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Electrochemical behavior of quinapril and its determination in pharmaceutical formulations by square-wave voltammetry at a mercury electrode

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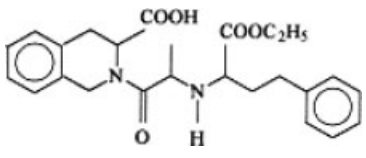
The electrochemical behavior of the antihypertensive drug quinapril was investigated at a hanging mercury drop electrode using different voltammetric techniques such as cyclic voltammetry, square-wave voltammetry and chronoamperometry. A simple and sensitive square-wave voltammetric method for the electrochemical analysis of quinapril in its pharmaceutical formulations was developed and validated. The experimental and instrumental parameters affecting the peak current of quinapril were investigated. Various buffers such as Britton Robinson, borate and phosphate buffers at different pH values (3.0–11.0) were examined as supporting electrolyte. The optimum conditions were obtained using Britton Robinson buffer at pH 10.0 and frequency: 50 Hz, scan increment: 4 mV and pulse amplitude: 25 mV. A well-defined peak current was observed at the hanging mercury drop electrode at −1100 mV vs. Ag/AgCl reference electrode. This proposed method was validated by evaluating linearity, sensitivity, repeatability, accuracy, precision, selectivity, recovery, robustness and ruggedness. The linear calibration range was 0.50–8.68 $\mu g\ mL^{-1}$ ($r = 0.9992$). The detection and quantification limits of this method were 0.22 and 0.50 $\mu g\ mL^{-1}$ and intra-day and inter-day precision were between 0.81–4.32% ($n = 7$), respectively. The developed method was applied successfully for the determination of quinapril in its tablet dosage forms. The average amount of quinapril in tablets was found as 20.26 ± 0.12 with RSD of 1.60% for 20 mg tablets and 40.55 ± 0.23 with RSD of 1.52% for 40 mg tablets.

1. Introduction

Quinapril hydrochloride (QUI), 2-(2-{[1-(ethoxycarbonyl)-3-phenyl-propyl]amino}-1-oxopropyl)-1,2,3,4-tetra-hydro-3-isoquinoline carboxylic acid monohydrochloride, is a nonpeptide, nonsulfhydryl angiotensin converting enzyme (ACE) inhibitor belonging to the third class of ACE inhibitors. The role of this kind of drugs is to inhibit the last step of the biosynthesis of angiotensin II, a potent vasoconstrictor, causing general vasodilatation. QUI is used for the treatment of mild to moderate hypertension and congestive heart failure, either alone or in conjunction with other drugs (Vertes and Haynie 1992; Forette et al. 1992; Cudina et al. 2006).



quinapril

Several analytical methods have been reported for the determination of QUI in pharmaceutical formulations and biological fluids, including densitometry (Kowalczuk et al. 2003), spectrophotometry (Bonazzi et al. 1997; Kowalczuk et al. 2004), HPLC (Bonazzi et al. 1997; Abbara et al. 2002; Hengy and Most 1988; Gumieniczek and Hopkala 1998; Prieto et al. 2001; Kugler et al. 1995), gas chromatography – mass spectrometry (Ferry et al. 1987; Goto et al. 1992; Goto et al. 1992), capillary electrophoresis (Cudina et al. 2006; Gotti et al. 2000; Hillaert et al. 2001; Hillaert and Van den Bossche 2001; Hillaert et al. 2002; Prieto et al. 2002) and voltammetry (Prieto et al. 2003). The main problems encountered using chromatographic methods are either the need for derivatization or time-consuming extraction procedures. Since these methods have a slightly expensive instrumentation and high running costs, the use of simpler, faster, less expensive, but sensitive, and stability to on-line measurements (give the repeatable results), electrochemical methods can be an alternative.

The main objective of this study was to investigate the electrochemical behavior and reduction mechanism of QUI and its determination possibilities at a hanging mercury drop electrode (HMDE) using the particularly simple, rapid and sensitive technique of square-wave voltammetric (SWV) method. The experimental and instrumental parameters were optimized in order to improve sensitivity. The proposed voltammetric method was also applied to the

quantitation of QUI in pharmaceutical formulations without the necessity of sample pre-treatment.

A voltammetric method concerning the reduction of QUI at the mercury electrode has been reported by Prieto et al. (2003). But in this study, electrochemical behavior and reduction mechanism of QUI were not investigated in detail and this method was not fully validated. In our study, reduction mechanism of QUI was investigated by cyclic voltammetry and the diffusion coefficient of QUI was calculated by chronoamperometry. Our method was fully validated and validity of the proposed method was also tested comparing the results to those of Prieto et al. (2003).

2. Investigations, results and discussion

The SWV method was used in this study because of its adequate sensitivity and the rapidity of the measurements.

The peak current intensity, shape and characteristics of all voltammograms were strongly dependent on various electrolytes and pH of the medium. Thus, the effect of pH on the peak current (i_p) and the reduction potential (E_p) of QUI was investigated over a range between 3.0 and 11.0. In acidic solutions, no reduction peak of QUI was observed. QUI exhibited a cathodic peak in Britton Robinson buffer at pH 6.0–11.0, but good peak shape was observed at pH 8.0–11.0 (Fig. 1). Peak current of QUI was increased with the increase of pH (Fig. 2). Maximum peak current and good peak shape were obtained in BR buffer at pH 10.0. In addition, BR, phosphate and borate buffers at pH 10.0 were investigated for the analytical determination of QUI (Fig. 3). The best results such as the maximum peak current, a well-defined cathodic peak, suitable sensitivity and repeatability were obtained with BR buffer at pH 10.0. Therefore, 0.04 M BR buffer at pH 10.0 was chosen as a supporting electrolyte for the rest of the present work.

The SWV response of the accumulated drug markedly depends on the instrumental parameters. Different parameters influencing peak current intensity and shape of the SWV peak of QUI were studied in order to improve sensitivity. Thus, frequency (f), scan increment (ΔE) and pulse amplitude (E_{SW}) were investigated for 3.38 $\mu g \cdot mL^{-1}$ of QUI solution in BR buffer at pH 10.0 in the proposed method.

f was varied from 40 to 120 Hz using ΔE of 5 mV and E_{SW} of 25 mV. A linear relationship was obtained between the peak current and the f up to 100 Hz. The best peak definition was found at f = 50 Hz, which is used in this study.

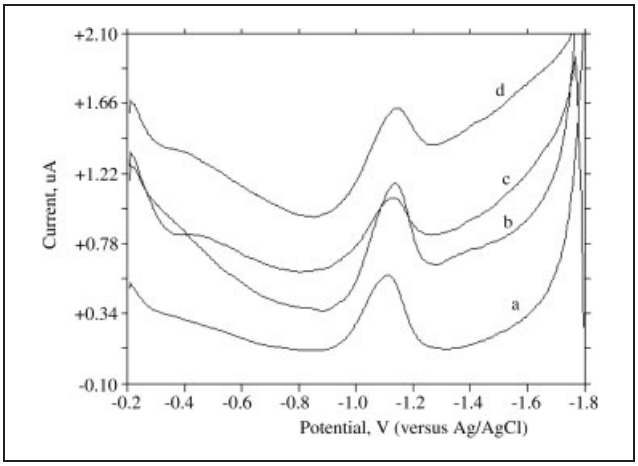


Fig. 1: Effect of BR buffer at different pH on the SWV peak of QUI (3.38 $\mu g \cdot mL^{-1}$) at f = 50 Hz, ΔE = 5 mV and E_{SW} = 25 mV. a) pH = 10.0, b) pH = 11.0, c) pH = 8.0, d) pH = 9.0

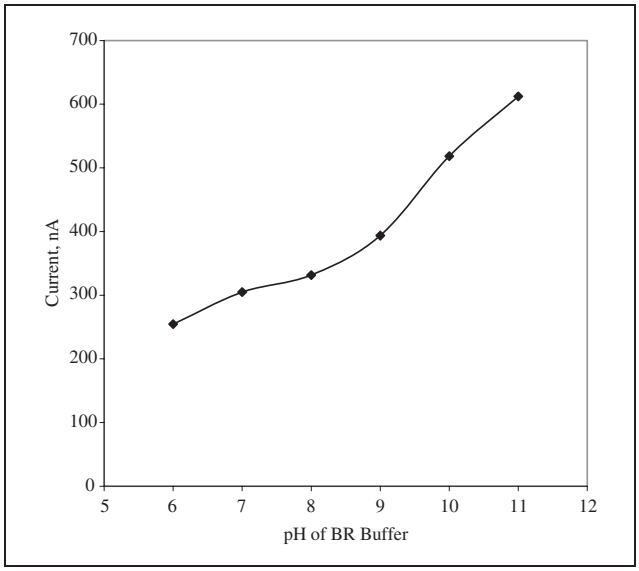


Fig. 2: Effect of BR buffer at different pH on the SWV peak of QUI (3.38 $\mu g \cdot mL^{-1}$) at f = 50 Hz, ΔE = 5 mV and E_{SW} = 25 mV

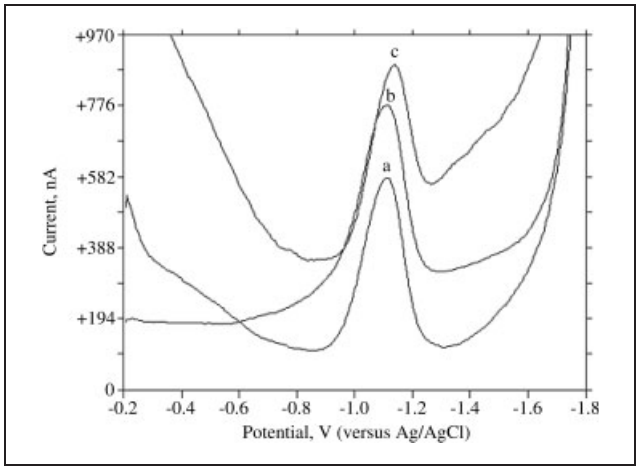


Fig. 3: Effect of different buffer at pH = 10.0 on the SWV peak of QUI (3.38 $\mu g \cdot mL^{-1}$) at f = 50 Hz, ΔE = 5 mV and E_{SW} = 25 mV. a) BR, b) Phosphate, c) Borate buffers

At f of 50 Hz and E_{SW} of 25 mV, ΔE was varied from 2 to 6 mV. The peak current increased to 4 mV and then it decreased; because the reduction peak of QUI was broad. Hence, ΔE of 4 mV was chosen for the determination of QUI.

At f of 50 Hz and ΔE of 4 mV, E_{SW} varied from 10 to 40 mV. Peak current of QUI was increased with the increase of E_{SW}, but the narrowest square-wave peak was obtained at 25 mV, and this was chosen as optimal value for analytical determination.

Consequently, the highest peak current values with the best peak definition were found as f = 50 Hz, ΔE = 4 mV and E_{SW} = 25 mV, and these values were used for further measurements of QUI. Under these optimal experimental and instrumental conditions, a well-defined SWV peak of QUI was observed at −1100 mV in the proposed method (Fig. 4).

The reversibility of the reduction process of QUI was investigated by using cyclic voltammetry. The cyclic voltammogram of 10.11 $\mu g \cdot mL^{-1}$ of QUI in BR buffer at

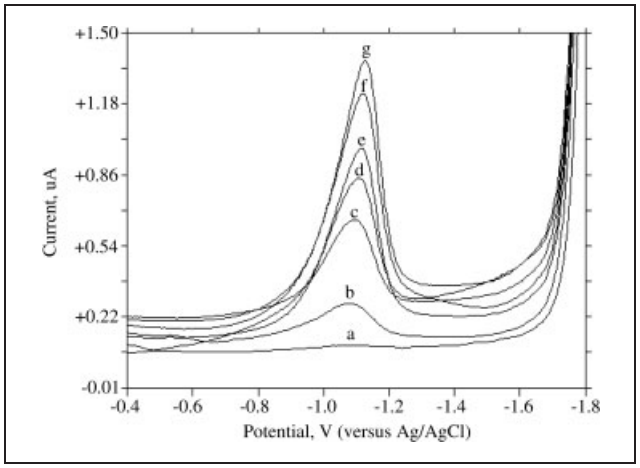


Fig. 4: SW voltammograms of QUI at different concentrations using the optimum conditions. a) Supporting electrolyte, b) 1.48, c) 3.38, d) 4.76, e) 6.10, f) 7.41 and g) 8.68 $\mu g \cdot mL^{-1}$ of QUI

pH 10.0 at HMDE exhibited a single well-defined peak at −1100 mV (Fig. 5). This peak may be attributed to the carbonyl group of the amide bound, activated by the neighboring nitrogen, might undergo reduction to alcohol, taking two electrons and two protons (Prieto et al. 2003).

No oxidation peak was observed on the reverse scan, indicating the irreversible nature of the electrode process (Fig. 5). The peak potential shifted to a more negative value on the increase of the scan rate, confirming the irreversible nature of the reduction process (Bard and Faulkner 1980).

Scan rate studies were carried out to assess whether the processes at the HMDE electrode was under diffusion or adsorption control. The effect of the potential scan rate between 20 and 1000 $mV \cdot s^{-1}$ on the peak current and the potential of QUI were evaluated. A 57 mV negative shift in the peak potential confirmed the irreversibility of the reduction process. When the scan rate was varied from 20 to 800 $mV \cdot s^{-1}$ in 8.68 $\mu g \cdot mL^{-1}$ solution of QUI, a linear dependence of the peak intensity i_p (μA) upon the square root of the scan rate $\nu^{1/2}$ ($mV \cdot s^{-1}$) was found, demonstrating a diffusional behavior (ip (μA) = 0.0224 $\nu^{1/2}$ ($mV \cdot s^{-1}$) − 0.0258, r = 0.9920, n = 6) (Bard and Faulkner 1980; Laviron et al. 1980).

A plot of log i_p (logarithm of peak current) versus log ν (logarithm of scan rate) gave a straight line with a slope of 0.5316, very close to the theoretical value of 0.5, which is expressed for an ideal reaction the diffusion controlled electrode process (Laviron et al. 1980). The following equation was obtained (scan rate range = 20–800 $mV \cdot s^{-1}$):

$$\log i_p\ (\mu A) = 0.5316 \log \nu\ (mV \cdot s^{-1}) - 1.7703\,,$$
$$r = 0.9885\ (n = 6)$$

The experimental Cottrell slope was determined from the chronoamperometric i_p versus $t^{-1/2}$ plot. The diffusion coefficient was calculated from Cottrell Equation (Baranski et al. 1985). The constant potential applied was slightly more cathodic than the cyclic voltammetric E_p from −1200 to −950 mV. A HMDE with a surface area of 0.0199 cm^2 was employed. The diffusion coefficient was calculated as $7.71 \times 10^{-6} \pm 2.41 \times 10^{-7}$ (n = 7).

Validation of the proposed SWV method for assay of QUI was examined via stability, linearity, sensitivity, precision, accuracy, recovery, selectivity, robustness, and ruggedness (ICH 2005; USP 2006; Ermer 2001; Taverniers et al. 2004; Ghoneim et al. 2006; Adhoum and Monser 2005; Hammam et al. 2006; Nouws et al. 2006).

The standard stock of QUI was kept in the dark at +4 °C. The stability of QUI stock solution (1000 $\mu g \cdot mL^{-1}$) was tested for two months and QUI in methanol solution was stable for at least two months period. Under the optimum conditions, the stability of 100.00 $\mu g \cdot mL^{-1}$ of QUI solution in BR buffer at pH 10.0 was evaluated for 52 h period by the proposed method (Table 1). This solution was kept in the dark at +4 °C. Repetition of sample analysis after 30 h did not show any significant changes in the peak potential and peak current of QUI. Nevertheless, 100.0 $\mu g \cdot mL^{-1}$ of QUI standard solution was prepared daily with BR at pH 10.0.

Under the optimum conditions, SWV voltammograms recorded with increasing amounts of QUI. As shown in

Table 1: Stability data of QUI standard solution (100.00 $\mu g \cdot mL^{-1}$)

	Peak current (nA)	Peak potential (mV)
Standard QUI	409.80 ± 6.37	−1100
1 h after	411.83 ± 4.55	−1100
2 h after	415.11 ± 3.38	−1100
3 h after	409.67 ± 5.00	−1096
4 h after	411.19 ± 4.35	−1100
5 h after	406.45 ± 4.96	−1100
23 h after	412.05 ± 6.07	−1108
30 h after	412.10 ± 5.40	−1100
48 h after	370.65 ± 2.31	−1112
50 h after	347.35 ± 4.86	−1108
52 h after	308.10 ± 6.12	−1100

Table 2: Analytical parameters for voltammetric determination of QUI using developed SWV method (n = 8)

	SWV Method
Regression equation*	y = 124.9965x − 13.8369
Correlation coefficient (r)	0.9992
Standard error of slope	0.81
Standard error of intercept	2.91
Linearity range ($\mu g \cdot mL^{-1}$)	0.50–8.68
Number of data points	9
Limit of detection (LOD) ($\mu g \cdot mL^{-1}$)	0.22
Limit of quantitation (LOQ) ($\mu g \cdot mL^{-1}$)	0.50

* y = bx + a; x = concentration ($\mu g \cdot mL^{-1}$), y = peak current (nA), a = intercept, b = slope

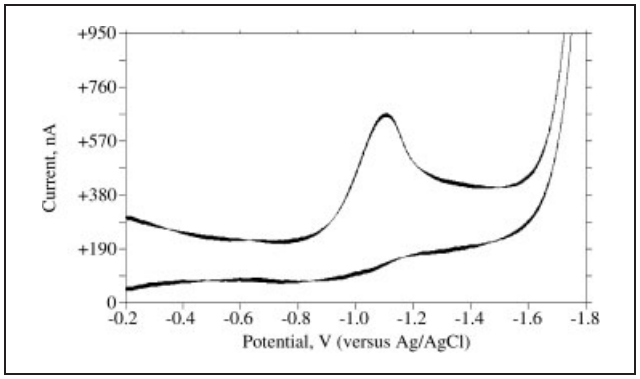


Fig. 5: Cyclic voltammogram of 10.11 $\mu g \cdot mL^{-1}$ QUI solution at HMDE

Table 3: Evaluation of precision and accuracy of the proposed method for the determination of QUI (n = 7)

	Intra-day			Inter-day		
Added ($\mu g \cdot mL^{-1}$)	Found[a] ($\mu g \cdot mL^{-1}$)	Precision RSD %	Accuracy[b] (Bias %)	Found[a] ($\mu g \cdot mL^{-1}$)	Precision RSD %	Accuracy[b] (Bias %)
0.99	1.02 ± 0.01	2.67	3.03	1.00 ± 0.02	4.32	1.01
3.38	3.41 ± 0.02	1.09	0.89	3.39 ± 0.02	1.79	0.30
7.41	7.44 ± 0.02	0.81	0.40	7.42 ± 0.03	0.96	0.13

[a] Found = $\bar{x}$ = mean ± standard error, RSD = Relative standard deviation,
[b] Accuracy = [(Found − Added)/Added] × 100

Fig. 4, peak currents increased linearly with increasing amounts of QUI. The calibration graphs of the peak current versus concentration were found to be linear over the range of 0.50–8.68 $\mu g \cdot mL^{-1}$. The linearity was checked by preparing standard solutions for 9 different concentrations. The calibration curve is described by the following regression equation:

$$i_p = 124.9965\,C - 13.8369\,, \quad r = 0.9992\ (n = 8)$$

where i_p is the SWV peak current (nA) and C is the QUI concentration ($\mu g \cdot mL^{-1}$), r is the correlation coefficient. Statistical evaluation of the regression lines regarding the standard error of the intercept and standard error of the slope and analytical characteristic of the proposed method are given in Table 2.

The sensitivity of the developed method was checked in terms of limit of detection (LOD) and limit of quantitation (LOQ) value. The LOD is defined as the lowest concentration of an analyte in a sample can be detected. LOD may be calculated according the formula:

$$LOD = 3.3\ (SD/S)$$

where SD is the standard deviation of y-intercepts of regression lines and S is the mean slope of the calibration curves. The calculated LOD value for the proposed method was 0.22 $\mu g \cdot mL^{-1}$.

The LOQ is defined as the lowest concentration of an analyte in a sample which can be determined quantitatively with an acceptable level of accuracy and precision under the optimum conditions of the method. The LOQ value of this method was found to be 0.50 $\mu g \cdot mL^{-1}$ (RSD = 5.88%) for the developed method (n = 8). These LOD and LOQ data indicated that the proposed method could be considered sensitive.

The precision of this method was investigated with respect to repeatability and intermediate precision. In order to measure repeatability of the voltammetric instrument, 12 consecutive measurements were made with the same standard solution 3.38 $\mu g \cdot mL^{-1}$ of QUI under the optimum condition on the same day. The mean of measured peak potential and peak current were found to be 1102.67 ± 0.75 with RSD of 0.24% and 412.22 ± 3.46 with RSD of 2.90%, respectively. These results confirmed the high repeatability and precision of the proposed method for the QUI analysis.

The intra- and inter-day precision of this method were evaluated at three different concentration levels of QUI (0.99, 3.38 and 7.41 $\mu g \cdot mL^{-1}$) in the linear range were used. The intra- and inter-day precision was studied on the same day and in 7 different days over a period one week. The RSD values of intra-day and inter-day precision of this method were in the range of 0.81–4.32% (Table 3). This indicates the high precision of the proposed method.

The accuracy of the proposed method was verified by calculating the percentage relative error (bias %) at three concentrations. The intra- and inter-day accuracy were carried out as mentioned in the precision section. The results obtained from intra- and inter-day accuracy of this developed method were found to be between 0.13 and 3.03% (Table 3).

To study the accuracy of the proposed method and to check the interference from excipients used in the dosage forms, recovery experiments were carried out using the standard addition method. This study was performed by addition of known amounts of QUI ($0.96 - 4.61\ \mu g \cdot mL^{-1}$) to known concentrations of the tablets and the mixtures were analyzed by the proposed method. The recovery results were calculated using the regression equation of the standard addition method. The recoveries of QUI were found to be from 100.44 to 100.96% (Table 4). These data showed that excipients presented in tablet dosage forms did not interfere with the analysis of QUI.

The mean regression equation of standard addition method was found to be

$$y = 130.2825\,C + 401.6324\,, \quad r = 0.9989$$

i_p is the SWV peak current (nA) and C is the added QUI concentration ($\mu g \cdot mL^{-1}$), r is the correlation coefficient. There was no difference between the slopes of the two methods with calibration curve and standard addition methods. These values showed that excipients from tablet dosage forms did not significantly interfere and the developed method could be considered selective. The calibration curve method, which is easier and quicker than the standard addition method, was used in quantitative analysis of QUI.

The selectivity of the developed method was tested by analysis of 3.38 $\mu g \cdot mL^{-1}$ of QUI standard solution and pharmaceutical formulation as tablet solution containing 3.38 $\mu g \cdot mL^{-1}$ of QUI. Comparison of the recorded voltammograms obtained from both solutions showed that the peak potential and peak current of QUI did not change (Fig. 6). Therefore, no significant excipient interference was observed and this SWV method could successfully be applied to the analysis of QUI in the presence of tablet excipients. Consequently, the proposed method could be considered selective.

The effect of small variables such as pH (9.9–10.1) and concentration of supporting electrolyte (0.03–0.05 M) were evaluated for 3.38 $\mu g \cdot mL^{-1}$ of QUI. Only one parameter was changed in each experiment. The obtained mean percent-

Table 4: Recovery data of the developed method for the analysis of QUI (n = 6)

Added ($\mu g \cdot mL^{-1}$)	Found ($\mu g \cdot mL^{-1}$)	Recovery (%)	RSD of Recovery (%)
0.96	0.97 ± 0.01	100.96 ± 0.17	0.28
1.90	1.92 ± 0.02	100.88 ± 0.83	1.43
3.27	3.29 ± 0.01	100.65 ± 0.34	0.58
4.61	4.63 ± 0.01	100.44 ± 0.20	0.34

Found = $\bar{x}$ = mean ± standard error, RSD % = Relative standard deviation

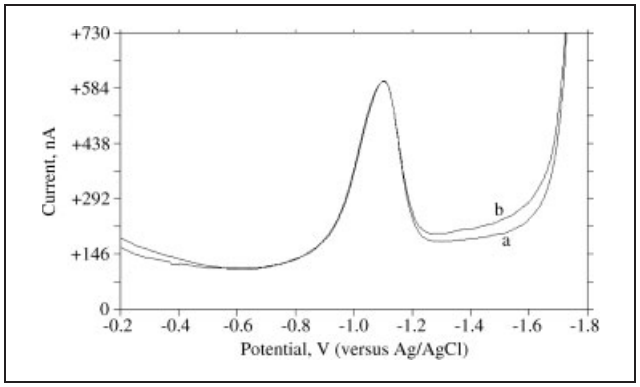


Fig. 6: The SW voltammograms of QUI (3.38 $\mu g \cdot mL^{-1}$) a) Standard solution, b) Tablet solution of QUI at optimum conditions

Table 5: Robustness data of SWV method (n = 7)

	Found ($\mu g \cdot mL^{-1}$)	RSD %	Recovery (%)
Standard (3.38 $\mu g \cdot mL^{-1}$)	3.40 ± 0.02	1.08	100.53 ± 0.41
pH 9.9	3.48 ± 0.02	1.28	103.05 ± 0.50
pH 10.1	3.44 ± 0.02	1.25	101.72 ± 0.48
Buffer Molarity (0.03 M)	3.44 ± 0.02	1.25	101.70 ± 0.48
Buffer Molarity (0.05 M)	3.40 ± 0.02	1.49	100.72 ± 0.57
Friedman analysis: $p = 0.072 > p = 0.05$			

$\bar{x}$ = Mean ± standard error, RSD = Relative standard deviation

Table 6: Ruggedness of the proposed method (Added of QUI 3.38 $\mu g \cdot mL^{-1}$) (n = 7)

1. Analyst found ($\mu g \cdot mL^{-1}$)	2. Analyst found ($\mu g \cdot mL^{-1}$)
$\bar{x} = 3.40 \pm 0.02$	$\bar{x} = 3.41 \pm 0.02$
SD = 0.04	SD = 0.05
RSD % = 1.08	RSD % = 1.57
$t_c = 0.42$, $t_t = 2.18$, $p > 0.05$	
$F_c = 1.56$, $F_t = 4.28$, $p > 0.05$	

$\bar{x}$ = Mean ± standard error, SD = Standard deviation, RSD % = Relative standard deviation
t_c = calculated t value, t_t = tabulated t value, F_c = calculated F value, F_t = tabulated F value

age recoveries and RSD % value based on the average of 7 replicate measurements were not significantly affected within the studied ranges of variations in the procedural operational conditions (Table 5). The statistical comparison was done with Friedman analysis and no difference was found between analysis results ($p = 0.072 > p = 0.05$). Consequently, this SWV was reliable for the analysis of QUI and the proposed method could be considered robust.

Two analysts analyzed 3.38 $\mu g \cdot mL^{-1}$ of QUI standard solution with the proposed method using the same instrument under the same optimized conditions at different days. The obtained results were found to reproducible, thus this developed method could be considered rugged with results of RSD % value of 1.08 and 1.57% for first and second analysts, respectively (Table 6). The statistical comparison of the results was done with the t- and F-tests ($t_c = 0.42$ and $F_c = 1.56$, $p > 0.05$). The results show no statistical differences between different analysts.

In order to evaluate the applicability of the proposed method, a commercial tablet formulation of Acuitel® Tablets at two different dosage forms as 20 mg and 40 mg containing QUI was studied. The QUI content of tablets was determined by the calibration curve method (Table 7). As shown in Table 7, the excipients presented in tablet dosage forms did not interfere with the analysis of QUI.

To test the reliability of the developed method, QUI tablets were also analyzed with a reported method (Prieto et al. 2003). The t- and F-tests were carried out on the data to statistically examine the validity of the obtained results (Table 7). Since the calculated t- and F-values did not exceed the theoretical values, which verified there was no significant difference between the proposed and reported methods.

The SWV method described here is sensitive, accurate, rapid, reliable and simple to perform and a low cost quantitative method, thus suitable for analysis of QUI in pharmaceutical formulations. Preparation of the sample is easy and no separation and extraction procedure is required. Therefore, the presented method can be recommended for routine analysis of QUI in quality control laboratories.

3. Experimental

3.1. Apparatus

All experiments were performed using a BAS 100 B/W (Bioanalytical System, USA) electrochemical analyzer. A three electrode system consisted of HMDE as working electrode; an Ag/AgCl with saturated KCl as reference electrode and a platinum wire as counter electrode were used. The peak heights were automatically or manually measured using the "tangent fit" capability of the instrument. All measurements were performed at room temperature. All pH measurements were made with a Mettler Orion Model 420A digital pH meter calibrated with standard buffers.

3.2. Chemicals and reagents

QUI was kindly provided from Dr. Reddy's Laboratories (Hyderabad, India) and it was used without further purification. Acuitel Tablets® (20 mg

Table 7: Application of the proposed and reported methods to the analysis of commercial pharmaceutical formulations (Acuitel® Tablets) of QUI (n = 7)

Labeled claim (mg)	Proposed method		Comparison method (Prieto et al. 2003)	
	20.00	40.00	20.00	40.00
Found (mg)	$\bar{x} = 20.26 \pm 0.12$	$\bar{x} = 40.55 \pm 0.23$	$\bar{x} = 20.02 \pm 0.14$	$\bar{x} = 39.95 \pm 0.29$
RSD %	1.60	1.52	1.83	1.94
t_c value	1.31	1.61		
t_t value	2.18	2.18		
F_c value	1.34	1.58		
F_t value	4.28	4.28		
Recovery %	$\bar{x} = 101.30 \pm 0.61$	$\bar{x} = 101.38 \pm 0.58$	$\bar{x} = 100.08 \pm 0.69$	$\bar{x} = 99.88 \pm 0.73$
RSD % of recovery	1.60	1.52	1.83	1.94

$\bar{x}$ = Mean ± standard error, RSD % = Relative standard deviation
t_c = calculated t value, t_t = tabulated t value, F_c = calculated F value, F_t = tabulated F value

and 40 mg QUI per tablet) were kindly supplied by Pfizer A. Ş. (Istanbul, Turkey). All chemicals for preparation of buffers were used analytical reagent grade (Merck or Sigma).

3.3. Standard solutions

The stock solution of QUI (1000 $\mu g \cdot mL^{-1}$) was prepared in MeOH and kept in the dark and at +4 °C. Standard solutions of QUI were prepared daily by appropriate dilution of the stock solution with (BR) buffer at pH 10.0.
Different buffers as supporting electrolytes, namely BR, phosphate and borate buffers were used. The investigated buffers were prepared in Milli-Q water. The pH of the solutions was adjusted with 0.1 M HCI or 0.1 M NaOH.

3.4. General analytical procedure

The supporting electrolyte (2 mL), containing BR buffer at pH 10.0, was pipetted into colored electrochemical cell. Dissolved oxygen was removed from the solution by a purified nitrogen gas stream through the cell for at least 10 min. After the voltammogram of supporting electrolyte was recorded, then aliquots standard solutions of QUI were added. Nitrogen was pressed through the solution for 30 s and the square-wave voltammograms of these solutions were recorded using a new mercury drop. The studied potential range was from −400 to −1800 mV versus Ag/AgCl. SWV optimum conditions were as follows: (f) = 50 Hz, (ΔE) = 4 mV and (E_{SW}) = 25 mV.

3.5. Tablet solutions and procedure

QUI determination was also performed in commercially available two different tablet dosage forms Acuitel® Tablets. The amount of QUI present in each tablet was 20 or 40 mg. Ten tablets were weighed accurately and finely powdered and mixed. A portion of the powder equivalent to the average weight of one tablet was transferred into a 50 mL volumetric flask and 50 mL of methanol was added. The content of the flask was sonicated for 15 min to provide dissolution and then completed to volume with methanol. This solution was centrifuged for 15 min at 5000 rpm to separate out the insoluble excipients. An aliquot of clear supernatant was taken and diluted BR buffer at pH 10.0 to achieve the desired concentration. Then the procedure was completed as mentioned under Section 3.4. The drug content per tablet was determined by using the calibration curve method.

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