# Quantification of Terbutaline in Pharmaceutical Formulation and Human Serum by Adsorptive Stripping Voltammetry at a Glassy Carbon Electrode

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**The electrochemical oxidative behavior of terbutaline at the glassy carbon electrode was studied in a series of the Britton-Robinson buffer of pH 2—11. Cyclic and square-wave voltammograms of terbutaline at the pH values ≤9 exhibited a single irreversible anodic peak. A fully validated, simple, sensitive and precise square-wave adsorptive anodic stripping voltammetric procedure was described for the determination of terbutaline in bulk form, tablets and human serum. For $5\times10^{-8}$ M bulk terbutaline a mean recovery of 98.78±0.94% (*n*=5) was achieved following its preconcentration by adsorptive accumulation onto the glassy carbon electrode at a +0.15 V (*vs.* Ag/AgCl/$KCl_s$) for 180 s. Limit of detection of $6\times10^{-9}$ M and limit of quantitation of $2\times10^{-8}$ M terbutaline were achieved in the bulk form or its formulations (Bricanyl® tablets). The described square-wave adsorption anodic stripping voltammetric procedure was successfully applied for the determination of terbutaline in human serum following medium exchange. Limit of detection of $1.41\times10^{-8}$ M (3.173 ng $ml^{-1}$) and limit of quantitation of $4.70\times10^{-8}$ M (10.575 ng $ml^{-1}$) were achieved in human serum with a mean recovery of 98.11±1.13%.**

**Key words** terbutaline; Bricanyl® tablet; human serum; determination; cyclic voltammetry; adsorptive stripping voltammetry

Terbutaline sulfate (Chart 1), 2-*tert*-butylamino-1-(3,5-dihydroxyphenyl) ethanol hemisulfate, is an adrenergic agonist which predominantly stimulates $\beta_2$-receptor widely used in the treatment of bronchial asthma, chronic bronchitis, emphysema and chronic obstructive pulmonary disease.[1,2] The drug is given orally and/or by injection or inhalation, thus producing relaxation of bronchial smooth muscle, inhibition of the release of endogenous spasmogens, inhibition of edema caused by endogenous mediators, increased mucociliary clearance and relaxation of the uterine muscle.[3] In some respiratory diseases, it can often be taken in overdoses which can cause tremor, tachycardia, hypokalamia and sometimes fatal consequences.[4] For this reason, trace analysis of terbutaline is important in pharmaceutical research and clinical chemistry.

Various techniques have been used for determination of terbutaline sulfate in its pharmaceutical formulations and biological fluids. These include capillary electrophoresis,[5—11] flow-injection chemiluminescence,[12,13] colorimetry,[14—17] spectrophotometry,[18—20] liquid chromatography,[21—24] gas chromatography,[25] high performance liquid chromatography[26—33] and cyclic voltammetry.[34] Most of the reported methods require time-consuming extraction steps prior to the analysis.

Here a square-wave adsorptive anodic stripping voltammetric procedure was described for determination of terbutaline in bulk form, pharmaceutical formulation and human serum at a glassy carbon electrode.

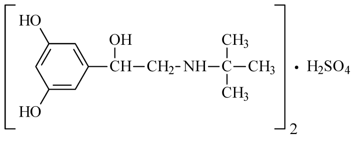

Chart 1

## Experimental

**Instrumentation** Computer-controlled Electrochemical Analyzers Models 263A and 394-PAR (Princeton Applied Research, Oak Ridge, TN., U.S.A.) were used for the voltammetric measurements. The electrode assembly (Model 303A-PAR) incorporated with a dark micro-electrolysis cell of three electrode system comprising of a glassy carbon disk electrode (G0197, 7 $mm^2$ surface area) as a working electrode, an Ag/AgCl/$KCl_s$ reference electrode and a platinum wire counter electrode, was used. Stirring of the solution in the micro-electrolysis cell was performed using a magnetic stirrer (305-PAR) with a star-shaped magnet to provide the convective transport during the preconcentration step. The whole measurements were automated and controlled through the programming capacity of the apparatus. The data were treated through a personal computer connected to the potentiostat and loaded with the 394 Analytical voltammetry software version 2.01-copyright© 1994 (PAR).

A Mettler balance (Toledo-AB104, Greifensee, Switzerland) was used for weighing the solid materials. A pH-meter (Crison, Barcelona, Spain) was used for the pH measurements of the supporting electrolytes. A centrifuge (Eppendorf-5417 C, Hamburg, Germanny) was used for separation of the precipitated proteins from the human serum samples before assay of the drug. A micopipetter (Eppendorf-Multipette® plus) was used for transfer of the reactant solutions throughout the present experimental work. The de-ionized water used throughout the present study was supplied from a Purite-Still Plus de-ionizer connected to a Hamilton-AquaMatic bi-distillation water system.

**Solutions** Supporting Electrolytes: Britton-Robinson (B-R) universal buffer (pH 2—11, 0.08 M), acetate buffer (pH 4.5—5.5, 0.1 M), phosphate buffer (pH 4.5—7.5, 0.1 M), sodium sulphate (0.1 M), sodium nitrate (0.1 M), sodium perchlorate (0.1 M) and potassium chloride (0.1 M) solutions (Analytical grade) were prepared in de-ionized water[35] and were used as supporting electrolytes.

Solutions of Bulk Terbutaline Sulfate: Bulk terbutaline sulfate was supplied from Chemical Industries Development, Egypt. A standard solution of $5\times10^{-3}$ M bulk terbutaline was prepared in methanol (Merck) and stored in a dark bottle at 4 °C. The desired working solutions ($1\times10^{-6}$—$1\times10^{-4}$ M) were prepared by appropriate dilution with methanol.

Solutions of Bricanyl® Tablets: Five Bricanyl® tablets (Chemical Industries Development, Egypt) as labeling to contain 2.5 and 5 mg terbutaline per tablet were weighed and the average mass per tablet was determined. A quantity of the finely ground terbutaline was accurately weighed and transferred into a 100-ml volume calibrated flask contains 70 ml methanol (Merck). The content of the flask was sonicated for about 15 min and then made up to the volume with methanol. The solution was then filtered

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through a 0.45 $\mu$m milli-pore filter (Gelman, Germany) to separate out the insoluble excipients, rejecting the first portion of the filtrate. The desired working solutions of the drug were obtained by accurate dilution with methanol and used as standard solutions. The solution was directly analyzed, according to the general analytical procedure.

Solutions of Human Serum: Serum sample of a healthy volunteer was stored frozen until assay. Samples of human serum (each of 1 ml) were fortified with various concentrations ($1\times10^{-8}$—$1\times10^{-5}$ M) of terbutaline in small centrifuge tubes, then each of these samples was completed to a 1.0 ml volume with methanol for denature and precipitate of proteins. After vortexing each of the serum samples for 2 min, the precipitated proteins were separated by centrifugation for 3 min at 14000 rpm. The clear supernatant layer was filtered through a 0.45 $\mu$m milli-pore filter to obtain protein-free human serum samples, which were used as standard spiked serum solutions. Then the analysis was followed up as indicated in the general analytical procedure.

**Cleaning of the Electrode** Before measurements, the glassy carbon electrode (GCE) was polished with aqueous slurry of 0.5 $\mu$m alumina powder on a damp silk cloth until a mirror-like finish was obtained. Then the electrode was activated before recording the voltammograms by scanning the applied potential from $-0.3$ to 1.3 V by cyclic voltammetry for 10 cycles in a blank solution of the B-R universal buffer till a low background current was obtained. For re-generation of the electrode surface after recording each voltammogram, the GCE was transferred to a blank electrolyte solution in the voltammetric cell and series of cyclic scans were continued until a voltammogram corresponding to the residual current was obtained. The electrode was then ready for use in the next measurement.

**General Analytical Procedure** Ten milliliters of the B-R universal buffer was introduced into the micro-electrolysis cell and a selected accumulation potential was then applied to the glassy carbon electrode for a selected preconcentration time period, while the solution was stirred at 400 rpm. At the end of the accumulation period, the stirring was stopped and a 5-s rest period was allowed for the solution to become quiescent. Then, the voltammogram was recorded by scanning the potential towards the positive direction using the selected waveform. Medium exchange method[36] was used during the determination of terbutaline in human serum to avoid blocking of the electrode surface with low molecular weight proteins may remain after centrifugation.

To study the reproducibility, accuracy and precision of the proposed stripping volammetric procedure for determination of the drug in bulk, tablet and human serum samples, recovery experiments were carried out, by means of both the calibration curve and standard addition methods. All the data were obtained at room temperature.

## Results and Discussion

**Cyclic Voltammetry** Cyclic voltammograms of terbutaline at a glassy carbon electrode in the B-R universal buffer of pH 2—9 exhibited a single irreversible anodic peak which may be attributed to oxidation of the –OH group of the aliphatic chain of the drug molecule. No peaks were observed in the reverse scan which indicated the irreversible nature of the electrode process. The peak current increased with an increase of pH up to pH 6 where a much developed peak current was achieved. In solutions of higher pH values the peak current decreased gradually till it almost vanished at pH >9.

The interfacial adsorptive character of terbutaline onto the GCE was examined by recording its cyclic voltammogram for $5\times10^{-5}$ M solution in a B-R universal buffer of pH 6 at scan rate of 0.10 V s$^{-1}$ following preconcentration of terbutaline by adsorptive accumulation onto the GCE under open circuit conditions (Fig. 1, dashed scan) and then at 0.15 V for 180 s (scan 1). A Substantial decrease of the anodic peak was observed in subsequent scans (scan 2). Such a behavior indicates the adsorption of terbutaline onto the GCE. Study of the influence of the scan rate shows that the peak current changes linearly with scan rate according to the equation $i_{pa}=\mathrm{A}v^x$, where $x$ is 1.0 as expected for adsorption-controlled reaction.[37] Moreover, the regression equation of

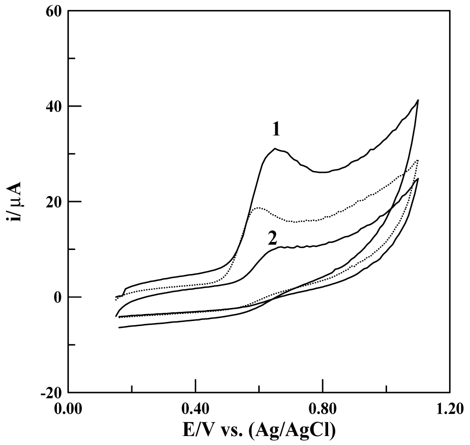

Fig. 1. Cyclic Voltammograms of $5\times10^{-5}$ M Terbutaline in a B-R Universal Buffer of pH 6 Recorded Following Preconcentration by Adsorptive Accumulation onto an Activated GCE: under Open Circuit Conditions (Dashed Scan) and Then at $E_{acc}=0.15$ V for 180 s (Scans 1 and 2); Scan Rate= 0.10 V s$^{-1}$

$\log i_{pa}$ *versus* $\log v$ plot gave a slope value of 0.90, confirming the adsorption nature of the oxidation process.[38] On the other hand, as the scan rate was increased from 0.025 to 0.50 V s$^{-1}$, the peak potential shifted towards more positive values as expected for an irreversible oxidation process.[39] Value of $\alpha n_a$, product of transfer coefficient $\alpha$ and number of electrons $n_a$ transferred in the rate-determining step, was determined from the linear correlation obtained between the peak potential $E_{pa}$ and the logarithm of the scan rate according to the equation of the totally irreversible electrode reaction[40]:

$$E_p=(2.303RT/\alpha n_a F)\log(RTk_f^o/\alpha n_a F)-(2.303RT/\alpha n_a F)\log v$$

A value of $\alpha n_a=0.90$ was obtained. Accordingly, the number of electrons, $n_a$, transferred in the rate-determining step should equal two ($n_a=2$) and hence, the transfer coefficient $\alpha$ should be 0.45.

**Adsorptive Stripping Voltammetry Study** Effect of Type and pH of the Medium: The influence of pH on the square-wave voltammetric response for $5\times10^{-7}$ M terbutaline was examined in the B-R universal buffer of various pH values following its preconcentration by adsorptive accumulation onto the GCE for 180 s. The voltammograms showed a single well-defined irreversible anodic peak over the pH range 2—8. At pH values higher than 8 the anodic peak became smaller, together with a poor peak definition. As mentioned before, terbutaline has an adsorptive behavior onto the glassy carbon electrode and the adsorption process reachs a maximum value at B-R buffer solution of pH 6, which was indicated from the $i_p$–pH relationship (Fig. 2a). Therefore, a much developed peak current was achieved at pH 6. The peak potential shifted to less positive values on the increase of pH of the medium (Fig. 2b) according to the following equation; $E_p\,(\mathrm{V})=1.078-0.065\mathrm{pH}$ ($r=0.999$), denoting that protons are involved in the electrode reaction process and that the proton-transfer reaction precedes the electrode process.[41] Some different buffers such as acetate and phosphate buffers, and also some salt solutions (0.1 M) such as sodium sulphate, sodium nitrate, sodium perchlorate and potassium chloride solutions were tested as supporting elec-

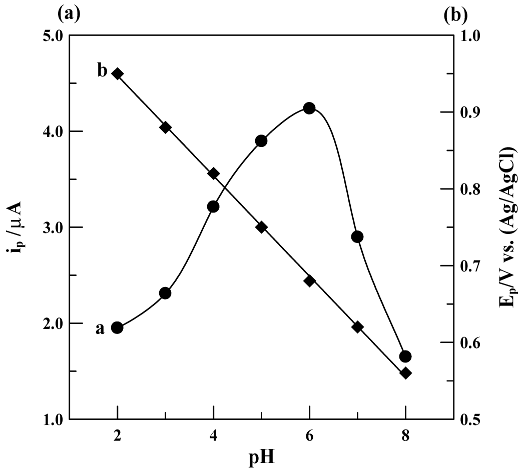

Fig. 2. Influence of pH of the B-R Universal Buffer on: (a) the SW-AdAS Votammetric Peak Current ($i_p$) of $5\times10^{-7}$ M Terbutaline and (b) Peak Potential ($E_p$) at Frequency $f$=60 Hz, Scan Increment $\Delta Es$=10 mV and Pulse-Amplitude $a$=25 mV, Following Preconcentration by Adsorptive Accumulation onto the GCE at +0.15 V for 180 s

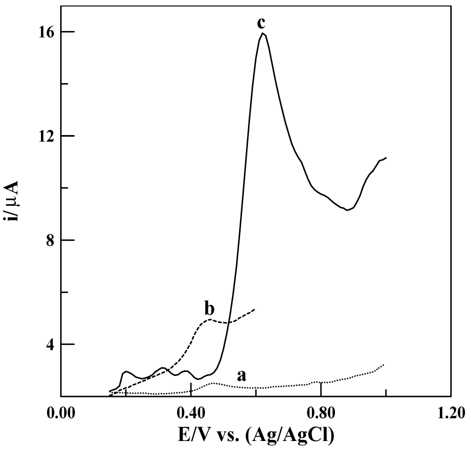

Fig. 3. Adsorptive Anodic Stripping Voltammograms of $1\times10^{-6}$ M Terbutaline in a B-R Universal Buffer of pH 6 Recorded Following Preconcentration by Adsorptive Accumulation onto the GCE at +0.15 for 90 s Using: (a) Differential-Pulse ($v$=10 mV s$^{-1}$ and $a$=25 mV), (b) Linear-Sweep ($v$=100 mV s$^{-1}$ and $a$=25 mV) and (c) Square-Wave ($f$=120 Hz, $\Delta Es$=10 mV and $a$=25 mV) Potential Waveforms

trolytes. A B-R universal buffer of pH 6 was the best compromise with respect to sharper response where a much enhanced adsorption of terbutaline onto the GCE was achieved and therefore it was used as a supporting electrolyte in the rest of the present analytical work.

Choice of the Applied Waveform: The ability to readily assay nanomolar concentrations was attributed not only to the effective accumulation conditions (accumulation potential and accumulation time), but also to the improved sensitivity of the applied waveform for monitoring of the accumulated analyte. Figure 3 shows the adsorptive anodic stripping (AdAS) voltammograms for $1\times10^{-6}$ M terbutaline recorded at the GCE in a B-R universal buffer of pH 6, following its preconcentration by adsorptive accumulation onto the GCE at 0.15 V (*vs.* Ag/AgCl/KCl$_s$) for 90 s, using the potential waveforms; (a) differential-pulse (DP), (b) linear-sweep (LS) and (c) square-wave (SW). The signal intensity of SW-AdAS voltammetry was found to be 67 and 25 times higher than those of the DP-AdAS and LS-AdAS voltammetry, respectively. Therefore, the SW potential waveform was applied in the present assay in order to improve the sensitivity and the rapidity of assaying terbutaline.

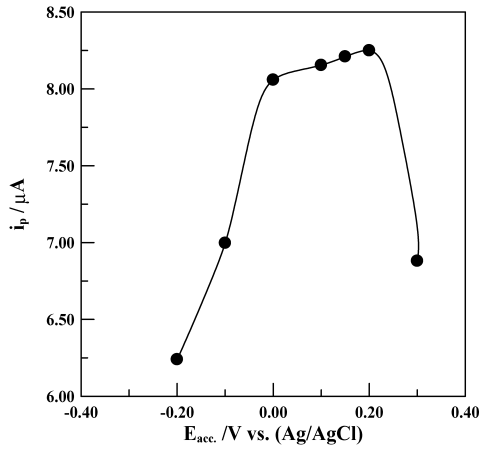

Fig. 4. Effect of Accumulation Potential ($E_{acc}$) on the SW-AdAS Voltammetric Peak Current ($i_p$) of $5\times10^{-7}$ M Terbutaline in a B-R Universal Buffer of pH 6; $f$=120 Hz, $\Delta Es$=10 mV and $a$=25 mV, Following Preconcentration by Adsorptive Accumulation onto the GCE at $E_{acc}$=0.15 V for for 90 s

Square-Wave Stripping Voltammetric Procedure:

- Instrumental parametres: The square-wave response markedly depends on the parameters of the excitement signal. In order to obtain a much developed square-wave adsorptive anodic stripping voltammetry peak current, the optimum instrumental conditions (frequency $f$, scan increment $\Delta Es$ and pulse amplitude $a$) were studied for $5\times10^{-7}$ M terbutaline in a B-R buffer of pH 6 following its preconcentration by adsorptive accumulation onto the GCE for 90 s. At a constant scan increment of 10 mV and a pulse amplitude of 25 mV, the peak current intensity increased linearly over the frequency range 20—120 Hz, following the relationship: $i_p\,(\mu\text{A})=0.054f(\text{Hz})+0.1458$ ($r$=0.997 and $n$=6). At frequency of 120 Hz, the peak current intensity increased linearly with the scan increment up to 10 mV, following the relationship: $i_p\,(\mu\text{A})=0.684\Delta s\,(\text{mV})+1.236$ ($r$=0.996 and $n$=5). The optimal pulse-amplitude was examined over the range 25—100 mV at $f$=120 Hz and $\Delta s$=10 mV and the best peak morphology and sharper one was obtained at 25 mV. Thus, pulse amplitude of 25 mV was applied, as it was better for analytical purposes. Therefore, the square wave optimal instrumental parameters which were used over all the rest of the present investigation can be concluded as; frequency $f$=120 Hz, scan increment $\Delta s$=10 mV and pulse amplitude $E_{sw}$=25 mV.
- Accumulation parameters: Effect of varying accumulation potential ($E_{acc}$) on the peak current of the SW-AdAS voltammogram for $5\times10^{-7}$ M terbutaline in a B-R universal buffer of pH 6 following its preconcentration by adsorptive accumulation onto the GCE for 90 s was studied from −0.2 to +0.3 V. The best developed peak current intensity was achieved over the potential range 0.0 to +0.2 V (Fig. 4). The observed gradual decrease in the peak current intensity may be attributed to the consequence of desorption of the drug at either higher or lower potential values than the zero charge potential, where a maximum adsorption of uncharged organic molecules can be expected. Therefore, accumulation

potential of $+0.15$ V (*vs.* Ag/AgCl/KCl$_s$) was chosen for the analytical studies.

On the other hand, square-wave adsorptive anodic stripping (SW-AdAS) voltammograms of $2\times10^{-7}$ M and $5\times10^{-7}$ M terbutaline were recorded under the optimal procedural conditions following increased accumulation duration (Fig. 5). The peak current intensity of the two concentrations gave linear relationships with $t_{acc}$ up 180 and 120 s for lower and higher concentrations, respectively. This means that the optimal accumulation duration should be chosen according to the concentration level of terbutaline in the investigated solution. The influence of rest period was also considered and a rest period of 5 s was applied.

- Method validation: The elements required for validation of an analytical procedure are: linearity range, limit of detection (LOD), limit of quantitation (LOQ), accuracy, precision, selectivity, robustness and intermediate precision.[42] Linear calibrations curves within the concentration range of $10^{-8}$—$10^{-6}$ M terbutaline were obtained on analysis of various concentrations of terbutaline by means of the described SW-AdAS voltammetric procedure following its preconcentration by adsorptive accumulation onto the GCE for 60 s, 120 s or 180 s. Limit of detection (LOD) and limit of quantitation (LOQ) were determined as 3 and 10 signal-to-noise ratio using the expression $k$ S.D./$b$,[42] where $k=3$ for LOD and 10 for LOQ, S.D. is the standard deviation of the intercept (or the blank) and $b$ is the slope of the calibration curve. The achieved LOD of $6\times10^{-9}$ M and LOQ of $2\times10^{-8}$ M following accumulation onto the GCE for 180 s, the linearity ranges and regression equations listed in Table 1 indicated the reliability of the described SW-AdAS voltammetric procedure for the determination of bulk terbutaline.

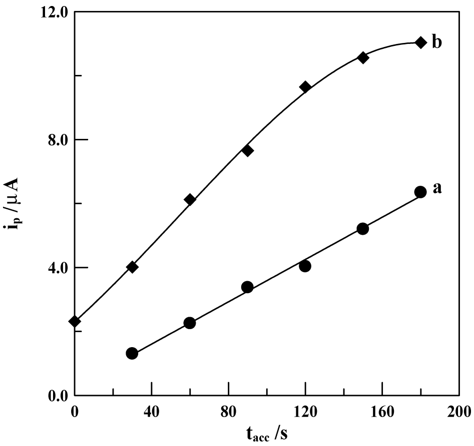

Fig. 5. Effect of the Accumulation Time ($t_{acc}$) on the SW-AdAS Voltammetric Peak Current (a) $2\times10^{-7}$ and (b) $5\times10^{-7}$ M Terbutaline in a B-R Buffer of pH 6 Following Preconcentration by Adsorptive Accumulation onto the GCE at 0.15 V; $f=120$ Hz, $\Delta Es=10$ mV and $a=25$ mV at $E_{acc}=0.15$ V

Repeatability of results using the proposed SW-AdAS voltammetry procedure was examined by performing five replicate measurements for $5\times10^{-8}$ M terbutaline following accumulation onto the GCE at $+0.15$ V for 180 s. A mean recovery of $98.78\pm0.94\%$ ($n=5$) was achieved.

Voltammetric techniques have found widespread use in drug analysis, since the voltammetric procedures usually involve a simple dilution step and most of the excipients used do not interfere in the subsequent determination.[43] The selectivity of the procedure for the assay of terbutaline was examined in the presence of the common excipients usually present in formulations (*e.g.* starch, gelatin, lactose, talc and magnesium stearate). The exipients are electro-inactive and its adsorption onto the GCE is very limited under the optimum procedural conditions. The mean recovery for $5\times10^{-8}$ M terbutaline in the presence of exipients was found to equal $97.61\pm1.52\%$ ($n=5$), which showed no significant interference from excipients. Accordingly, the proposed stripping voltammetric procedure can be considered selective.

The robustness[42] of the measurements by means of the proposed SW-AdAS voltammetric procedure was examined by studying the effect of small variation of some important procedural conditions (pH $6\pm0.5$, and accumulation potential $E_{acc}=+0.15\pm0.05$ V). As shown in Table 2, the achieved recoveries were reliable and the proposed procedure could be considered robust.

The intermediate precision[42] of the proposed procedure

Table 2. Influence of Small Variation in Some of the Optimal Procedural Conditions on Recovery and Standard Deviation (%R±S.D.) of $5\times10^{-8}$ M Terbutaline, Following Accumulation onto a GCE for 180 s; $f=120$ Hz, $\Delta Es=10$ mV and $a=25$ mV at $E_{acc}=0.15$ V

| Variable | Conditions | %R±S.D. ($n=3$) |
|---|---|---|
| Robustness | | |
| pH of the medium | | |
| 5.5 | | $101.52\pm1.28$ |
| 6.0 | $E_{acc}=+0.15$ V<br>pH=6 | $98.78\pm0.94$ |
| 6.5 | | $99.01\pm1.13$ |
| Accumulation potential ($E_{acc}$) | | |
| $+0.10$ V | | $98.52\pm1.34$ |
| $+0.15$ V | | $98.78\pm0.94$ |
| $+0.20$ V | | $97.66\pm1.40$ |
| Intermediate precision | | |
| Potentiostat 394-PAR | | $98.78\pm0.94$ |
| Potentiostat 263A-PAR | pH=6.0<br>$E_{acc}=+0.15$ V | $102.76\pm1.91$ |
| Day (1) | | $98.78\pm0.94$ |
| Day (2) | | $99.16\pm0.56$ |
| Day (3) | | $97.85\pm1.16$ |

Table 1. Characteristics of the Calibration Curves of the SW-AdAS Voltammetric Assay of Bulk Terbutaline under the Optimal Procedural Conditions

| Acc. duration (s) | Linearity range (M) | Least square equation[a] | | Corr. coeff. ($r$) | LOD (M) | LOQ (M) |
|---|---|---|---|---|---|---|
| | | Intercept (μA) | Slope (μA/μM) | | | |
| 60 | $5\times10^{-7}$—$1\times10^{-6}$ | 0.263 | 15.49 | 0.998 | $1.5\times10^{-7}$ | $5\times10^{-7}$ |
| 120 | $5\times10^{-8}$—$8\times10^{-7}$ | 0.087 | 21.21 | 0.998 | $1.5\times10^{-8}$ | $5\times10^{-8}$ |
| 180 | $2\times10^{-8}$—$5\times10^{-7}$ | 0.046 | 38.33 | 0.995 | $6.6\times10^{-9}$ | $2\times10^{-8}$ |

[a] Average of three determinations.

Table 3. Assay of Terbutaline in Its Pharmaceutical Formulations by the Proposed SW-AdAS Voltammetric Procedure and a Reported USP Spectrophotometric Official Method[20)]

| Sample | Claimed value (mg/tablet) | Described procedure (%R±S.D.) | | Reported USP |
|---|---|---|---|---|
| | | Calibration curve | Standard addition | |
| Bricanyl® | 2.5 | 97.9±1.1<br>$F=1.72$<br>$t=1.36$ | 98.7±1.7 | 96.8±1.4 |
| | 5 | 101.6±0.9<br>$F=3.74$<br>$t=0.62$ | 99.3±1.2 | 102.1±1.7 |

Theoretical $F$-value$=6.39$ and $t$-test$=2.3$ at 95% confidence limit for $n_1=5$ and $n_2=5$.

was examined by applying the procedure to assay of terbutaline using two Potentiostats, 394-PAR (Lab. 1) and 263A-PAR (Lab. 2), at different elapsed time. The results obtained due to Lab. (1) and Lab. (2) and even day to day were found reproducible (Table 2), since there was no significant difference in the recoveries of terbutaline or the standard deviations.

**Applications** Analysis of Terbutaline in Bricanyl® Tablets: The described SW-AdAS voltammetric procedure was successfully applied for the determination of terbutaline in its pharmaceutical formulations (Bricanyl® tablets of 2.5 and 5 mg terbutaline/tablet). The obtained results (Table 3) were statistically compared with those obtained by the official USP spectrophotometric method.[20)] Since calculated value of $F$ does not exceed the theoretical value, there was no significant difference between the proposed and reported methods with respect to reproducibility.[44)] Also, no significant difference was noticed between the two methods regarding accuracy and precision as revealed by $t$-value.[44)] The accuracy of the described SW-AdAS procedure was also judged by applying the standard addition method.[45)] This means that the proposed procedure should be applicable to the analysis of this and other similar formulation products containing terbutaline.

Assay of Terbutaline in Human Serum: The described SW-AdAS voltammetric procedure was also successfully applied to the assay of terbutaline in spiked human serum. Medium exchange method was used following accumulation of terbutaline onto the GCE and before recording each voltammogram to minimize interferences resulting from macro solution constituents and to increase the efficiency of the stripping step. Variation of the peak current *versus* terbutaline concentration was linear within the concentration range $5\times10^{-8}$—$1\times10^{-6}$ M (Fig. 6) which can be represented by a straight line following the equation; $i_p(\mu A)=35.62C(\mu M)+1.066$ ($r=0.999$ and $n=7$). A mean percentage recovery of terbutaline in human serum was found to equal 98.11±1.13%. The achieved LOD and LOQ of terbutaline were $1.41\times10^{-8}$ M ($3.173\ \text{ng ml}^{-1}$) and $4.70\times10^{-8}$ M ($10.575\ \text{ng ml}^{-1}$), respectively.

## Conclusion

A square-wave adsorptive anodic stripping voltammetric procedure was described for the assay of terbutaline in bulk form, pharmaceutical formulation and spiked human serum at a glassy carbon electrode. The described procedure is simple, sensitive, rapid, selective and reproducible.

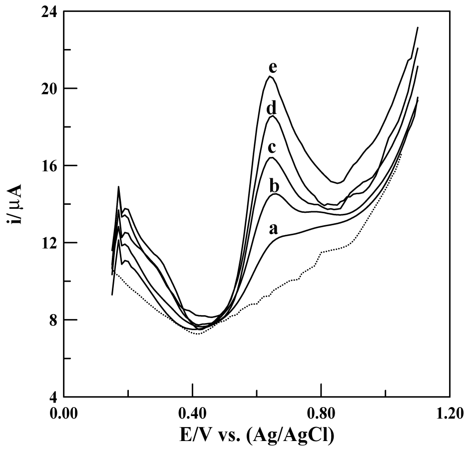

Fig. 6. SW-AdAS Voltammograms for Successive Additions of Terbutaline Spiked in Human Serum Samples, Recorded in a B-R Buffer of pH 6 Following Preconcentration by Adsorptive Accumulation onto the GCE at 0.15 V for 180 s

Each addition affected a $5\times10^{-8}$ M terbutaline and the dotted line represents the blank solution. Other instrumental parameters are as those given in Fig. 5.

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