 1st peak current intensity for 5×10^{-7} M amiloride in B–R buffer at pH 8. Other operational conditions are as those indicated in Fig. 5.

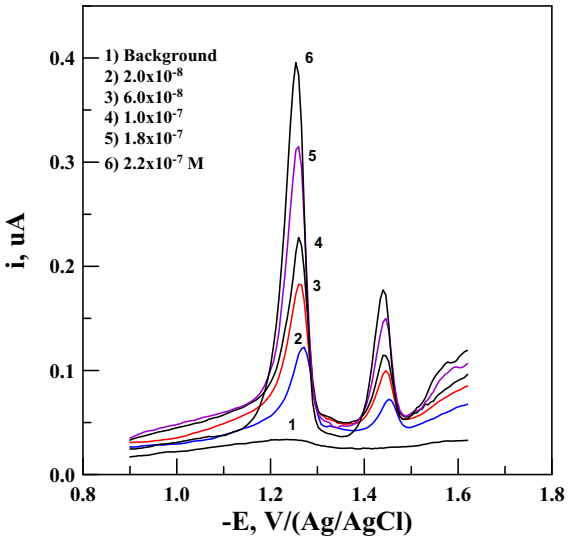

Fig. 8. DPCAdS voltammograms for different concentration of bulk amiloride in B–R buffer of pH 8.0, $t_{acc} = 30$ s, $E_{acc} = -0.9$ V, scan rate = 20 mV/s and pulse-height = 90 mV.

Accordingly, the optimum conditions for the proposed DPAdCS voltammetric procedure to determination of amiloride drug were found to be; preconcentration potential (E_{acc}) = −0.9 V, preconcentration time (t_{acc}) = 30 s, scan rate = 10–20 mV/s, pulse-height = 90 mV, mercury drop surface area = 0.026 cm^2, rest period = 10 s and a Britton–Robinson buffer at pH 8 as a supporting electrolyte.

The DPCAdCS voltammograms were recorded for different concentrations of amiloride under the optimized conditions (Fig. 8). The linear variation of i_p (μA) of the 1st peak with amiloride concentration was represented by the equation $i_p(\mu A) = 6.3552 \times 10^3 C$ (mM) + 0.09 (correlation coefficient $r = 0.998$ and $n = 14$). The calibration curves were obtained over the concentration range 2×10^{-8} to 1×10^{-6} M amiloride.

Validation of the proposed DPAdCS voltammetric procedure was examined via evaluation of the limit of detection (LOD), limit of quantitation (LOQ), repeatability, recovery, specificity, robustness and ruggedness. The LOD and LOQ were calculated from the calibration curves using the relations (1) and (2) [25], respectively. The LOD and LOQ of 7.1×10^{-9} and 2.4×10^{-8} M bulk amiloride, respectively, were achieved. Both LOD and LOQ values confirmed the sensitivity of the proposed procedure compared to a reported spectrophotometric method [5].

The repeatability and recovery were examined by performing five replicate measurements for 5.0×10^{-8} M bulk amiloride following pre-concentration for 30 s. A mean percentage recovery of 99.47 ± 0.71 was achieved which indicated a high precision of the proposed procedure.

The selectivity [26] of the optimized procedure for the assay of amiloride was examined for 2×10^{-7} M bulk amiloride in the presence of some common excepients usually present in pharmaceutical formulations (starch, gelatin, lactose, talc and magnesium stearate) and hydrochlorothiazide (as a co-formulated drug). The obtained mean percentage recovery based on the average of five replicate determinations of 97.42 ± 0.77 showed no significant interference from excepients or hydrochlorothiazide (as an electro-inactive compound under the experimental conditions). Thus, the procedure was able to assay amiloride in the presence of the excepeints and/or hydrochlorothiazide and it can be considered selective.

The robustness [26] of the measurements was examined by evaluating the influence of small variations in some of the most important operational conditions of the procedure included pH (7–8), preconcentration

Table 2
Influence of variation of some of the operational parameters of the proposed DPAdCS votammetric procedure on the mean percentage recovery of 5×10^{-7} M bulk amiloride; $t_{acc} = 30$ s, frequency = 120 Hz and pulse-height = 90 mV

Parameters	$R \pm$ S.D.[b] (%)	Operational conditions
pH of the medium[a]		
7	99.25 ± 0.65	$E_{acc} = -0.9$ V, $\Delta E = 20$ mV/s
8	99.50 ± 0.72	
Preconcentration potential (E_{acc})[a]		
−0.8 V	99.45 ± 0.67	pH = 8, $\Delta E = 20$ mV/s
−0.9 V	99.50 ± 0.72	
Scan rate ΔE[a]		
10 mV	99.39 ± 0.85	pH = 8, $E_{acc} = -0.9$ V
20 mV	99.50 ± 0.72	
Potentiostat (PAR)		
Lab (1) model 394	99.50 ± 0.72	pH = 8, $E_{acc} = -0.9$ V, $\Delta E = 20$ mV/s
Lab (2) model 263 A	99.28 ± 0.88	

[a] Using potentiostat 394.
[b] Average of five replicate measurements.

potential (−0.8 to −0.9 V) and scan rate (10–20 mV). The results shown in Table 2 indicated that none of these variables significantly affect the percentage recovery of amiloride. These results provided an indication of the reliability of the proposed DPAdCS voltammetric procedure to assay amiloride, and it can be considered robust.

The ruggedness [26] of the measurements was examined by applying the optimized DPAdCS voltammetric procedure to assay amiloride using two Electrochemical Analyzers models 263A and 394-PAR under the same optimized experimental conditions at different elapsed time. The recoveries obtained due to lab-to-lab and even day-to-day variations were found reproducible since there was no significant difference between the recovery and standard deviation results (Table 2).

3.3. Assay of amiloride in tablets

The proposed polarographic procedure was applied to the assay of amiloride in Yostriretic® tablets. Fig. 9 illustrate the polarograpgic response of successive additions of amiloride of tablet solution in B–R buffer at pH 2. A mean percentage recovery, based on three replicate determination, of 101 ± 1.27 was achieved.

The proposed DPAdCS voltammetric procedure was also applied to determination of the drug in tablets. A mean percentage recovery based on the average of five replicate measurements was found to be 98.65 ± 1.05. The recovery of the drug in tablets by means of the proposed DPAdCS voltammeric procedure was favorably compared with that obtained by a reported

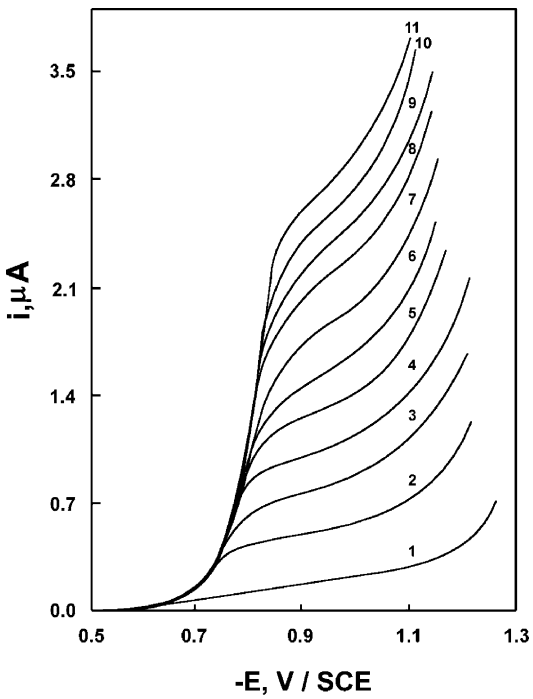

Fig. 9. dc-Polarograms for different concentrations of amiloride in tablet solutions in B–R buffer at pH 2.

spectrophtometric method [5]. Both the proposed polarographic and DPAdCS voltammetric procedures did not require sample pretreatment or any extraction or evaporation steps prior to the drug analysis.

In addition, preliminary studies on spiked human serum samples indicated that the proposed DPAdCS voltammetric procedure might also have application to analysis of the drug in plasma samples.

4. Conclusion

The electrochemical behavior of amiloride drug at the dropping mercury and hanging mercury drop electrodes has been studied and its electrode reaction pathway was discussed. A polarographic procedure of enough sensitivity has been developed and successfully applied to determination of amiloride drug in bulk form and tablets. Moreover, a differential-pulse adsorptive cathodic stripping voltammetric procedure has been developed and successfully applied to assay of the drug in tablets without interference from excipients and/or the co-formulated hydrochlorothiazide. The developed procedures did not require sample pretreatment or any time-consuming extraction or evaporation steps prior to the drug analysis.

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