Electrochemical Characterization and Determination of Tramadol drug using Graphite Pencil Electrode

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Abstract - Electrochemical oxidation of tramadol at pencil graphite electrode has been investigated using cyclic, differential pulse and square wave voltammetric techniques. In pH 9.2 phosphate buffer, tramadol showed an irreversible oxidation peak at 0.77 V. The dependence of the current on pH, concentration and scan rate was investigated to optimize the experimental conditions for the determination of tramadol. Differential pulse voltammetry was further exploited as a sensitive method for the detection of tramadol. Under optimized conditions, the concentration range and detection limit were $1.0 \times 10^{-7}$ to $1.5 \times 10^{-6}$ M and $0.38 \times 10^{-8}$ M, respectively. The proposed method was applied to determine the tramadol assay in pharmaceutical samples and human biological fluids such as urine as a real sample.

Keywords - Voltammetry, Tramadol, Pencil, pH, Electrochemical, Tablet

1. INTRODUCTION

Drug analysis is an important tool for drug quality control. Hence, the development of simple, sensitive and rapid method is of great importance. Tramadol(TRA),(1R,2R)-2-[(dimethylamino)methyl]-1-(3methoxyphenyl) cyclohexanol (Scheme 1), is a synthetic monoamine uptake inhibitor and centrally acting analgesic, used for treating moderate to severe pain and it appears to have actions at the µ-opioid receptor as well as the
noradrenergic and serotonergic systems[1]. However, their overdose is toxic in nature and may cause dizziness, nausea and omitting. The graphite pencil electrode (GPE) has been successfully used as a biosensor in modern electroanalytical field due to its high electrochemical reactivity, good mechanical rigidity, low cost, low technology and ease of modification, renewal and low background current[2,3]. The GPE has good applications in the analysis of neurotransmitter and detection of traces of metal ions and drugs.

![Scheme 1. Structure of Tramadol](image)

Most of the analytical methods available in literature are based on chromatographic procedures, HPLC and capillary electrophoresis, being used to quantify tramadol in different biological fluids, namely urine, plasma and whole blood samples [4-7]. For determination of tramadol in pharmaceutical dosage forms a few analytical methodologies were proposed and were mainly based on spectrophotometry [8,9], HPLC[10], capillary isotachophoresis [11] and potentiometry [12]. However, spectrophotometry suffers from low sensitivity while liquid chromatography, although more sensitive, requires expensive apparatus, long and time-consuming procedures and costly chemicals. In ion-selective electrode, the response is affected by electrical properties of the film and electric double-layer capacitance while it also suffers from low sensitivity.

 Electroanalytical techniques, however, have been shown to be excellent for the determination of pharmaceutical compounds in different matrices. The advances made in the experimental electro-chemical techniques used in the field of drug analysis owe much to their simplicity, low cost, and relatively short analysis time compared to other techniques.

 Electrochemical methods, especially differential pulse voltammetry (DPV) and square wave voltammetry (SWV), make it possible to decrease analytical time as compared to the time required by chromatographic methods. The advantages of DPV over other electroanatical techniques are greater speed of analysis, lower consumption of electroactive species and fewer problems with blocking of the electrode surface.

 Literature survey revealed that no electroanalytical method for determination of TRA by using GPE was reported. Hence the title reaction was undertaken to investigate the oxidation
mechanism of TRA and to optimize the conditions for determination of TRA in pharmaceutical dosage forms and human biological fluids using CV, DPV and SWV techniques.

2. EXPERIMENTAL

2.1. Reagents and chemicals

The TRA was purchased from Sigma-Aldrich (India) and used as such. A 1.0 mM stock solution was made in millipore water and then stored in the dark at low temperature. The studies were conducted in the pH range 3.0–11.2 phosphate buffer solutions prepared by mixing the stock solutions of Na₂HPO₄ and NaH₂PO₄ (Sd. Fine, India) [13]. The pencil-lead rods (HB 0.5mm in diameter and 6cm length) were purchased from local bookstall. All other chemicals and reagents were of analytical grade and millipore water was used throughout the experiment.

2.2. Instrumentation

Electrochemical measurements were carried out on a CHI 630D electrochemical analyzer (CH Instruments Inc., USA). The voltammetric measurements were carried out in a 10 mL single compartment three-electrode glass cell with Ag/AgCl as a reference electrode, a platinum wire as counter electrode and a graphite pencil electrode as working electrode. All the potentials were given against the Ag/AgCl (3.0 M KCl). pH measurements were performed with an Elico LI 120 pH meter (Elico Ltd., India).

2.3. Area of the electrode

The area of the electrode was obtained by the cyclic voltammetric technique using 1.0 mM K₄Fe(CN)₆ as a probe at different scan rates. For a reversible process, the following Randles-Sevcik formula was used [14].

\[ I_{pa} = (2.69 \times 10^5) n^{3/2}A_0D_0^{1/2} C_0^{1/2} \sqrt{v} \]  

(1)

where \( I_{pa} \) refers to the anodic peak current, \( n \) is the number of electrons transferred, \( A_0 \) is the surface area of the electrode, \( D_0 \) is diffusion coefficient, \( v \) is the scan rate and \( C_0 \) is the concentration of K₄Fe(CN)₆. For 1.0 mM K₄Fe(CN)₆ in 0.1 M KCl electrolyte, \( n=1 \), \( D_0=7.6 \times 10^{-6} \text{ cm}^2\text{s}^{-1} \), then from the slope of the plot of \( I_{pa} \) vs. \( \sqrt{v} \), the electro active area was calculated. In our experiment electro active area for graphite pencil electrode was found to be 0.298 cm² and for carbon paste electrode was found to be 0.0421 cm². Electro active area of GPE is higher than the electro active area of CPE, hence greater response of peak current was observed for GPE towards tramadol.
2.4. Analytical Procedure

All experiments were carried out at an ambient temperature of 25±0.1 °C. The parameters for differential pulse voltammetry (DPV) were initial potential E: 0.40 V; final potential E: 1.0 V; sample interval: 0.01 V; amplitude: 0.05 V; frequency: 15 Hz; quiet time: 2 s; sensitivity: 1.0×10^{-4} A/V. The parameters for square wave voltammetry (SWV) were initial potential E: 0.40; final potential E: 1.0 V; amplitude: 0.025 V; frequency: 15 Hz; quiet time: 2 s; sensitivity: 1.0×10^{-4} A/V.

2.5. Procedure for Pharmaceutical preparations

Ten pieces of Tramol® (100 mg) tablets were powered in a mortar. A portion equivalent to a stock solution of a concentration of about 1.0×10^{-3} M was accurately weighed and transferred into a 100 ml calibrated flask and completed to the volume with millipore water. The contents of the flask were sonicated for 10 min to affect complete dissolution. Appropriate solutions were prepared by taking suitable aliquots of the clear supernatant liquid and diluting with them with the phosphate buffer solutions. Each solution was transferred to the voltammetric cell and analyzed by standard addition method. The differential pulse voltammograms were recorded between 0.40 and 0.80 V after open-circuit accumulation for 150 s with stirring. The oxidation peak current of TRA was measured. To study the accuracy of the proposed method and to check the interference from excipients used in the dosage form, recovery experiments were carried out. The concentration of TRA was calculated using standard addition method.

2.6. Analysis of urine sample

Human urine was obtained from four healthy volunteers of similar sex and age. Aliquots were centrifuged at 7000 rpm for 5 min at room temperature (25±0.2 °C). These urine samples were analyzed immediately or they were stored at -4 °C until analysis.

3. RESULTS AND DISCUSSION

3.1. Voltammetric behavior of tramadol

The electrochemical behavior of TRA at graphite pencil electrode was studied by cyclic voltammetry (CV) at pH 9.2. The cyclic voltammograms obtained for 1.0 mM TRA solution at a scan rate of 50 mV s^{-1} exhibits a well-defined anodic peak at about 0.77 V at GPE. The results are shown in Fig. 1. On the reverse scan, no corresponding reduction peak was observed indicating that, the electrode process of TRA is an irreversible one. The voltammograms corresponding to the first cycle was generally recorded.
3.2. Effect of pH

The electrode reaction might be affected by pH of the medium. The electro-oxidation of 1.0 mM TRA was studied over the pH range of 3.0–11.2 in phosphate buffer solution by cyclic voltammetry which is as shown in Fig. 2A. However, no sharp peaks were obtained for pH 3.0-6.0. The solution pH influenced the peak current and peak potential considerably. With the increase in pH of the solution, peak potential shifted to less positive values, (Fig. 2B) and obeys the following equation:

\[ E_P (V) = -0.042 \text{pH} + 1.167 \quad (r=0.974) \]  

(2)

From the plot of \( I_{pa} \) vs. pH (Fig. 2C) it is clear that the intensity increased to a high value at pH 9.2, then the peak intensity decreased. Because the best result with respect to sensitivity accompanied with sharper response was obtained with pH 9.2, it was selected for further experiments.

3.3. Effect of scan rate

The effect of the scan rate on the peak current of the compound was investigated in buffer solution of pH 9.2 containing 1.0 mM of the compound. The cyclic voltammetric results indicated that the anodic peak current of TRA showed a linear relationship with the square root of the potential sweep rate over a wide range of 50–300 mVs\(^{-1}\) with correlation coefficient values \((r)\) of 0.995 (Fig. 3A). This indicates that the electrode process was controlled by diffusion. In addition there was a linear relation between \( \log I_{pa}(\mu A) \) and \( \log \upsilon(Vs^{-1}) \), corresponding to the following equation:
\[ \log I_r(\mu A) = 0.35 \log \nu(Vs^{-1}) - 0.45; \quad r=0.991 \quad \text{(Fig. 3B)} \]  

(3)

The slope of 0.35 was very close to the theoretically expected value of 0.5 for a diffusion-controlled process [15]. The peak potential shifted to more positive values with increasing of the scan rates. The linear relation between peak potential and log of scan rate can be expressed as \( E_p/V = 0.074 \log \left( \nu/Vs^{-1} \right) + 0.79; \quad r=0.990 \) (Fig. 3C).

![Graph showing the influence of pH on the shape of the anodic peak](image1.png)

**Fig. 2.** (A) Influence of pH on the shape of the anodic peak, pH: (a) 7.0; (b) 8.0; (c)9.2; (d) 10.4; (e) 11.2; (B) Influence of pH on the peak potential \( E_p(V) \) of TRA. Other conditions are as in Fig. 1; (C) Variations of peak currents \( I_{pa}(\mu A) \) of TRA with pH. Other conditions are as in Fig. 1
For an irreversible electrode process, \( E_p \) is defined by the following equation:

\[
E_p = E^0 + \left( \frac{2.303RT}{\alpha n_f} \right) \log \left( \frac{RTk^0}{\alpha n_f} \right) + \left( \frac{2.303RT}{\alpha n_f} \right) \log \nu
\]  

(4)

where ‘\( \alpha \)’ is the electron transfer coefficient, ‘\( k^0 \)’ the standard heterogeneous rate constant of the reaction, ‘\( \nu \)’ the scan rate, ‘\( n \)’ the number of electrons transferred and ‘\( E^0 \)’ is the formal redox potential. Other symbols have usual meanings. The value of ‘\( \alpha n \)’ can be easily calculated from the slope of \( E_p(V) \) vs. \( \log \nu(Vs^{-1}) \). In this system, the slope was 0.074, taking \( T=298 \text{ K}, \ R=8.314 \text{ J K}^{-1} \text{ mol}^{-1} \) and \( F=96485 \text{ C/mol} \), \( \alpha n \) was calculated to be 0.799.

According to Bard and Faulkner [16], \( \alpha \) can be given by

\[
\alpha=47.7/E_p-E_{p1/2} \text{ mV}
\]  

(5)

Here \( E_{p1/2} \) is the potential when the current is at half the peak value. From this, the value of \( \alpha \) was calculated as 0.431. Further, the number of electrons (\( n \)) transferred in the electro-oxidation of TRA was calculated to be 1.85≈2. The value of \( k^0 \) can be determined from the intercept of the above plot if the value of \( E^0 \) is known. The value of \( E^0 \) can be obtained from the intercept of \( E_p(V) \) vs. \( \log \nu(Vs^{-1}) \) curve by extrapolating to the vertical axis at \( \nu=0 \) [17]. The intercept for \( E_p(V) \) vs. \( \log \nu(Vs^{-1}) \) plot was 0.795 and \( E^0 \) was obtained to be 0.704, the \( k^0 \) was calculated to be \( 7.06\times10^2 \text{ s}^{-1} \).

![Graphs](image)

Fig. 3. (A) Dependence of oxidation peak current on the square root of scan rate; (B) Dependence of the logarithm of peak current on logarithm of scan rate; (C) Linear relationship between \( E_p \) vs. \( \log \nu \)

3.4. Mechanism

In the proposed method, the electro-oxidation of TRA involves two electrons and one proton transfer process. Based on this a mechanism for electro-oxidation of TRA is proposed as in Scheme 2. In the first step there is a removal of electron which leads to the formation of
positive charge and free radical on nitrogen. Second step contains removal of one proton from the CH₃ group to form the free radical and again removal of one electron leads to the formation of positive charge on Nitrogen. In next step with an addition of H₂O and addition of two electrons which leads to the final product 2-(((hydroxymethyl) (methyl)(amino) methyl)-1-(3-methoxyphenyl) cyclohexanol. The product was confirmed by its GC-mass spectra which shows molecular ion peak at 279 m/z as shown in Fig. 4. This type of mechanism is also observed in previous report [18].

\[
\begin{align*}
\text{OH} & \quad \text{N} \\
\text{OMe} & \quad \text{OH} \\
\text{N} & \quad \text{OMe}
\end{align*}
\]

\[
\text{e}^- \quad \text{H}^+ \\
\text{OH} & \quad \text{N} \\
\text{OMe} & \quad \text{OH}
\]

\[
\begin{align*}
\text{OH} & \quad \text{N} \\
\text{OMe} & \quad \text{OH}
\end{align*}
\]

\[
\text{e}^- \quad \text{H}_2\text{O}
\]

\[
\begin{align*}
\text{OH} & \quad \text{N} \\
\text{OMe} & \quad \text{OH}
\end{align*}
\]

2-(((hydroxymethyl) (methyl)(amino)methyl)-1-(3-methoxyphenyl)cyclohexanol

\[
\begin{align*}
\text{OH} & \quad \text{N} \\
\text{OMe} & \quad \text{OH}
\end{align*}
\]

2-(((dimethylamino)methyl)-1-(3-methoxyphenyl)cyclohexanol

\[
\begin{align*}
\text{OH} & \quad \text{N} \\
\text{OMe} & \quad \text{OH}
\end{align*}
\]

2-(((hydroxymethyl)(methyl)amino)methyl)-1-(3-methoxyphenyl)cyclohexanol

\[
\begin{align*}
\text{OH} & \quad \text{N} \\
\text{OMe} & \quad \text{OH}
\end{align*}
\]

Scheme 2. Probable electrode oxidation mechanism of TRA

3.5. Construction of calibration curve

DPV and SWV techniques were used to develop a rapid and sensitive voltammetric method for the determination of TRA under the optimized experimental conditions. The peaks obtained are better defined at lower concentrations of TRA (than those obtained by cyclic voltammetry) with a lower background current, resulting in improved resolution and pH 9.2 was selected as the supporting electrolyte for the quantification of TRA.

The peak current increased linearly with increase in concentration of TRA and the corresponding results are shown in Fig. 5A and 5B for DPV and SWV, respectively. The linear relationship between the current density and concentration in the range of 0.01–0.13 µM for DPV (Fig. 5C) and 0.01–0.11 µM for SWV (Fig. 5D) respectively.

Deviation from linearity was observed at higher concentrations of TRA owing to the adsorption of TRA or its oxidation products on the electrode surface. The values of limit of
detection (LOD) and limit of quantification (LOQ) were calculated using the following equations, LOD=3 s/m; LOQ=10s/m, where s is the standard deviation of intercept of the calibration plot (Five replicates), and m is the slope of the calibration curve [19].

![Graph](image)

**Fig. 4.** GC-mass spectrum of 2-(((hydroxymethyl)(methyl)(amino)methyl)-1-(3-methoxyphenyl)cyclohexanol with its molecular ion peak at 279 m/z

The values of LOD and LOQ were calculated to be $0.38 \times 10^{-8}$ and $1.2 \times 10^{-8}$ for DPV, $0.42 \times 10^{-8}$ and $1.4 \times 10^{-8}$ for SWV respectively. Characteristics of calibration plots for TRA using DPV and SWV are shown in Table 1. DPV showed good response as compared to SWV in view of low intercept and low LOD value.

The LOD and LOQ values calculated by the present method are better compared to the reported work [10-11] (Table 2). In the proposed method, environment friendly electrode was used for the determination of TRA. Reproducibility, repeatability, linearity range, LOD and LOQ of the proposed method are better than earlier methods. The method also offered the advantages of accuracy and time saving.

**Table 1.** Characteristics of calibration plots for TRA

<table>
<thead>
<tr>
<th></th>
<th>SWV</th>
<th>DPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linearity (µM)</td>
<td>0.01–0.11</td>
<td>0.01-0.11</td>
</tr>
<tr>
<td>Slope</td>
<td>0.715</td>
<td>0.454</td>
</tr>
<tr>
<td>Intercept</td>
<td>1.263</td>
<td>0.769</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>0.982</td>
<td>0.935</td>
</tr>
<tr>
<td>RSD% (slope)a</td>
<td>0.455</td>
<td>0.715</td>
</tr>
<tr>
<td>RSD% (intercept)a</td>
<td>0.768</td>
<td>1.263</td>
</tr>
<tr>
<td>LOD</td>
<td>$0.42 \times 10^{-8}$</td>
<td>$0.38 \times 10^{-8}$</td>
</tr>
</tbody>
</table>

*a Mean average of five determinations*
Fig. 5. (A) Differential Pulse Voltammograms of TRA solution at different concentrations at GPE (a) 0.1, (b) 0.3, (c) 0.5, (d) 0.7, (e) 0.9, (f) 1.2 (g) 1.5 and (h) 2.0×10^{-6} M; (B) Square Wave Voltammograms of TRA solution at different concentrations at GPE (a) 0.1, (b) 0.3, (c) 0.5, (d) 0.7, (e) 0.9, (f) 1.1, (g) 1.3 (h) 1.5, (i) 1.7, (j) 1.9, (k) 2.1 and (l) 2.3×10^{-6} M; (C) Plot of the peak currents against concentrations of TRA for DPV; (D) Plot of the peak currents against concentrations of TRA for SWV

3.6. Effect of excipients

For the possible analytical application of the proposed method, the effect of some common excipients used in pharmaceutical preparations was examined. The tolerance limit was defined as the maximum concentration of the interfering substance that caused an error less than 5% for determination of TRA. The effects of these excipients on the voltammetric response was carried by analyzing sample solutions containing a fixed amount of TRA (1.0×10^{-6} M) spiked with various excess amount of each excipient under the same
experimental conditions. The experimental results (Table 3) showed that hundred-fold excess of citric acid, oxalic acid, glucose, gum acacia, lactose, starch, tartaric acid, sucrose and diclofenac did not interfere with the voltammetric signal of TRA. Thus, the procedures were able to assay TRA in the presence of excipients, and hence it can be considered specific.

Table 2. Comparison between various electroanalytical methods for the determination of TRA with the proposed method

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Modified electrodes</th>
<th>Linear working range (M)</th>
<th>Limit of detection (M)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRA</td>
<td>Glassy carbon electrode</td>
<td>$1.50 \times 10^{-5}$ to $7.5 \times 10^{-5}$</td>
<td>$2.2 \times 10^{-6}$</td>
<td>[10]</td>
</tr>
<tr>
<td>Carbon nanoparticles modified glassy carbon electrode</td>
<td>$1.0 \times 10^{-5}$ to $1.0 \times 10^{-3}$</td>
<td>$5.0 \times 10^{-6}$</td>
<td>[11]</td>
<td></td>
</tr>
<tr>
<td>D50wx2–GNP–GCPE</td>
<td></td>
<td>$3.34 \times 10^{-8}$ to $4.55 \times 10^{-5}$</td>
<td>$1.12 \times 10^{-8}$</td>
<td>[18]</td>
</tr>
<tr>
<td>GPE</td>
<td></td>
<td>$1.0 \times 10^{-7}$ to $1.1 \times 10^{-6}$ M</td>
<td>$0.38 \times 10^{-8}$</td>
<td>This work</td>
</tr>
</tbody>
</table>

Table 3. Influence of potential interferents on the voltammetric response of $1.0 \times 10^{-6}$ M TRA

<table>
<thead>
<tr>
<th>Samples</th>
<th>Interferents</th>
<th>Concentration ($1.0 \times 10^{-6}$M)</th>
<th>Signal change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Glucose</td>
<td>1.0</td>
<td>+1.76</td>
</tr>
<tr>
<td>2</td>
<td>Starch</td>
<td>1.0</td>
<td>+0.74</td>
</tr>
<tr>
<td>3</td>
<td>Sucrose</td>
<td>1.0</td>
<td>+1.20</td>
</tr>
<tr>
<td>4</td>
<td>Citric acid</td>
<td>1.0</td>
<td>+0.90</td>
</tr>
<tr>
<td>5</td>
<td>Gum acacia</td>
<td>1.0</td>
<td>-0.77</td>
</tr>
<tr>
<td>6</td>
<td>Lactose</td>
<td>1.0</td>
<td>+2.41</td>
</tr>
<tr>
<td>7</td>
<td>Tartaric acid</td>
<td>1.0</td>
<td>+3.10</td>
</tr>
<tr>
<td>8</td>
<td>Oxalic acid</td>
<td>1.0</td>
<td>-0.76</td>
</tr>
<tr>
<td>9</td>
<td>diclofenac</td>
<td>1.0</td>
<td>+4.4</td>
</tr>
</tbody>
</table>
3.7. Determination of TRA in tablet

An aliquot of the standard solution of the drug was added to 10 mL phosphate buffer (pH 9.2) in the voltammetric cell and the measurement of its drug content was performed according to the general analytical procedure. The results are given in Table 4. The recovery determined was in the range from 98.7% to 100.1%.

Table 4. Analysis and recovery studies of TRA in tablet by DPV

<table>
<thead>
<tr>
<th>Labeled claim (mg)</th>
<th>100.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount found (mg)</td>
<td>98.8</td>
</tr>
<tr>
<td>RSD (%)</td>
<td>1.21</td>
</tr>
<tr>
<td>Added (mg)</td>
<td>4.00</td>
</tr>
<tr>
<td>Found (mg)</td>
<td>3.95</td>
</tr>
<tr>
<td>Recovered (%)</td>
<td>98.7</td>
</tr>
<tr>
<td>RSD (%)</td>
<td>1.10</td>
</tr>
<tr>
<td>Bias (%)</td>
<td>1.25</td>
</tr>
</tbody>
</table>

((a) Mean average of five determinations)

3.8. Detection of TRA in urine samples

The developed differential pulse voltammetric method for the TRA determination was applied to urine samples. The recoveries from urine were by spiking drug free urine with known amounts of TRA. The urine samples were diluted 100 times with the phosphate buffer solution before analysis without further pretreatments. A quantitative analysis can be carried out by adding the standard solution of TRA into the direct system of urine sample. The calibration graph was used for the determination of spiked TRA in urine samples. The detection results of four urine samples obtained are listed in Table 5. The recovery determined was in the range from 99.1% to 100.3%.

Table 5. Determination of TRA in urine samples

<table>
<thead>
<tr>
<th>Spiked(µM)</th>
<th>Detected((a) (µM)</th>
<th>Recovery (%)</th>
<th>SD±RSD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>0.24</td>
<td>98.4</td>
<td>0.002</td>
</tr>
<tr>
<td>0.45</td>
<td>0.44</td>
<td>98.2</td>
<td>0.002</td>
</tr>
<tr>
<td>0.65</td>
<td>0.64</td>
<td>99.2</td>
<td>0.001</td>
</tr>
</tbody>
</table>

((a) Mean average of five determinations)
3.9. Stability and repeatability

The stability and repeatability of the sensor were evaluated by monitoring the response currents in the presence of 1.0 mM TRA. The relative standard deviation (RSD) of the sensor was 1.0% for five successive measurements. From RSD values of peak current and peak potential between day reproducibility are similar to that of within a day if the temperature was kept almost unchanged which could be attributed to the excellent stability and reproducibility of GPE.

4. CONCLUSIONS

The voltammetric behavior and oxidation mechanism of TRA were investigated at a GPE by CV in phosphate buffer solution (pH 9.2). Based on the study, influence of several physico-chemical parameters like potential scan rate, pH and concentration were investigated. The oxidation of TRA was found to be an irreversible two-electron and one-proton process with diffusion character. This method has been successfully used to determine TRA in the pharmaceutical sample. The proposed method offered the advantages of accuracy and time saving as well as simplicity of reagents and apparatus. In addition, the results obtained in the analysis of TRA in spiked urine samples demonstrated the applicability of the method for real sample analysis.

REFERENCES