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# Development of square-wave adsorptive stripping voltammetric method for determination of acebutolol in pharmaceutical formulations and biological fluids

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## Abstract

A validated simple, rapid, sensitive and specific square-wave voltammetric technique is described for the determination of acebutolol (AC) following its accumulation onto a hanging mercury drop electrode in a Britton-Robinson universal buffer of pH 7.5. The optimal procedural conditions were: accumulation potential $E_{acc}$ = - 0.8 V versus Ag/AgCl/KCl, accumulation duration $t_{acc}$ = 30 s, pulse-amplitude = 70 mV, scan rate = 100 mV/s, frequency = 30 Hz, surface area of the working electrode = 0.6 $mm^2$ and the convection rate = 2000 rpm. Under these optimized conditions, the adsorptive stripping voltammetry (AdSV) peak current was proportional over the concentration range $5 \times 10^{-7}$ - $6 \times 10^{-6}$ M (r = 0.999). Recoveries for acebutolol from human plasma and urine were in the range 97-103% and 96-104% respectively. The method proved to be precise (intra-day precision expressed as %RSD in human plasma ranged from 2.9 - 3.2% and inter-day precision expressed as %RSD ranged from 3.4 - 3.8%) and accurate (intra-day accuracies expressed as % error in human urine ranged from -3.3 - 2.8% and inter-day accuracies ranged from -3.3 - 1.7%). The limit of quantitation (LOQ) and limit of detection (LOD) for acebutolol were $1.7 \times 10^{-7}$ and $5 \times 10^{-7}$ M, respectively. Possible interferences by substances usually present in the pharmaceutical formulations were investigated with a mean recovery of 101.6 ± 0.64%. Results of the developed square-wave adsorptive stripping voltammetry (SW-AdSV) method were comparable with those obtained by reference analytical method.

**Keywords:** Acebutolol, Square wave voltammetry, Adsorptive stripping voltammetry, Pharmaceutical formulations, Biological fluids

## Background

Acebotolol, (RS)-N-(3-acetyl-4-[2-hydroxy-3-(propan-2-ylamino)propoxy]phenyl)butanamide is a cardioselective, lipophilic β-adrenoreceptor blocking agent with mild intrinsic sympathomimetric activity. It is therefore more suitable than non cardioselective β-blockers, if a patient with asthma or chronic obstructive pulmonary disease needs treatment with a β-blocker. It is marketed in tablets form for oral admininstration [1].Various techniques have been concerned with the development of rapid and sensitive methods for the separation, identification or

determination of AC and others β-blockers in human urine. These techniques included high performance liquid chromatography (HPLC) [2,3], HPLC-mass spectrometry (MS) [4], gas chromatography-mass spectrometry (GC-MS) [5] and capillary electrophoresis (CE) [6]. On the other hand, existing publications concerning the individual determination of AC in pharmaceutical preparations were based on, spectrophotometry [7-10], spectrofluorimetry [8], thin layer chromatography (TLC) [9], HPLC [9-11], GC [10] and CE [12]. The analytical methods reported for chiral separation of AC included CE [13-19] and HPLC [20-25]. Since, some of these methods required expensive equipment(s) and/or special treatment.

Adsorptive cathodic stripping voltammetry has been shown to be an efficient electroanalytical technique for

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the determination of sub-nanomolar levels of a wide range of drugs that have an interfacial adsorptive character onto the working electrode surface. It usually involves a simple accumulation step, and most of the excipients used do not interfere in the subsequent determination of drugs [26]. The technique is easy to use, saves of time and costs, low detection limit, high accuracy, wide concentration range, applicability to colored and turbid solution. According to our knowledge, there are only two reported papers for the determination of AC by the electrochemical method based on potentiometry [27,28]. The first reported method [27] was a coated wire electrode for some β-blockers (AC one of them) and calcium blockers has been suggested based on the use of dinonylnaphthaline sulphonic acid as ion exchanger material, the selectivity behavior was accurately predicted from calculated distribution coefficient constant for each drug. The second method [28] based on the use of ion-association complexes of AC with tetraphenylborate and phosphomolybdate as exchange sites in a polyvinyl chloride matrix. Therefore, there has been no report concerning the determination of AC by voltammetric method. The proposed method is a highly sensitive, simple, fast and accurate method with lower detection limits for the determination of AC in human plasma and urine.

## Experimental
### Instrumentation and Chemicals
All adsorptive stripping measurements were carried out with 797 VA Computrace (Metrohm, Switzerland) in connection with Dell computer and controlled by (VA computrace 2.0) control software. Stripping voltammograms were obtained via a HP color laserjet CP 1215 printer. A conventional three electrode system was used in the hanging mercury drop electrode (HMDE) mode. pH values were measured with Hanna pH 211 (Romania made). Biohit adjustable micropipette (AU), and Brand adjustable micropipette (Germany), were used to measure microliter volumes of the standard solutions. All chemicals used were of analytical reagent grade and were used without further purification. (±) Acebutolol hydrochloride was obtained from Sigma Chemical Co. (St Louis, MO, USA). AC stock solution of $1 \times 10^{-2}$ mol $L^{-1}$ was prepared by dissolving the appropriate amount of AC in methanol in 25 ml volumetric flask and this stock solution was stored in the dark. Britton-Robinson (B-R) supporting buffer (pH 7.5, 0.04 M in each constituent) was prepared by dissolving 2.47 g of boric acid (Winlab, UK) in 500 ml distilled water containing 2.3 ml of glacial acetic acid (BDH, UK) and then adding 2.7 ml of ortho-phosphoric acid (Riedal-deHaen, Germany) and diluting to one liter with distilled water. In addition, phosphate supporting buffer [0.1 M $NaH_2PO_4$ (Winlab,

UK) and 0.1 M $H_3PO_4$] was prepared by dissolving 12 g of $NaH_2PO_4$ and 6.78 g of $H_3PO_4$ in 1000 ml distilled water. Acetate supporting buffer (0.02 M in each constituent) was prepared by dissolving 1.68 g of sodium acetate (Winlab, UK) in 500 ml distilled water containing 1.12 ml of acetic acid and diluting to one liter with distilled water. Finally, carbonate supporting buffer (0.1 M in each constituent) was prepared by dissolving 10.6 g of sodium carbonate (BDH, UK) and 8.4 g of sodium hydrogen carbonate (Winlab, UK) in one liter distilled water.

### Procedures and Analysis
#### Analysis of Standard AC
The general procedure adopted for obtaining square wave adsorptive stripping voltammograms was as follows: A 10 ml aliquot of B-R supporting buffer (unless otherwise stated) at desired pH was pipetted in a clean and dry voltammetric cell and the required standard solutions of AC were added. The test solutions were purged with nitrogen for 5 min initially, while the solution was stirred. The accumulation potential of - 0.8 V vs. Ag/AgCl was applied to a new mercury drop while the solution was stirred for 30 s. Following the preconcentration period, the stripping was stopped and after 20 s had elapsed, cathodic scans were carried out over the range 0.0 to -1.7 V. All measurements were made at room temperature.

#### Analysis of AC in Tablets
Twenty tablets of Sectral® (Alexandria Pharm. & Chem. Ind. Co., Egypt) labeled to contain 200 mg AC per tablet were powdered. An adequate amount of the homogenous powder, corresponding to $5 \times 10^{-6}$ M, was accurately weighed and transferred into a calibrated flask and then dissolved in 25 ml of methanol by sonication for 10 min, followed by mechanical shaking for 10 min and lastly centrifuged for 5 min at 10,000 rpm. A portion of the clear solution was diluted with the supporting electrolyte to achieve the desired concentration. Then AC was quantified by means of the proposed stripping voltammetric procedure.

#### Analysis of AC in Spiked Human Plasma and Urine
Accurately measured aliquots of AC solutions were pipette into centrifugation tubes containing 300 μl human plasma and/or urine, then vortex were done for 5 min. Into each tube, 0.5 ml of acetontrile, 0.1 ml NaOH (0.1 M), 0.5 ml $ZnSO_4.7 H_2O$ (5% w/v) were added, where most of the interfering substances (mainly proteins) were simply removed and eliminated by precipitation, then centrifuged for 30 min at 3500 rpm [29]. The clear supernatant layer was filtered through 0.45 μm Millipore filter. A 0.1 ml volume of the supernatant liquor was transferred into the voltammetric cell then completed to a 10 ml volume with a pH 7.5 B-R universal

buffer. Then AC was quantified by means of the proposed stripping voltammetric procedure.

## Results and Discussion
### The Electrochemical Behavior of AC

The cyclic voltammetric behavior of $5 \times 10^{-6}$ mol $L^{-1}$ AC in Britton-Robinson buffer pH 7.5 at the hanging mercury drop electrode monitored in the cathodic direction yielded a single well-defined peak at -1237 mV probably attributed to the cathodic reduction of the carbonyl group between the methyl and phenyl groups present in the analyte molecule (Scheme 1). No oxidation peak was observed in the positive scanning half-cycle, indicating the irreversible nature of the electrode process. The interfacial accumulation of the drug was designated from repetitive cyclic voltammograms for AC recorded following stirring for 30 s at 0.0 V prior to the first scan produced considerable cathodic peak (scan 1). As can be seen from Figure 1, a substantial decrease of the monitored electrochemical signal was observed in subsequent repetitive scans. Such behavior indicated rapid adsorption of AC from the working electrode surface. The voltammetric cycles carried out for increasing scan rate values over the range 50-500 mVs$^{-1}$ gave rise to an electrochemical response with increased peak current intensities. The plot of log $i$p versus log $v$, gave a straight line with slope value of 0.85, which is to some degree close to the theoretical value of 1.0 that is expected for an adsorption-controlled process [30,31], indicating the interfacial adsorptive character of AC onto the surface electrode. In addition, the observed peak potential shift to a more negative values on the increase of scan rate confirmed the irreversible nature of the studied cathodic reduction process. The strong adsorption phenomenon of AC can be used as an effective preconcentration step prior to the actual voltammetric quantification of the analyte. The adsorptive stripping voltammetric response of AC at HMDE was examined in Britton-Robinson buffer pH 7.5 using the differential pulse (DP) and square wave (SW) excitation waveforms. The electrochemical current intensity for the cathodic reduction of AC recorded by the square wave voltammetric technique was nearly 10 times higher than that generated by the differential pulse excitation mode. Due to its intense sensitivity, therefore SWAdSV approach was used in all the subsequent experiments. Figure 2 shows a square-wave adsorptive stripping voltammogram for AC after 60 s accumulation period at 0.0 V, which illustrates a single well-defined AdSV peak at -1237 mV versus Ag/AgCl reference electrode.

### Optimum Parameters and Experimental Conditions
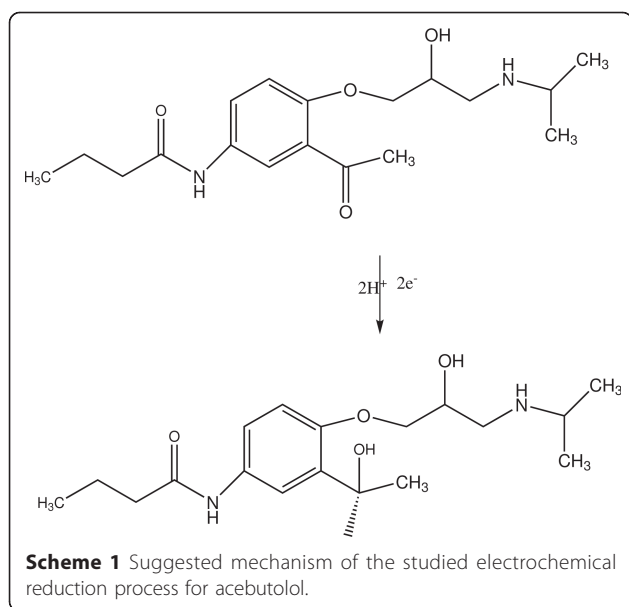#### Effect of Supporting Electrolyte and pH

Since the adsorptive phenomenon of AC on the HMDE was utilized as a suitable collection step prior to its electrochemical determination, it was rational to characterize various variables and experimental conditions that affecting the engaged adsorption process. In fact, the sensitivity of the adsorptive stripping procedure for a particular analyte is usually significantly influenced by the composition of the supporting buffer and pH value. Consequently, several supporting buffers such as Britton-Robinson, phosphate, acetate and carbonate buffers at different pH values were evaluated after 60 s accumulation time at 0.0 V accumulation potential. Among these supporting electrolytes the best electroanalytical signal in terms of SW-AdSV peak current intensity and shape was obtained with B-R buffer, which was selected as optimal for further works. Generally, the AdSV signal was mainly pH dependent since the monitored voltammetric signal was only observed at low alkaline media. When the stripping voltammetric peak current was measured as a function of pH over the range 5-9, the peak current increased gradually at first and enhanced
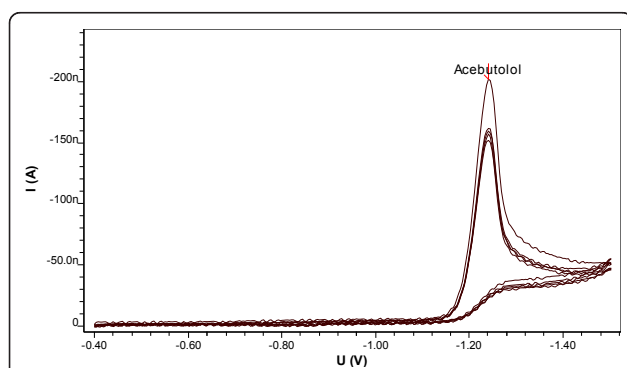


**Figure 1** Repetitive cyclic voltammograms for $5 \times 10^{-6}$ mol $L^{-1}$ acebutolol in pH 7.5 B-R buffer, scan rate 50 mV$^{-1}$, accumulation potential 0.0 V and preconcentration time 30 s (scan A).
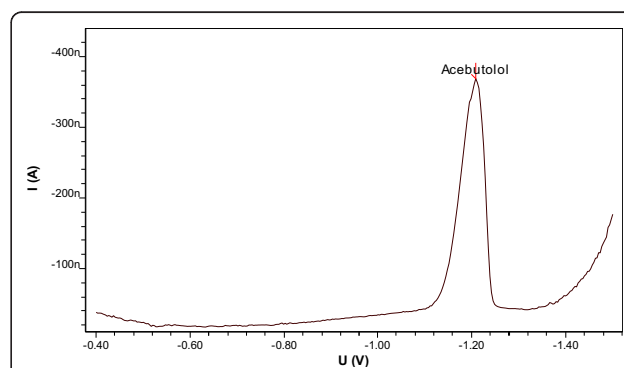


**Figure 2** SW-AdSV voltammogram for acebutolol in B-R buffer (pH 7.5), $t_{acc}$: 60 s, $E_{acc}$: -0.8 V, scan rate: 100 mVs$^{-1}$, SW frequency: 30 Hz and pulse amplitude: 70 mV. acebutolol concentration: (A) $5.0 \times 10^{-6}$ 10 mol $L^{-1}$.

**Scheme 1** Suggested mechanism of the studied electrochemical reduction process for acebutolol.

sharply beyond pH 7 then it reached its maximum value at pH 7.5, which was adopted as optimum pH value for subsequent investigations. The influence of pH factor on the SW-AdSV signal is illustrated in Figure 3. In addition, it was observed that the voltammetric peak potential of AC did not shifted when pH was varied over the studied pH rang, which indicates that $E_p$ was pH independent as expected for an electrochemical reaction in which hydrogen ions did not consumed.
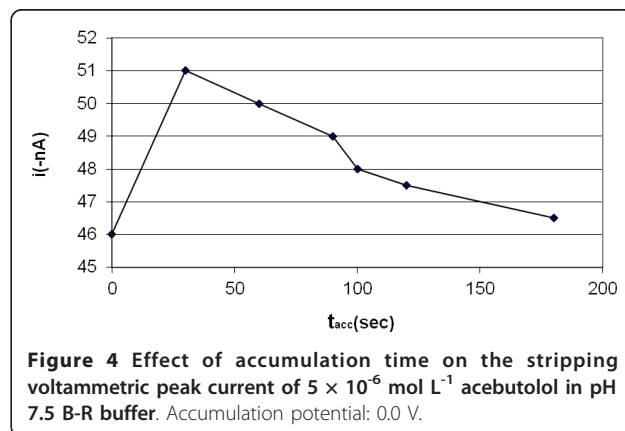
### Effect of Accumulation Time and Potential

The interfacial accumulation of AC onto the HMDE surface depends on some operational factors, which worth additional investigations in order to ensure high sensitive determinations of AC. Therefore, the effect of accumulation time on the efficiency of the collection of $5 \times 10^{-6}$ mol $L^{-1}$ AC onto the working electrode was evaluated by rising the accumulation time over the range 0 - 150 s. The resulting peak current-accumulation time ($i_p$-$t_{acc}$)

profile is exhibited in Figure 4 and as can be seen from this plot, a steadily enhancement in the peak current was observed over the range 0 - 30 s and thereafter the peak intensity nearly decreased probably due to the saturation of the HMDE. Hence, 30 s accumulation times was selected for all future experiments. Furthermore, variation of the accumulation potential over the range from +0.4 to -1.2 V (Figure 5) at 30 s accumulation time revealed that a preconcentration potential of -0.8 V was the ideal choice for optimal sensitivity.

### Effect of Potential Sweep Conditions

The observed stripping voltammetric signal can be further maximized by adjusting the way the applied potential was scanned. The relationship between the measured peak intensity and scan rate was found to be directly proportional over 10-100 mV s$^{-1}$ scan arte (from studied range 10-250 mV s$^{-1}$). However, when scan rates faster than 100 mV s$^{-1}$ were employed, the peak current decreased slightly. The influence of scan rate on the observed voltammetric signal is illustrated in Figure 6,



**Figure 4 Effect of accumulation time on the stripping voltammetric peak current of $5 \times 10^{-6}$ mol $L^{-1}$ acebutolol in pH 7.5 B-R buffer**. Accumulation potential: 0.0 V.
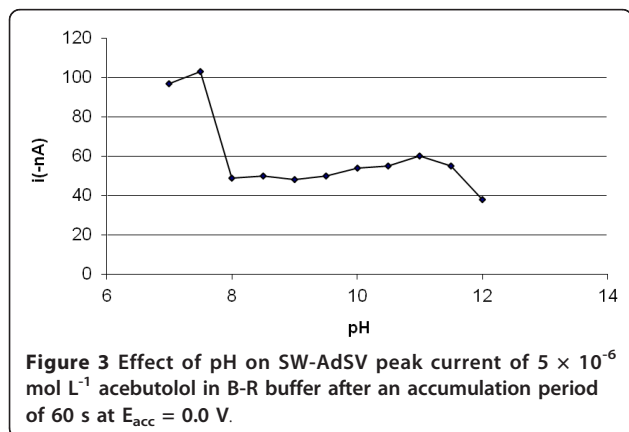


**Figure 3 Effect of pH on SW-AdSV peak current of $5 \times 10^{-6}$ mol $L^{-1}$ acebutolol in B-R buffer after an accumulation period of 60 s at $E_{acc}$ = 0.0 V**.
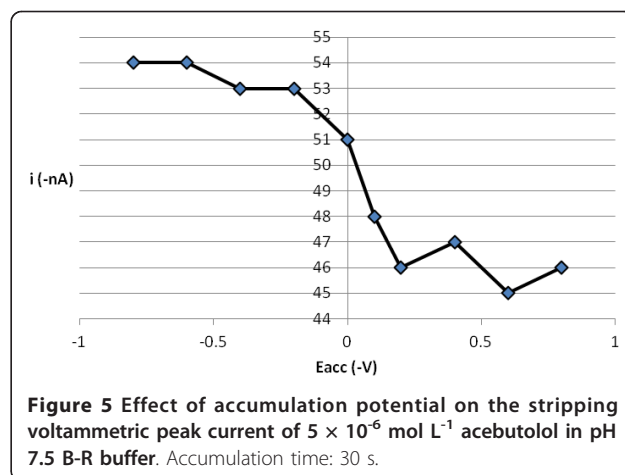


**Figure 5 Effect of accumulation potential on the stripping voltammetric peak current of $5 \times 10^{-6}$ mol $L^{-1}$ acebutolol in pH 7.5 B-R buffer**. Accumulation time: 30 s.
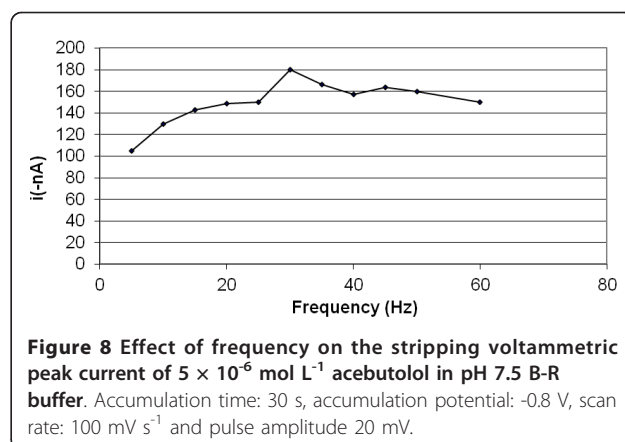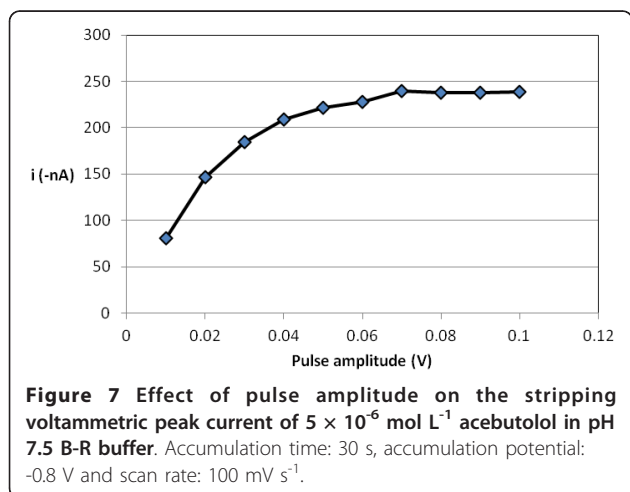
**Figure 6 Effect of scan rate on AdSV peak current of 5 × 10⁻⁶ mol L⁻¹ acebutolol in pH 7.5 B-R buffer**. Accumulation time: 30 s and accumulation potential: -0.8 V.
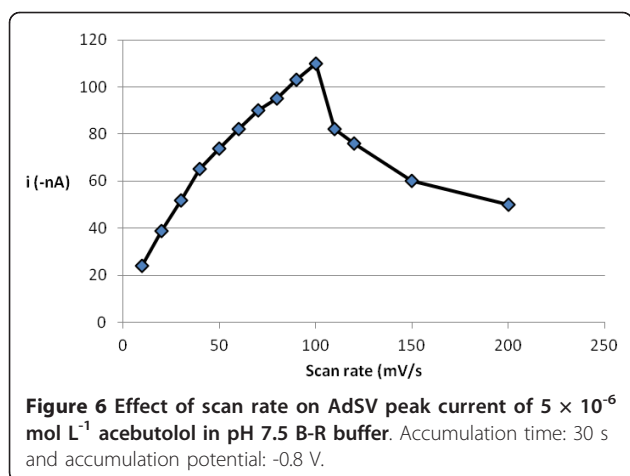
which indicates that scan rate value of 100 mV s⁻¹ would be adequate optimum for succeeding investigations.

In addition, the impact of varying the excitation wave pulse amplitude on the voltammetric current intensity was also evaluated. The effect of this operating variable was studied over the range 10-100 mV (Figure 7) and it was concluded that in order to assure maximum peak current, 70 mV pulse amplitude is the ideal choice for this operational parameter. Moreover, varying the value of square wave frequency also plays an important role for the measured signal of SW-AdSV approach. Varying this parameter over the range 5-60 Hz resulted in a substantial enhancement of the voltammetric peak current particularly at range 5-45 Hz as can be seen from Figure 8, then the peak of current become constant. Accordingly, for future work 30 Hz SW frequency value was adopted.

### Effect of Other Instrumental Variables
The influence of other operating parameters such as the size of the adsorption area (HMDE) and convection rate on the efficiency of the adsorption accumulation of AC



**Figure 8 Effect of frequency on the stripping voltammetric peak current of 5 × 10⁻⁶ mol L⁻¹ acebutolol in pH 7.5 B-R buffer**. Accumulation time: 30 s, accumulation potential: -0.8 V, scan rate: 100 mV s⁻¹ and pulse amplitude 20 mV.

was additionally checked. As expected, a linear enhancement for the electrochemical peak intensity was observed when the surface area of HMDE was increased over the range 0.15-0.6 mm² drop size area. Besides, the SW-AdSV peak current can be maximized further by increasing the stirring rate of the rotating rod over the range 0-2000 rpm. Hence, for optimal sensitivity, 0.6 mm² drop size and 2000 rpm stirring speed were selected.

In conclusion, for electroanalytical purposes, the optimized experimental conditions for SW-AdSV measurements of AC were accumulating for 30 s at -8.0 V preconcentration potential with stirring rate of 2000 rpm. These voltammetric measurements were carried out in Britton-Robinson buffer at pH 7.5. The applied potential was scanned at 100 mV s⁻¹ with 30 Hz SW frequency rate and 70 mV pulse amplitude.

### Validation of the Method
#### Linearity
Once the optimal chemical conditions and instrumental parameters for the SW-AdSV determination of AC were established, several analytical characteristics of the proposed were evaluated. Under the optimized conditions, a linear correlation between SW-AdSV peak intensity and the drug concentration was obtained over the range $5 \times 10^{-7}$ to $6 \times 10^{-6}$ mol L⁻¹, (Figure 9). The calibration equation was calculated by least-squares method and it has the form:
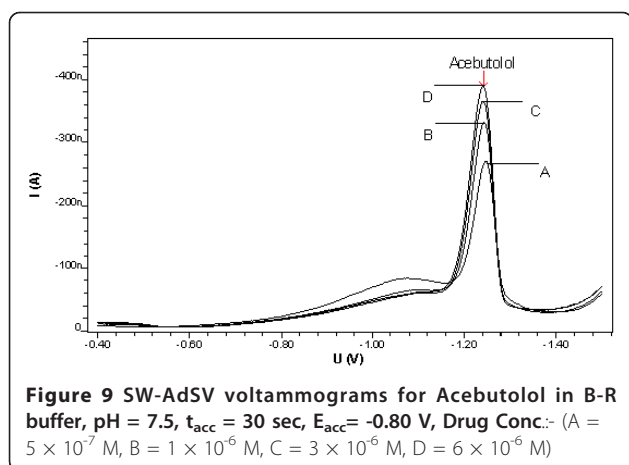
$$I_p(-nA) = 2.33 \times 10^{-7}\,C\,(mol\,L^{-1}) + 209.63 \qquad r = 0:99, \qquad n = 4.$$

where $I_p$ is the stripping voltammetric peak current in nano-amperes, C is AC concentration and r is the correlation coefficient.

#### Limit of quantification and limit of detection
The limits of detection (LOD) and limits of quantification (LOQ) were determined using the formula: LOD or LOQ = $k$ S.D.a/b, where k = 3 for LOD and 10 for



**Figure 7 Effect of pulse amplitude on the stripping voltammetric peak current of 5 × 10⁻⁶ mol L⁻¹ acebutolol in pH 7.5 B-R buffer**. Accumulation time: 30 s, accumulation potential: -0.8 V and scan rate: 100 mV s⁻¹.

**Figure 9 SW-AdSV voltammograms for Acebutolol in B-R buffer, pH = 7.5, $t_{acc}$ = 30 sec, $E_{acc}$= -0.80 V, Drug Conc.:- (A = $5 \times 10^{-7}$ M, B = $1 \times 10^{-6}$ M, C = $3 \times 10^{-6}$ M, D = $6 \times 10^{-6}$ M)**

**Table 1 Accuracy and precision data for acebutolol in spiked human plasma and urine by the proposed SW-AdSV method.**

| Analyte | Actual conc. ($\mu$g mL$^{-1}$) | Experimental conc. ($\mu$g mL$^{-1}$) | RSD (%)[c] | Error (%)[d] |
|---|---|---|---|---|
| Intra-day[a] | | | | |
| Plasma | 0.4 | 0.39 ± 0.012 | 3.1 | - 2.5 |
| | 1.0 | 0.98 ± 0.028 | 2.9 | -2.0 |
| | 2.0 | 2.04 ± 0.065 | 3.2 | 2.0 |
| Urine | 0.3 | 0.29 ± 0.011 | 3.8 | -3.3 |
| | 0.9 | 0.88 ± 0.024 | 2.7 | - 2.0 |
| | 1.8 | 1.85 ± 0.039 | 2.1 | 2.8 |
| Intra-day[b] | | | | |
| Plasma | 0.4 | 0.39 ± 0.012 | 3.8 | - 2.5 |
| | 1.0 | 0.97 ± 0.033 | 3.4 | -3.0 |
| | 2.0 | 2.06 ± 0.072 | 3.5 | 3.0 |
| Urine | 0.3 | 0.29 ± 0.014 | 4.8 | -3.3 |
| | 0.9 | 0.89 ± 0.031 | 3.5 | - 1.1 |
| | 1.8 | 1.83 ± 0.045 | 2.5 | 1.7 |

[a] Mean ± SD based on n = 6.
[b] Mean ± SD based on n = 6.
[c] Expressed as % RSD: (S.D./mean) × 100
[d] Calculated as (mean determined concentration/nominal concentration) × 100

LOQ, S.D.a is the standard deviation of the intercept, and b is the slope. Also lower limit of detection (LOD) defined as the concentration of AC corresponding to the intersection of the extrapolated linear segment of the calibration graph which is $1.7 \times 10^{-7}$ M.

This obtained sensitivity was significantly preferable than those reported for other analytical technique used for determination of AC such as potentiometric method [28] with $6 \times 10^{-6}$ mol L$^{-1}$.

### Precision, Accuracy

A summary of the accuracy and precision results is given in Table 1. The acceptance criteria (within-run and between-run % RSD of less than 15% and an accuracy between 85 and 115%) were met in all cases. The intra-day precision and accuracy (n = 6) expressed as % RSD and % error were 2.9 - 3.2% and -2.5 - 2.0%, respectively, for human plasma and 2.1 - 3.8% and -3.3 - 2.8%, respectively, for human urine. The inter-day precision and accuracy (n = 6) expressed as % RSD and % error were 3.4 - 3.8% and -2.5 - 3.0% for human plasma, respectively, and 2.5 - 4.8% and -3.3 - 1.7% for human urine, respectively.

### Ruggedness

The ruggedness of the SW-AdSV method was evaluated by carrying out the analysis using two different analyst (operator) and different instruments on different days. The RSD of less than 2.5% were observed for repetitive measurements in three different day time periods using two different instruments and operators. The results indicate that the method is capable of producing results with high precision.

### Robustness

The robustness of the method was explained by the evaluation the influence of small variation of some of the most important procedure variables including pH, scan rate, accumulation potential and duration. Preliminary inspection of the results under various conditions suggested that the method is fairly robust, but the pH of the measuring solution should be 7.5.

### Selectivity

The competitive co-adsorption interference was evaluated in the presence of various substances that are usually found in the pharmaceutical tablets and formulations. For these investigations, the interfering species were added at different concentrations (twice, 5-fold and 50-fold) higher than the concentration of AC (5 ×10$^{-6}$mol L$^{-1}$). The additions of filling materials (sucrose, lactose and cellulose), disintegrate agent (starch) and lubricants such as magnesium stearate caused no significant effects on the SW-AdSV response of AC. Hence, this compound may need not to be extracted from these tablet ingredients or additives prior to its determination in tablets.

### Analytical Applications

Following the developed electroanalytical procedure described above, AC was analysed in pharmaceutical formulations. The AC content of commercially available tablets was determination directly by the SW-AdSV method after the required dissolving and filtration steps. Five aliquots of the dissolved sample were diluted to the required concentration level and measured via the standard additions approach. For these studies, results obtained gave a recovery mean 101.6% with standard deviation of ± 0.64%. As can be seen from Table 2, these results achieved by the optimized AdSV procedure were in good agreement with those obtained by

**Table 2 Comparative determination of acebutolol tablet by the proposed SW- AdSV method and the reference potentiometric method.**

| AdSV method | | Reference method[28] | |
|---|---|---|---|
| Found (mg) | % Recovery | Found (mg) | % Recovery |
| Labeled content of Sectral® Tablet* (200 mg acebutolol) | | | |
| 200 | 101 | 200 | 104 |
| 201 | 102 | 200 | 105 |
| 202 | 101 | 201 | 104 |
| 202 | 102.5 | 202 | 104 |
| Mean | 101.6 | Mean | 104.25 |
| Standard deviation | ± 0.64 | Standard deviation | ± 0.43 |

* Product of Alexandria Pharm. & Chem. Ind. Co., Egypt.

potentiometric technique for the analysis of the same pharmaceutical tablets [28]. Based on the statistical evaluation (F-test approach) for these results, there is no significant difference between the results obtained by the developed AdSV procedure and that obtained by the reference method [28]. The calculated F value is 6.76 which was less than the critical value (9.28) at the 95% confidence level.

In addition, the applicability of the AdSV procedure for the analysis of AC in biological samples was also evaluated by estimating its recovery from spiked human urine and plasma samples. Recoveries for acebutolol from human plasma and urine were in the range 97-103% and 96-104% respectively (Table 1). A simple and fast pretreatment procedure [29] was used. By adding a small amount of 5% $ZnSO_4.7 H_2O$ solution, NaOH and acetonitrile to the urine or plasma samples and centrifuging the mixture, most of the interfering substances (mainly proteins) were simply removed and eliminated by precipitation (Figures 10 and 11).

## Conclusion

Square-wave adsorptive stripping voltammetric (SW-AdSV) method has been developed for the determination
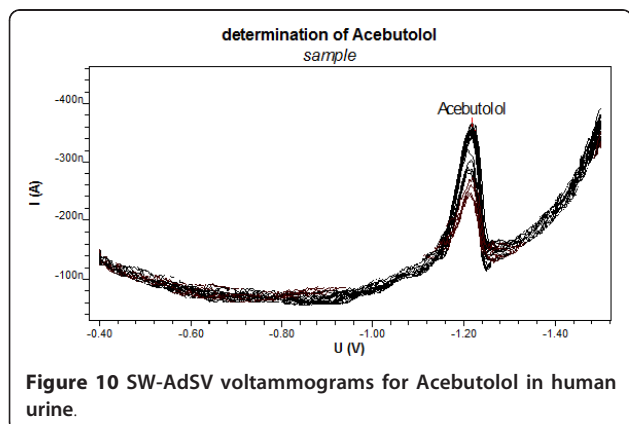


**Figure 10 SW-AdSV voltammograms for Acebutolol in human urine.**
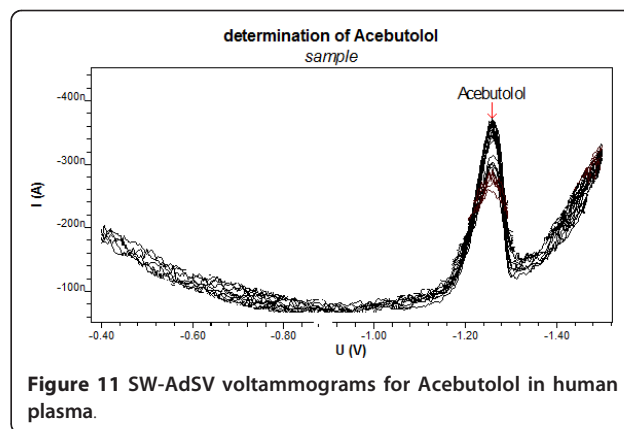


**Figure 11 SW-AdSV voltammograms for Acebutolol in human plasma**.

of acebutolol in biological fluids and pharmaceutical formulation for first time. The principal advantage of the proposed method over the reference potentiometric method is sensitivity and specificity. The proposed voltammetric technique has the advantages of being simpler, faster, more selective and more cost-effective than potentiometric procedure. The SW-AdSV method are rapid, requiring about 5 min to run sample, and involve no sample preparation other than dissolving, diluting and transferring an aliquot to the supporting electrolyte. The possibility of monitoring of the compound in human urine and plasma makes the voltammetric method useful for pharmacokinetic and pharmacodynamic purposes.

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### Authors' contributions
AA participated in the design of the study, carried out the experimental work and manuscript drafting. MH proposed and supervised the program, and participated in data analysis and draft revision. AM coordinated the study and modified the text. FB participated in the design of this study and analyzed the experimental data. All authors read and approved the final manuscript.

### Competing interests
The authors declare that they have no competing interests.

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