ACADEMIA ROMÂNĂ
Revue Roumaine de Chimie
http://web.icf.ro/rrch/

Rev. Roum. Chim.,
2017, *62*(6-7), 559-567

VOLTAMMETRIC DETERMINATION OF ROPINIROLE AT GLASSY CARBON ELECTRODE EMPLOYING PULSED TECHNIQUES

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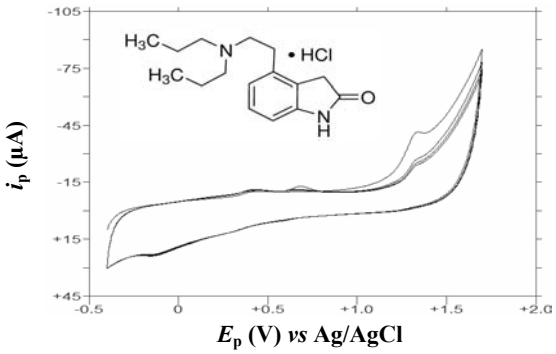
Received November 1, 2016

In this study electrochemical studies were performed for ropinirole, which is used for the treatment of Parkinson's disease. In order to obtain rapid, simple and repeatable determination for ropinirole at glassy carbon electrode differential pulse voltammetry and square wave voltammetry were used. The oxidation behavior of this drug was analyzed with different supporting electrolytes between pH 0.3 – 12.0 by using cyclic voltammetry, differential pulse voltammetry and square wave voltammetry. The regression and the required validation parameters were studied in 0.1 M H_2SO_4 and pH 7.0 Britton-Robinson buffer solutions. Linearity was found between 8×10^{-6} M and 2×10^{-4} M for differential pulse and 4×10^{-6} M and 2×10^{-4} M for square wave voltammetry in 0.1 M H_2SO_4 with detection limits of 1.06×10^{-6} M and 1.04×10^{-6} M, respectively. Linear range was found 2×10^{-6} – 6×10^{-5} M for differential pulse and 4×10^{-6} – 6×10^{-5} M for square wave voltammetry in pH 7.0 Britton-Robinson buffer solution with detection limits of 4.73×10^{-7} M and 2.65×10^{-7} M, respectively. The applicability of developed techniques was shown through analyzing from pharmaceutical dosage forms and serum samples as well. Average recovery values were found between 99.65 % – 100.55 % which showed the accuracy of the developed techniques.



INTRODUCTION

As a neurodegenerative disease, Parkinson's disease is very widely encountered and affect approximately one per cent of post-65 people.[1] The treatment procedures of the disease generally focus on increasing dopamine levels in patients' brains since it is determined that dopamine levels declined tremendously in the patients diagnosed with Parkinson's. In order to increase dopamine levels, dopamine agonists, which activate the dopamine receptors in brain, are commonly preferred. Among them, ropinirole hydrochloride (Scheme 1), 4-[dipropylamino)ethyl]-1,3-dihydro-2H-indol-2-one, which is a one of the non-ergoline dopamine agonists, binds specially to D2 and D3 receptors as selective as dopamine. In treating the Parkinson's disease's symptoms, ropinirole is used in the earlier therapeutic phases as well as an adjustment therapy with levodopa.[2]

Additionally, ropinirole is very effective in the treatment of more advanced phases of Parkinson's disease; it is particularly used at patients who have significant motor complications caused by long-term use of levodopa. When applied to the patients at the earlier stages of the disease, ropinirole seems to be an influential option for lowering the risk of dyskinesia as well as for protecting the nerves, and it may delay the need for supplemental levodopa.[3]

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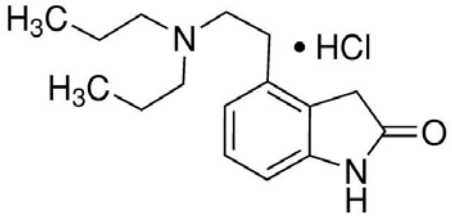

Scheme – Structure of ropinirole HCl.

Until now, a number of analytical methods have been offered for the analysis of ropinirole, such as spectrophotometry,[4-7] spectrofluorimetry,[5] ultra-performance liquid chromatography (UPLC),[8-10] liquid chromatography (LC)[7, 11-24] and capillary zone electrophoresis[25] and voltammetry. European or other pharmacopoeias has not approved one of these methods as the official methods for the determination of ropinirole.

The literature notes four studies for the voltammetric determination of ropinirole.[26-29] According these studies that used square wave (SW) and differential pulse (DP) techniques reached 10^{-7} M detection limits.[26] Stripping and open circuit DP voltammetric techniques had 10^{-8} – 10^{-9} M detection limit values.[27-29] In this study detection limits reached to the level of 10^{-7} M using DP and SW voltammetric techniques. Since there are no optimization steps in these techniques used for stripping, an analysis at the level of 10^{-7} M could be achieved simply and at a short period. This quantity is enough for pharmaceutical form analysis. When the literature was examined, it was observed that only two of them include application towards biological samples.[27, 29] One of them, in which adsorptive SW voltammetric technique was used with the modified GC electrode was applied on serum.[27] This study made by Sadikovic *et al*. the % recovery results were found 98.66 % – 101.07 % while the relative standard deviation values were found between 1.84 and 2.47.[27] In the other study made by Salama *et al.* modified carbon paste electrode was used and the developed DP voltammetric technique (with 4 minutes of accumulation time) was applied to urine and the limit of detection was found 6.12×10^{-7} M.[29] In our study, the developed DP and SW voltammetric techniques were applied to serum, because it was thought that urine study would be useless since less than 10 % of ropinirole is removed from body via urine without any change.[30] The limit of detection for serum studies were found 3.85×10^{-7} M and 2.69×10^{-7} M. Moreover, % recovery studies were performed and the results were found 100.08 % and 101.05 % with the relative standard deviation value of 0.50. The results demonstrate that the developed techniques give quicker and better outcomes compared to literature methods when applied to biological samples.

Compared to the widely-preferred separation techniques such as chromatography and electrophoresis, electroanalytical techniques seem to be more promising when samples containing a single physiologically active component in pharmaceutical dosage forms are analyzed. Major advantageous of electroanalytical techniques include higher sensitivity, higher speed of analysis and wider linear range. Moreover, these techniques employ low-cost, portable and relatively simpler instruments, environmental-friendly organic solvents and a wide range of electrodes that can be used in various media.[31]

The electrochemical techniques can be used for making the redox behavior of many pharmaceutically active drugs clear.[32-36] In electrochemical studies, the glassy carbon (GC) is the one of the most frequently preferred carbon based working electrode for the analysis of the redox mechanism of pharmaceutically active compounds. GC electrodes belong to the group of homogenous carbon electrodes combining glass-like mechanical qualities and graphite's physical characteristics.[37] It is designed with the ribbon-like formation of thin graphite layers and it is similar to polycrystalline graphite in terms of its composition, bonding mechanism and resistance. GC has a greater strength against high temperatures and chemicals; it is also impermeable against gases and liquids. Among other advantages of GC for electroanalytical purposes, wide potential window and relatively reproducible performance can be enlisted.[31]

In this study the electrochemical determination of ropinirole was studied in detail on bare glassy carbon electrode based on pH, scan rate by cyclic voltammetric (CV), DP and SW voltammetric techniques. DP and SW voltammetric techniques are successfully used in the rapid, basic and precise determination of ropinirole in pharmaceutical dosage forms.

RESULTS AND DISCUSSION

Electrochemical behavior of ropinirole

The oxidation behavior of ropinirole was examined through a GC electrode via CV, DPV and SWV techniques by using four types of buffer solutions: (1) 0.1 M and 0.5 M H_2SO_4 solutions, (2) phosphate buffer solutions between the pH range of 2.0 and 8.0, (3) acetate buffer solutions between the pH range of 3.7 and 5.7, (4) Britton-Robinson (BR) buffer solutions between the pH range of 2.0 and 12.0. In these pH ranges, no cathodic peak for ropinirole was observed; while after pH 3.0, two peaks emerged for ropinirole. The peak at less positive potential was called the peak 1, while the peak at positive potential was called the peak 2. The peak observed at pH values lower than 3.0 was peak 2.

As a result of the pH scan through CV, it was observed that the increase in pH values resulted in the shift of two anodic peaks of ropinirole towards less positive potentials. The equations of the peak potential (E_p) – pH lines for peak 1 and peak 2 were as follows:

E_p (mV) = -67.65 pH +1293.9; r = 0.987
(pH 3.7 – 10.0) (Peak 1) (CV)

E_p (mV) = -64.83 pH +1493.1; r = 0.995
(pH 2.0 – 11.0) (Peak 2) (CV)

DPV and SWV gave same results and two anodic peaks of ropinirole shifted towards less positive potentials. Figure 1 shows the E_p – pH and peak current (i_p) – pH graphs of two anodic peaks using DPV. The equations belong to DPV and SWV were given below:

E_p (mV) = -70.05 pH +1257.9; r = 0.989
(pH 3.0 – 10.0) (Peak 1) (DPV)

E_p (mV) = -61.36 pH +1428.0; r = 0.996
(pH 2.0 – 11.0) (Peak 2) (DPV)

E_p (mV) = -72.22 pH +1307.7; r = 0.990
(pH 3.0 – 9.0) (Peak 1) (SWV)

E_p (mV) = -63.60 pH +1477.1; r = 0.995
(pH 2.0 – 11.0) (Peak 2) (SWV)

The slopes between 61.36 – 72.22 mV per pH, which were close to 59 mV per pH indicates that proton and electron number involved in the ropinirole oxidation is equal.

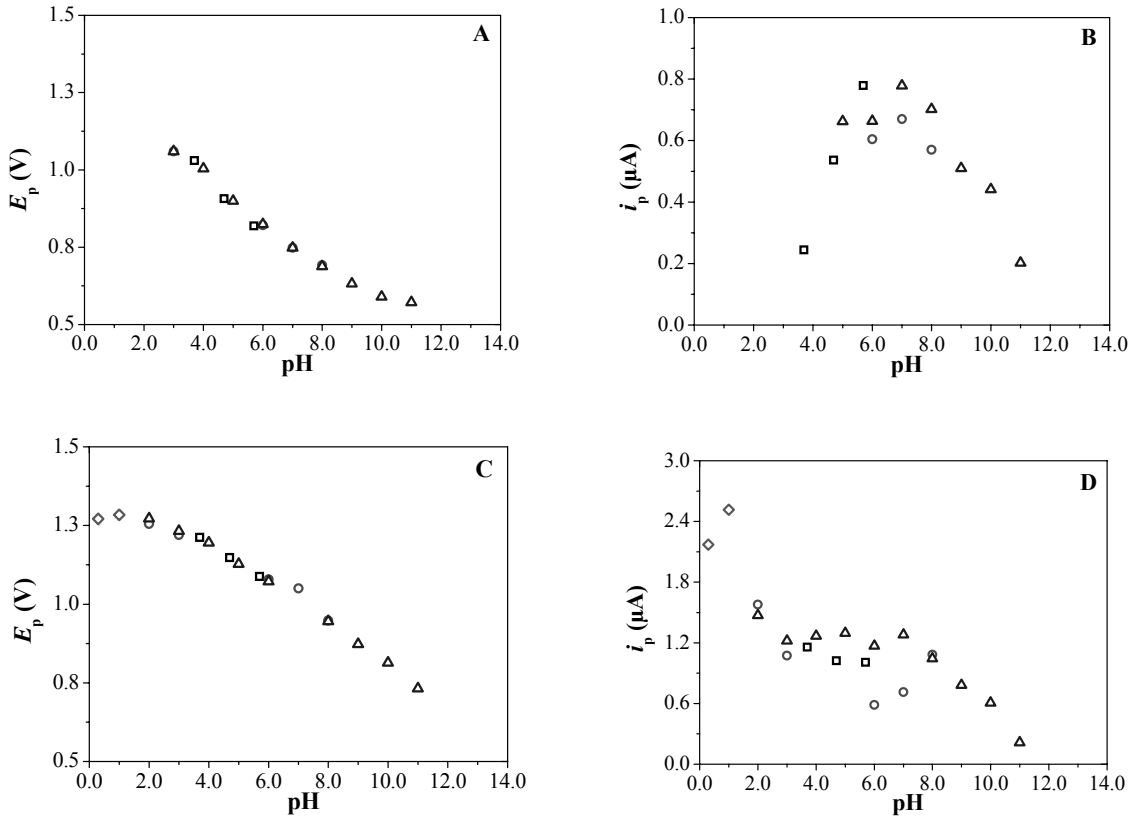

Fig. 1 – Effect of pH on ropinirole (4×10^{-5} M) peak potentials (E_p) and peak currents (i_p) obtained with GC electrode using DPV. A and B belong to peak 1; C and D belong to peak 2. (Δ): Britton-Robinson buffer; (○): phosphate buffer; (◊): sulphuric acid solution; (□): acetate buffer.

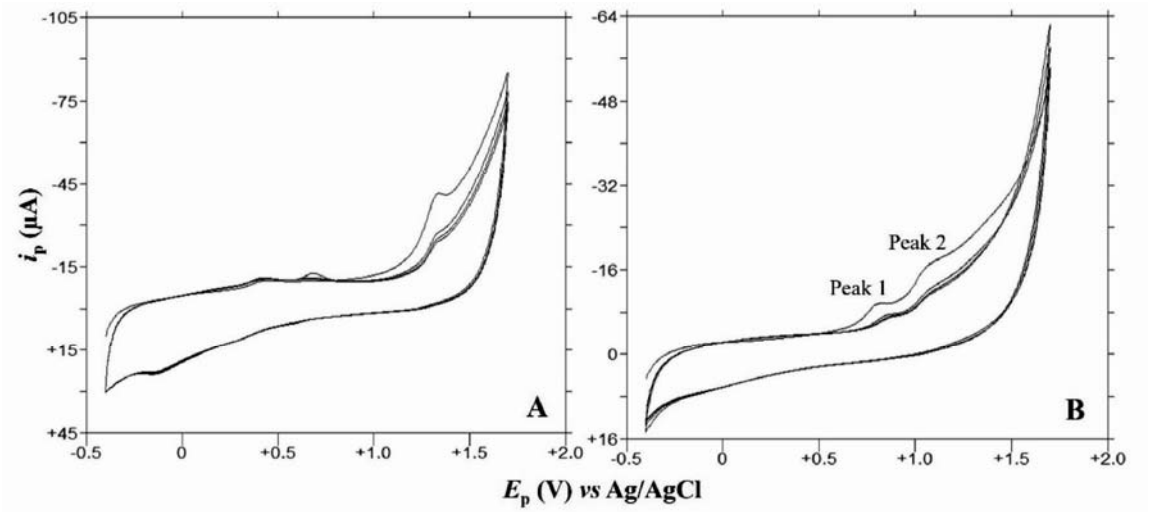

Fig. 2 – Repetitive cyclic voltammograms of 8×10^{-5} M ropinirole at GC electrode in 0.1 M H_2SO_4 (A) and pH 7.0 BR buffer solution (B). Scan rate: 100 mV s^{-1}.

As a result of the pH scan, 0.1 M H_2SO_4 and pH 7.0 BR buffer solutions were chosen. The latter was the medium at which both peaks for ropinirole together had the highest peak currents. The peak at the positive potential, on the other hand, showed the highest current value alone in 0.1 M H_2SO_4. The cyclic voltammograms of ropinirole in 0.1 M H_2SO_4 and pH 7.0 BR buffer solution were presented at Figure 2.

The effect of different scan rates (v) on the oxidation behavior of ropinirole was examined by CV in 0.1 M H_2SO_4 and pH 7.0 BR buffer solutions between the ranges of 5 – 750 mV s^{-1} and 5 – 500 mV s^{-1} were considered, respectively. When the scan rate studies in 0.1 M H_2SO_4 were considered, the slope value of $\log i_p - \log v$ curve was found 0.463, and in pH 7.0 BR buffer solutions were considered, the values of the slope of $\log i_p - \log v$ curves were found 0.586 and 0.454 for peak 1 and peak 2, respectively. Since these values were quite to the theoretical value of 0.5, it can be inferred that the reaction was diffusion controlled.[38]

The linear equations of $\log i_p - \log v$ curves obtained were as follows:

$\log i_p$ (µA) = 0.463 $\log v$ (mV s^{-1}) – 0.4814;
r = 0.997 (n = 9) (0.1 M H_2SO_4)
$\log i_p$ (µA) = 0.586 $\log v$ (mV s^{-1}) – 0.9514;
r = 0.997 (n = 8) (Peak 1) (pH 7.0 BR buffer)
$\log i_p$ (µA) = 0.454 $\log v$ (mV s^{-1}) – 0.7256;
r = 0.996 (n = 8) (Peak 2) (pH 7.0 BR buffer)

The results obtained via scan rate measurements for 8×10^{-5} M ropinirole in 0.1 M H_2SO_4 and pH 7.0 BR buffer solutions demonstrated a linear relationship between the square root of the scan rate and the peak current for both peaks of ropinirole at the range of 5 – 750 mV s^{-1} and 5 – 500 mV s^{-1}, respectively. The linear equation based on these data is as follows:

i_p (µA) = 0.260 $v^{1/2}$ (mV s^{-1}) + 0.1451;
r = 0.994 (n = 9) (0.1 M H_2SO_4)
i_p (µA) = 0.2049 $v^{1/2}$ (mV s^{-1}) + 0.2961;
r = 0.994 (n = 8) (Peak 1) (pH 7.0 BR buffer)
i_p (µA) = 0.1258 $v^{1/2}$ (mV s^{-1}) + 0.2164;
r = 0.986 (n = 8) (Peak 2) (pH 7.0 BR buffer)

With an increase in the scan rate at the range between 5 – 750 mV s^{-1}, it was observed that the potential was shifted to 44 mV more positive potentials. The results showed that the increase in the scan rate at the range of 5 – 500 mV s^{-1} resulted in a shift of the peak potentials to 73 and 53 mV more positive potential values for peak 1 and peak 2, respectively. The peak potentials were shifted to 44 mV, 73 mV and 53 mV positive values on an increasing scan rate. This means that the reaction process is irreversible.

Analytical application and validation of proposed methods

For ropinirole, analyses were performed with a glassy carbon electrode in 0.1 M H_2SO_4 and pH 7.0 BR buffer solutions by employing DPV and SWV techniques. Linearity was obtained at the concentration range of 8×10^{-6} – 2×10^{-4} M for DPV and 4×10^{-6} – 2×10^{-4} M for SWV in 0.1 M H_2SO_4 solution. The linear equations obtained between the ropinirole concentration and peak current with DPV and SWV techniques and the correlation coefficient values are as follows:

i_p (µA) = 4.56×10^4 C (M) + 0.0225; r = 0.999 (n = 8) (for DPV)
i_p (µA) = 5.09×10^4 C (M) – 0.0339; r = 0.999 (n = 10) (for SWV)

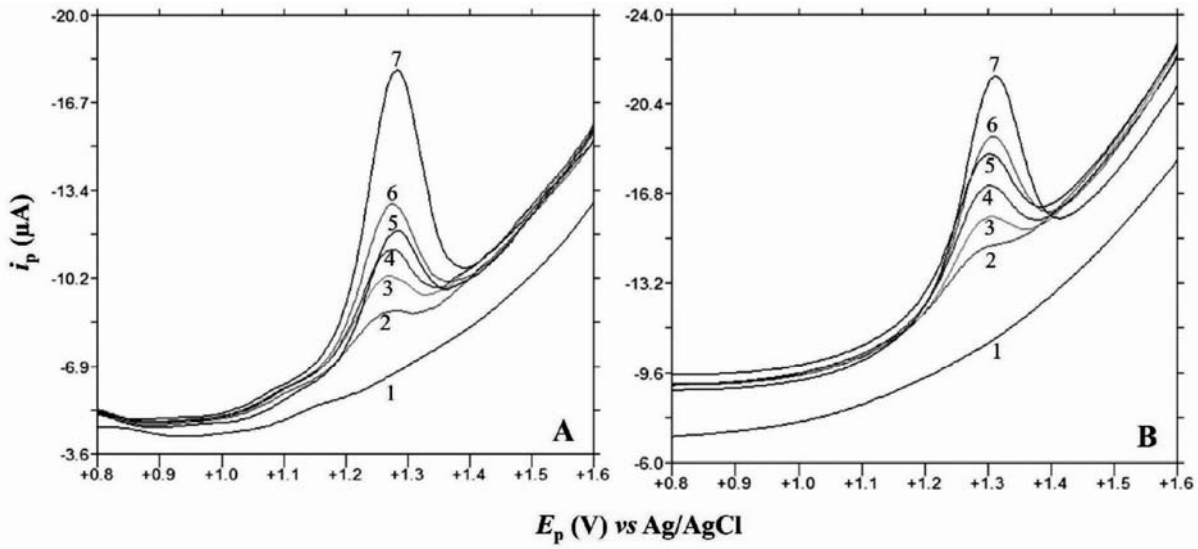

Fig. 3 – DP voltammograms (A) and SW voltammograms (B) of ropinirole standard solutions in 0.1 M H_2SO_4. (1) Blank; (2) 2×10^{-5} M; (3) 4×10^{-5} M; (4) 6×10^{-5} M; (5) 8×10^{-5} M; (6) 1×10^{-4} M; (7) 2×10^{-4} M.

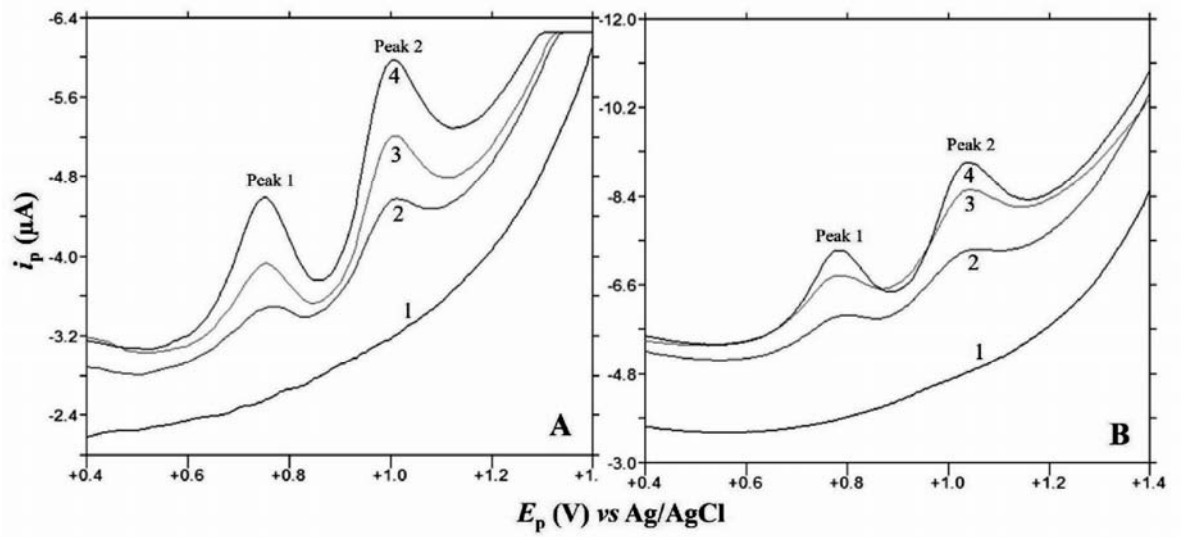

Fig. 4 – DP voltammograms (A) and SW voltammograms (B) of ropinirole standard solutions in pH 7.0 BR buffer solution. (1) Blank; (2) 2×10^{-5} M; (3) 4×10^{-5} M; (4) 6×10^{-5} M.

Figure 3 shows the voltammograms chosen within the calibration range and obtained by DPV and SWV for increasing concentrations of ropinirole in 0.1 M H_2SO_4 solution.

For peak 2, linearity was obtained between the concentration range of 2×10^{-6} – 6×10^{-5} M for DPV and 4×10^{-6} – 6×10^{-5} M for SWV in pH 7.0 BR buffer solution. The linear equations and correlation coefficient values obtained between ropinirole concentration and peak current via DPV and SWV techniques are as follows:

$$i_p\ (\mu A) = 2.55\times10^4\ C\ (M) - 0.0048;$$
$$r = 0.999\ (n = 8)\ \text{(for DPV)}$$
$$i_p\ (\mu A) = 2.98\times10^4\ C\ (M) - 0.0560;$$
$$r = 0.999\ (n = 7)\ \text{(for SWV)}$$

Figure 4 shows the voltammograms chosen within the calibration range and obtained by DPV and SWV for increasing concentrations of ropinirole in pH 7.0 BR buffer solution.

Table 1 summarizes the regression analysis results for the calibration curve obtained via DPV and SWV techniques in 0.1 M H_2SO_4 and pH 7.0 BR buffer solutions together with relevant calculated validation parameters. Limit of detection (LOD) and limit of quantification (LOQ) were calculated via the formulas of 3 *ss/m* and 10 *ss/m* respectively.[39] The "*ss*" in the formulas represented the standard deviation of the three repeated measurement of the lowest concentration of calibration, whereas "*m*" represented the calibration curve's slope.

Table 1

Regression analysis results and required validation studies of the quantitative determination of ropinirole using DPV and SWV in standard solutions

	0.1 M H_2SO_4		**pH 7.0 BR buffer**	
	DPV	**SWV**	**DPV**	**SWV**
Measured potential (V)	1.268	1.295	1.012	1.073
Linear range (M)	8×10^{-6}–2×10^{-4}	4×10^{-6}–2×10^{-4}	2×10^{-6}–6×10^{-5}	4×10^{-6}–6×10^{-5}
Slope (μA M^{-1})	4.56×10^{4}	5.09×10^{4}	2.55×10^{4}	2.98×10^{4}
Intercept (μA)	2.25×10^{-2}	-3.39×10^{-2}	-4.77×10^{-3}	-5.69×10^{-2}
Correlation coefficient (*r*)	0.999	0.999	0.999	0.999
Standard error of slope	1.90×10^{2}	4.12×10^{2}	4.43×10^{2}	3.77×10^{2}
Standard error of intercept	1.68×10^{-2}	3.25×10^{-2}	1.19×10^{-2}	1.08×10^{-2}
LOD (M)	1.06×10^{-6}	1.04×10^{-6}	4.73×10^{-7}	2.65×10^{-7}
LOQ (M)	3.53×10^{-6}	3.45×10^{-6}	1.57×10^{-6}	8.85×10^{-7}
Within day precision of current (RSD %)*	0.63	0.58	0.79	0.81
Between days precision of current (RSD %)*	0.91	1.29	1.49	1.16
Within day precision of potential (RSD %)*	0.29	0.12	0.23	0.49
Between days precision of potential (RSD %)*	0.13	0.51	0.20	0.72

* Obtained from five experiments for 4×10^{-5} M ropinirole in 0.1 M H_2SO_4 and for 2×10^{-5} M ropinirole in pH 7.0 BR buffer solutions.

Table 2

DP and SW voltammetric analysis results of ropinirole from Requip® tablets and recovery studies in 0.1 M H_2SO_4 and pH 7.0 BR buffer solution

	0.1 M H_2SO_4		pH 7.0 BR buffer	
	DPV	**SWV**	**DPV**	**SWV**
Labelled claim (mg)	5.00	5.00	5.00	5.00
Amount found (mg)*	4.96	5.005	5.05	5.01
RSD %	1.06	0.82	0.84	0.31
Bias %	0.80	-0.10	-1.00	-0.20
Added (mg)	1.00	1.00	1.00	1.00
Found (mg)*	0.97	1.005	0.99	0.99
Average recovered %*	99.88	100.55	99.65	99.93
RSD % of recovery	0.42	1.31	0.38	0.97
Bias %	0.12	-0.55	0.35	0.08

* Obtained from five measurements.

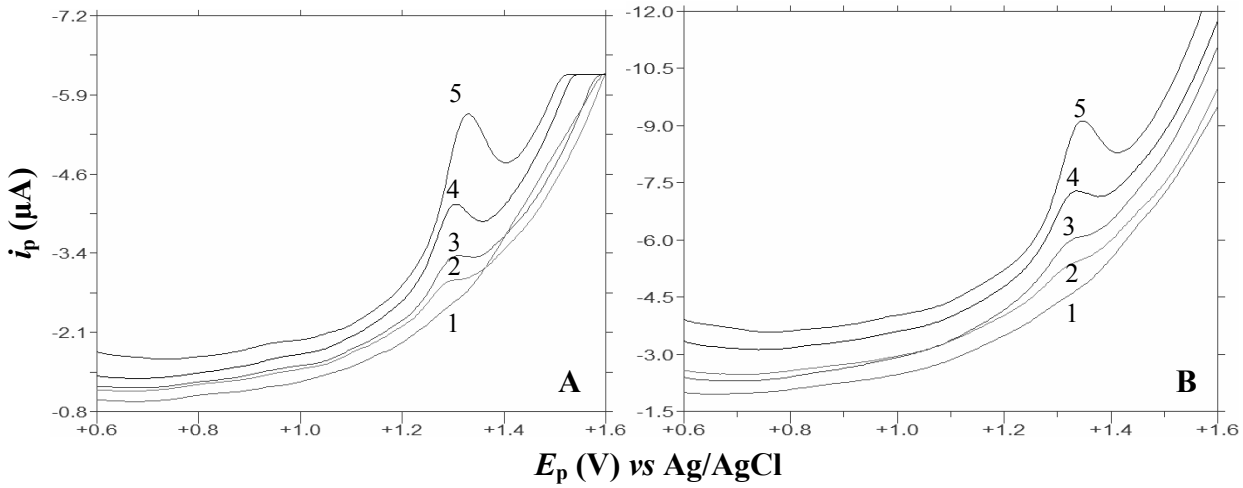

Fig. 5 – DP voltammograms (A) and SW voltammograms (B) of ropinirole serum solutions in 0.1 M H_2SO_4. (1) Blank; (2) 6×10^{-6} M; (3) 1×10^{-5} M; (4) 2×10^{-5} M; (5) 4×10^{-5} M.

Table 3

DP and SW voltammetric analysis results of ropinirole from spiked serum samples and recovery studies in 0.1 M H_2SO_4

	0.1 M H_2SO_4	
	DPV	**SWV**
Measured potential (V)	1.280	1.308
Linear range (M)	4×10^{-6}–4×10^{-5}	4×10^{-6}–6×10^{-5}
Slope (μA M^{-1})	4.12×10^{4}	5.01×10^{4}
Intercept (μA)	-4.59×10^{-2}	-1.14×10^{-1}
Correlation coefficient (r)	0.999	0.998
Standard error of slope	3.75×10^{2}	1.13×10^{3}
Standard error of intercept	7.20×10^{-3}	3.25×10^{-2}
LOD (M)	3.85×10^{-7}	2.69×10^{-7}
LOQ (M)	1.28×10^{-6}	8.99×10^{-7}
Added concentration (M)	1.00×10^{-5}	1.0×10^{-5}
Found concentration (M)	1.01×10^{-5}	1.0×10^{-5}
Average recovered %	101.05	100.08
Number of experiment	5	5
RSD % of recovery	0.55	0.51
Bias %	-1.05	-0.08

To show the precision of the techniques that were developed for 4×10^{-5} M ropinirole solution in 0.1 M H_2SO_4 buffer solution and 2×10^{-5} M ropinirole solution in pH 7.0 BR buffer solution. In order to calculate the % relative standard deviation (RSD %) of within-day and between-days

precision, five repeated measurements were made. When the results shown in Table 1 was examined, it was observed that the RSD % for within-day precision is lower than 1.0, whereas the RSD % for between-days precision is lower than 2.0. These results proved that the developed techniques had good precision.

For demonstrating the applicability of the techniques developed, the tablet dosage forms of ropinirole (Requip® tablet, 5 mg per tablet) were analyzed via DPV and SWV methods. In doing that, related calibration equations were used considering solely with a dilution step and this process did not require the steps of the preparation, extraction, filtration or evaporation. In order to determine the accuracy of the proposed method, the recovery during spiked experiments is calculated. Pure drugs with known amounts were added to several pre-analyzed formulations of ropinirole for carrying out recovery studies. For detecting the interference of the excipients, preparation processes similar to those made for calibration studies were preferred including the standard addition technique.

The results shown in Table 2 demonstrate that the optimized DPV and SWV techniques were applied successfully to ropinirole's pharmaceutical dosage forms. These results were promising for the application of the proposed methods for ropinirole studies in tablet because of non-interference of excipients.

The developed techniques were also applied to the spiked serum samples. The linearity was obtained between the concentration range of 4×10^{-6} – 4×10^{-5} M for DPV and 4×10^{-6} – 6×10^{-5} M for SWV from spiked serum samples in 0.1 M H_2SO_4. Some of the DP and SW voltammograms from the linear range were given in Fig. 5. The linear equations and correlation coefficient values obtained between ropinirole concentration in serum and peak current via DPV and SWV techniques are as follows:

$$i_p\ (\mu A) = 4.12\times10^4\ C\ (M) - 0.046;$$
$$r = 0.999\ (n = 6)\ \text{(for DPV)}$$
$$i_p\ (\mu A) = 5.01\times10^4\ C\ (M) - 0.114;$$
$$r = 0.998\ (n = 7)\ \text{(for SWV)}$$

LOD values were obtained as 3.85×10^{-7} M and 2.69×10^{-7} M for DPV and SWV, respectively. Recovery studies of serum samples from five repetitive analyzes were realized and results were found as 101.05 % and 100.08 % for the developed techniques. All results obtained from the serum studies were summarized in Table 3.

EXPERIMENTAL

Apparatus

In this study, for performing the electroanalytical measurements, BAS 100W (Bioanalytical System, USA) electrochemical analyzer was used. Cyclic voltammetry, differential pulse voltammetry and square wave voltammetry were preferred. The study was based on a conventional three-electrode system. In the system used in this study, a GC (BASi MF 2012) is the working electrode, a platinum wire (BASi) is the auxiliary electrode, and an Ag/AgCl (BASi; 3 M NaCl) is the reference electrode.

The pH measurements were made with a pH meter Model 526 (WTW, Austria) which uses a combined electrode (glass electrode–reference electrode).

While the DPV conditions were determined as follows; step potential: 0.00795 V; modulation amplitude: 0.0505 V; modulation time: 0.050 s; interval time: 0.500 s, the SWV conditions were set as follows; step potential: 0.004 V; amplitude: 0.025 V; frequency: 15 Hz.

Reagents and chemicals

Ropinirole hydrochloride was supplied by GlaxoSmithKline (Istanbul, Turkey) and so was the Requip® tablets (5 mg per tablet).

For electrochemical measurements, three types of supporting electrolytes were used, being acetate (1.0 M CH_3COOH; pH 3.7–5.7), phosphate (0.2 M H_3PO_4; 0.2 M $NaH_2PO_4{\cdot}2H_2O$; pH 2.0–8.0) and BR (0.04 M H_3BO_3; 0.04 M H_3PO_4 and 0.04 M CH_3COOH; pH 2.0–12.0) buffers and 0.1 M and 0.5 M H_2SO_4 solutions. Other reagents, which were prepared by distilled water, were of analytical grade. While acetic and phosphoric acids were bought from Sigma-Aldrich, methanol and acetonitrile were obtained from Merck, boric acid was purchased from Pancreac; sodium dihydrogen phosphate and disodium hydrogen phosphate was obtained from Riedel-de Haen. Human serum (from human male AB plasma, USA origin, sterile-filtered) was purchased from Sigma.

Tablet and recovery assay procedure

For tablet studies, ten Requip® tablets were crushed in a mortar to obtain a fine powder. Then, a sufficient amount of this powder, corresponding to a stock solution with a concentration of 1.0×10^{-3} M, was weighed precisely and put into a 25.0 mL flask. After that, the flask was completed with 0.1 M H_2SO_4 solution and pH 7.0 BR buffer solution separately, and sonicated for 30 min. The analyzed solutions were prepared through taking aliquots from the stock solutions and by diluting these aliquots with the selected supporting electrolytes. Known amounts of the pure drug were added to the tablet formulation before the analysis in order to investigate the interferences of the excipients. In order to determine the recovery results, five parallel analyses were performed.

Serum Analysis

A required volume of the serum sample and ropinirole was dissolved in acetonitrile to reach the final concentration of 1×10^{-3} M. Acetonitrile was used as serum precipitating agent. This agent removed serum proteins more effectively. The mixture was centrifuged for 15 min and then for 15 min at 5000 rpm to eliminate the residues of serum protein. Then the supernatant was taken out carefully and appropriate volumes of it were put into the volumetric flask and diluted to the

chosen volumes with 0.1 M H_2SO_4. Via the DP and SW voltammetric techniques, the ropinirole concentration in 0.1 M H_2SO_4 varied in the range between 4×10^{-6} M and 4×10^{-5} M and between 4×10^{-6} and 6×10^{-5} M using GC electrode, respectively.

CONCLUSIONS

Ropinirole showed irreversible oxidation behavior in the studied buffer solutions and pH values. In this study, DP and SW voltammetric techniques were developed and successfully applied to the determination of ropinirole from tablet formulations without pretreatment, extraction or evaporation process. The proposed techniques were also fully validated. The applicability of the developed methods was proposed via tablet and spiked serum studies. High percentage values indicated that the analyses were performed without any interference from the matrix. Developed techniques can be suitable for quality control because of economic and time consuming reasons.

Acknowledgments: The financial support of the Ankara University, Department of Scientific Research Projects (Project No: 13L3336001) was essential for the conduct of this work, to which the authors were extending their gratitude. This study was a product of the PhD Dissertation of Burçin Bozal-Palabiyik (Ankara University, Health Sciences Institute).

REFERENCES

1. W.J. Weiner, M.D. Shulman and A.E. Lang, "Parkinson's Disease: A Complete Guide for Patients and Families", 4th edition. The Johns Hopkins University Press, Baltimore, MD, 2013.
2. K. Fukuzaki, T. Kamenosono and R. Nagata, *Pharmacol. Biochem. Behavior.*, **2000**, *65*, 503–508.
3. G. Park, Y.-J. Park, H.O. Yang and M.S. Oh, *Pharmacol. Biochem. Behavior.*, **2013**, *104*, 163–168.
4. L.P. Kothapalli, M.E. Choudhari, A.B. Thomas, R.K. Nanda, A.D. Deshpande and P.S. Gaidhani, *Der Pharma Chemica*, **2012**, *4*, 574–580.
5. Z. Aydoğmuş, *Spectrochim. Acta A*, **2008**, *70*, 69–78.
6. A. Önal and S. Çağlar, *Chem. Pharm. Bull*., **2007**, *55*, 629–631.
7. J.V. Susheel, S. Malathi and T.K. Ravi, *Indian J. Pharm. Sci*., **2007**, *69*, 589–591.
8. S. Mohamed, R. Riva and M. Contin, *J. Chromatogr. B*., **2016**, *1017-1018*, 114–119.
9. H.-Y. Wang, M. Liu, P. Hu and J. Jiang, *J. Chinese Mass Spectrom. Soc.*, **2015**, *36*, 296–301.
10. Ch. Krishnaiah, M.V. Murthy, A.R. Reddy, R. Kumar and K. Mukkanti, *J. Chin. Chem. Soc*., **2010**, *57*, 348–355.
11. X. Yan, S. Zhao, W. Zhu, J. Rao, L. Kang, J. Xu, D. Li, L. Qui, G. Li, J. Huang and L. Si, *Bioanalysis*, **2016**, *8*, 1823–1835.
12. Z.-T. Wang, C.-R. Huang, Q.-Q. XU, S.B. Liu and L.-Y. Miao, *Chinese J. New Drugs*, **2015**, *24*, 1412–1417 and 1422.
13. P.S. Reddy, A.M. Reddy, S.J. Reddy, S. Sait and K. Vyas, *J. Liq. Chromatogr. R. T*., **2014**, *37*, 2490–2505.
14. A. Kakouris, V. Samara, A. Kalaskani and I. Panderi, *Chromatographia*, **2014**, *77*, 447–457.
15. G. Mustafa, S. Baboota, J. Ali and A. Ahuja, *J. Pharm. Innov.*, **2012**, *7*, 47–55.
16. N. Adib, M. Shekarchi and A. Dabirsiaghi, *Biosci. Biotechnol. Res. Asia*, **2011**, *8*, 617–621.
17. N. Sreekanth, Ch.B. Rao and K. Mukkanti, *Int. J. Pharm. Pharm. Sci*., **2009**, *1(Suppl 1)*, 186–192.
18. D.V. Bharathi, B. Jagadeesh, S.S. Kumar, R.N. Lakshmi, K.K. Hotha, A. Naidu and R. Mullangi, *Biomed. Chromatogr.*, **2009**, *23*, 557–562.
19. B. Jancic-Stojanovic, A. Malenovic, D. Ivanovic, T. Rakic and M. Medenica, *J. Chromatogr. A*, **2009**, *1216*, 1263–1269.
20. A. Azeem, Z. Iqbal, F.J. Ahmad, R.K. Khar and S. Talegaonkar, *Acta Chromatogr*., **2008**, *20*, 95–107.
21. A. Önal, *Chromatographia*, **2006**, *64*, 459–461.
22. A. Nagarjuna, S.D.V. Rao, S. Eswaraiah, K. Mukkanti and M.V. Suryanarayana, *Indian Drugs*, **2006**, *43*, 813–820.
23. J. Bhatt, A. Jangid, R. Shetty, B. Shah, S. Kambli, G. Subbaiah and S. Singh, *J. Pharm. Biomed. Anal*., **2006**, *40*, 1202–1208.
24. P. Coufal, K. Stulik, H.A. Claessens, M.J. Hardy and M. Webb, *J. Chromatogr. B*, **1999**, *732*, 437–444
25. P. Coufal, K. Stulik, H.A. Claessens, M.J. Hardy and M. Webb, *J. Chromatogr. B*, **1998**, *720*, 197–204.
26. B. Nigovic, S. Juric, A. Mornar and I. Malenica, *J. Chem. Sci*, 2013, 125 (5), 1197–1205.
27. M. Sadikovic, B. Nigovic, S. Juric and A. Mornar, *J. Electroanal. Chem*., **2014**, *733*, 60–68.
28. B. Bozal-Palabiyik and B. Uslu, *Ionics*, **2016**, *22*, 115–123.
29. N.N. Salama, H.E. Zaazaa, S.M. Azab, S.A. Atty, N.M. El-Kosy and M.Y. Salem, *Sens. Actuator. B-Chem*., **2017**, *240*, 1291–1301.
30. J.C. Bloomer, S.E. Clarke and R.J. Chenery, *Drug Metab. Dispos.*, **1997**, *25*, 840–844.
31. J. Wang, "Analytical Electrochemistry", 3rd edition. John Wiley and Sons., Hoboken, NJ, 2006.
32. B. Dogan-Topal, B. Bozal-Palabiyik, S.A. Ozkan and B. Uslu, *Sens. Actuator. B-Chem*., **2014**, *194*, 185–194.
33. N. Karadas, B. Bozal-Palabiyik, B. Uslu and S.A. Ozkan, *Sens. Actuator. B-Chem*., **2013**, *186*, 486–494.
34. B. Dogan-Topal, B. Bozal-Palabıyık, B. Uslu and S.A. Ozkan, *Sens. Actuator. B-Chem*., **2013**, *177*, 841–847.
35. B. Dogan-Topal, B. Bozal-Palabiyik, S.A. Ozkan and B. Uslu, *Rev. Roum. Chim.*, **2015**, *60*, 467–475.
36. E. Demir, R. Inam, S.A. Ozkan and B. Uslu, *J. Solid State Electrochem*., **2014**, *18*, 2709–2720.
37. B. Uslu and S.A. Ozkan, *Comb. Chem. High T. Scr.*, **2007**, *10*, 495–513.
38. E. Laviron, L. Roullier and C.A. Degrand, *J. Electroanal. Chem*., **1980**, *112*, 11–23.
39. S.A. Özkan, "Electroanalytical Methods in Pharmaceutical Analysis and Their Validation", HNB Pub., USA, 2012.