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Electrocatalytic oxidation of moxifloxacin hydrochloride on modified glassy carbon surface and determination in Avelox tablets

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This work presents an electroanalytical method for the determination of moxifloxacin hydrochloride (MOX) in tablets. The surface of the glassy carbon electrode (GCE) was modified by electrochemical polymerization of 4-aminobenzene sulfonic acid in phosphate buffer solution (pH 7.0).The oxidative behavior of MOX was studied at glassy carbon and modified glassy carbon electrodes in different buffer systems using the cyclic voltammetry technique. The modified glassy carbon electrode (poly(4-ABSA/GCE) has very high catalytic ability for electrooxidation of MOX. Acetate buffer (pH 5.0) was selected as the optimum medium for the oxidation of MOX at poly(4-ABSA/GCE) due to the highest electronic signal increase obtained. Differential pulse voltammetry (DPV) and chronoamperometry (CA) techniques were used for voltammetric determination of MOX. The values of limit of detection (LOD) and limit of quantification (LOQ) were determined to be 3.19×10^{-7}M and 1.06×10^{-6}M for DPV; and 5.50×10^{-7}M and 1.83×10^{-6}M for CA, respectively. A highly sensitive electroanalytical method for the determination of MOX in Avelox tablets by DPV was described.

Keywords: 4-Aminobenzene sulfonic acid, Modified glassy carbon electrode, Electropolymerization, Electrocatalytic ability, Moxifloxacin hydrochloride, Voltammetry

INTRODUCTION

Moxifloxacin hydrochloride {1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, monohydrochloride} (Fig. 1) is a new 8-methoxyquinolone derivative of fluoroquinolones with enhanced activity *in vitro* against gram-positive bacteria and maintenance of activity against gram-negative bacteria [1-3]. MOX has various beneficial effects on human health. The drug, which is used to treat acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis and community-acquired pneumonia [3-6], is rapidly absorbed and reaches the maximum concentration values in plasma between 1 and 6 h after oral administration [7].

Several techniques such as HPLC [8], LC-MS/MS [9], sensitive kinetic spectrophotometry [10], liquid chromatography with column switching [11], capillary electrophoresis with laser-induced fluorescence [12] and spectrofluorimetry [13] have been used for the determination of MOX. Furthermore, several electrochemical techniques involving economic, sensitive and rapid methodologies were reported for determination of MOX [13-17].

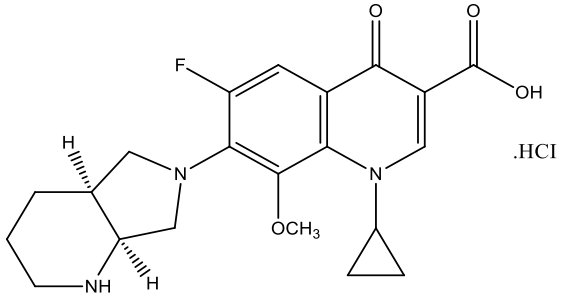

Fig. 1. Structure of moxifloxacin hydrochloride

However, the electrooxidation of MOX at carbon electrodes is kinetically slow. Therefore, the use of modified electrodes is preferred for the oxidation of MOX. Until today, the modified electrodes such as chloranil modified carbon paste electrode [18], molecularly imprinted polymer modified carbon paste electrode [19], and carbon paste modified with silver nanoparticles [20] were used to determine MOX. Furthermore, it is known that poly(4-ABSA/GCE) was used to determine samples such as phenylephrine and chlorprothixene [21], hydroquinone in the presence of catechol and resorcinol [22], uric acid [23], acyclovir [24],

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phenazopyridine hydrocloride [25] and ornidazole [26].

In this work, the surface of the glassy carbon electrode modified by electrochemical polymerization of 4-aminobenzene sulfonic acid (4-ABSA) in PBS buffer solution (pH 7.0) was investigated for determination of MOX by using different voltammetric techniques. Poly(4-ABSA/GCE) shows a high electrocatalytic ability for the oxidation of MOX in the pH range from 2 to 10. The acetate buffer (pH 5.0) was selected as the optimum medium for determination of MOX. Moreover, MOX in Avelox tablets was successfully determined with the modified glassy carbon electrode using a simple, sensitive and rapid method.

EXPERIMENTAL

Instrumentation

A potentiostat meter (VersaSTAT^3, Princeton Applied Research, USA) was used for the voltammetric measurements. All experiments were carried out with a three-electrode system. Glassy carbon electrodes (GCE) (3.0 mm diameter) were purchased from BAS and used as a working electrode. A platinum wire auxiliary electrode and an Ag/AgCl (NaCl 3 M, BAS) reference electrode were used.

All pH measurements were made using an EZDO 5011 model digital pH-meter. The deionized water was obtained from water purified with an aqua MAX^{TM}-Ultra water purification system (young Lin Inst.) 18.2 MΩ cm.

Reagents and materials

MOX and Avelox were supplied from Basel Kimyevi Maddeler ve Ilac. San. Tic. A.S. Istanbul-Turkey. A stock solution of 1.0×10^{-3}M MOX was prepared by dissolving an accurate mass in methanol and was used to prepare the diluted solutions. The working solutions were obtained by dilution of the stock solution with acetate buffer solution (pH 5.0). All solutions were protected from light and were used within 24 h to avoid decomposition. 0.2M acetate buffer (pH 5.0) was selected as the supporting electrolyte solution to investigate the voltammetric behavior of MOX. All other chemical substances were reagent-grade commercial products.

PROCEDURES

Polishing and cleaning of glassy carbon electrode

The GCE was polished successively in 1 μm, 0.3 μm and 0.05 μm alumina slurries on Buehler polishing microcloth. The polished GCE was sonicated in ultrapure water, in a mixture of 1:1 (v/v) nitric acid/water (HNO_3+H_2O) (Fluka) and then in ethanol (Aldrich) for 10 min each. Then, the cleaned GCE was rinsed with water and dried under a stream of argon. The polished and cleaned GCE was used for the derivatization.

Modification of glassy carbon electrode

The surface derivatization of the bare GC electrode was performed in 0.10 M PBS (pH 7.0) containing 2.0×10^{-3} M 4-ABSA. The oxygen in the 4-ABSA solution was removed with argon for at least 10 min before the derivatization. Then, the bare GCE was immersed in the 4-ABSA solution. The GC surface was modified using cyclic voltammetry for five cycles at a scan rate of 100 mV s^{-1} in the potential range from -1.5 to +2.5 V. Finally, the modified electrode was activated by cyclic voltammetry from -1.0 to +1.0 V at a scan rate of 100 mV s^{-1} for ten cycles in 0.10 M PBS (pH 7.0). Bare GC and modified GC electrodes were used as working electrodes.

Calibration graph for quantitative determination

The stock solution of 10^{-3} M MOX was prepared by dissolving an accurate amount of the substance in methanol and diluting with 0.1 M acetate buffer solution (pH 5.0) to obtain different MOX concentrations. The calibration graphs were constructed by using the data recorded under the optimum conditions described in the experimental section. The concentration ranges of the linear calibration curves for DPV and CA techniques are from 1×10^{-6} M to 9×10^{-6} M and from 5×10^{-6} M to 9×10^{-5} M, respectively. The DPV technique, which has lower limits of detection, was used to determine the amount of MOX in tablets.

Procedure for Avelox® tablets

Each Avelox® tablet contains 436.80 mg of moxifloxacin hydrochloride, equivalent to 400.00 mg of moxifloxacin drug and some inactive excipients. One Avelox® tablet, which weighs 0.7069 g, was powdered. The stock solution of 25.8 mg of the powdered drug tablet dosage form was prepared in methanol. The stock solution of 30 μL was transferred to a volumetric flask of 10 mL and then, the volume was diluted to 10 mL with 0.2 M acetate buffer (pH 5.0). The DPV and CV voltammograms of the sample were recorded. The content of the drug in the tablet was determined by using the drawn calibration graph.

RESULTS AND DISCUSSION

Electropolymerization of 4-ABSA on the GCE surface

The cyclic voltammogram of 10 cycles recorded in 0.10 M PBS (pH 7.0) containing 4-ABSA of 2.0×10^{-3} M for electrochemical polymerization of 4-ABSA on the GCE surface are given in Fig. 2. In the first cycle, a weak anodic and a cathodic peak were observed with a peak potential value at E_{pa} = 1.70 V and E_{pc} = -0.60 V, respectively. The two anodic peaks in the second cycle of the voltammogram appeared at peak potential values of +0.13 V and +1.45 V, respectively. The peak current increases in the subsequent cycles. Therefore, it is understood that the surface of GCE is modified with the polymerization film. The modified surface is a blue polymer film [23-26]. Furthermore, the modified GC electrode was activated with the CV voltammogram of 10 cycles at 100 mV s^{-1} scan rate in the potential range from -1.0 V to+1.0 V in 0.1 M phosphate buffer (pH 7.0) medium. After the activation process was completed, the prepared, modified and activated electrode was used for voltammetric studies. The poly(p-ABSA) modified electrode was thoroughly washed with double-distilled water and stored in 0.1 M PBS (pH 7.0) before use.

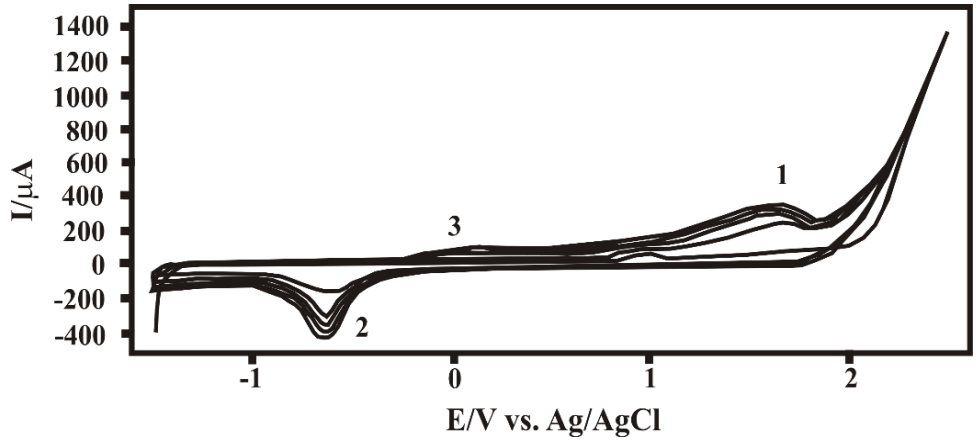

Fig. 2. The cyclic voltammogram of 10 cycles of the solution in 0.10 M PBS (pH 7.0) of 4-ABSA of 2.0×10^{-3} M in the potential range from-1.5 V to +2.4 V (scan rate 100 mV s^{-1}).

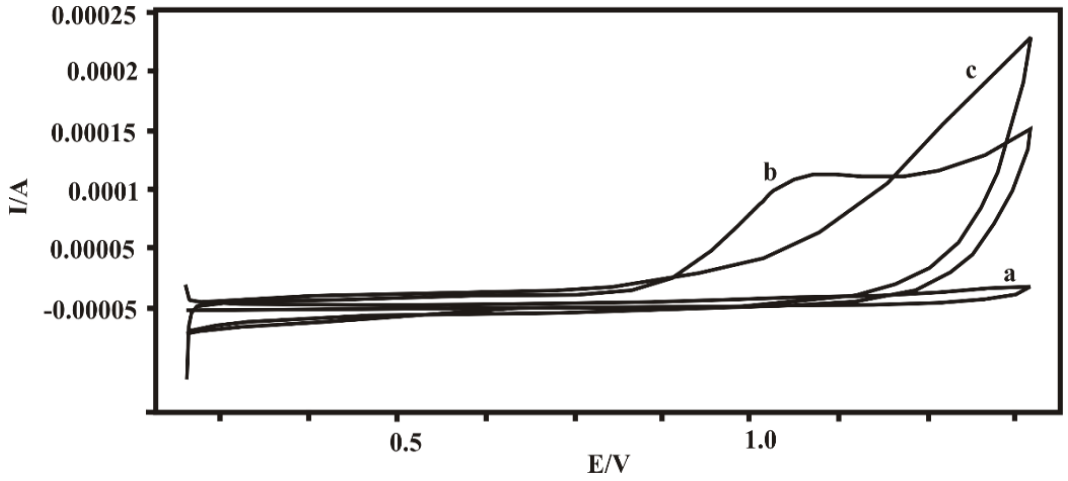

Fig. 3. Cyclic voltammograms of 1×10^{-4} M MOX recorded at the bare GC (a) and poly(4-ABSA/GC) (b) electrodes in 0.2 M acetate buffer (pH 5.0). The voltammogram of 0.2 M acetate buffer (pH 5.0) (c) is the background obtained by using the modified glassy carbon (scan rate: 50 mV s^{-1}).

Electrochemical oxidation of MOX on 4-ABSA modified glassy carbon electrode

The electrochemical responses of MOX on the bare GC and the poly(p-ABSA) modified electrodes were studied by using cyclic voltammetry. The cyclic voltammograms recorded at the GC (a) and poly(4-ABSA/GCE) (b) electrode of 1×10^{-4} M MOX in 0.2 M acetate buffer (pH 5.0) at the scan rate of 50 mV s^{-1} are given in Fig. 3.

At the bare GC electrode, MOX shows a featureless voltammogram (Fig. 3a). When the CV voltammogram of MOX is recorded at the bare GC electrode, the smaller oxidation CV peak was obtained at more negative potential values.

However, if the poly(4-ABSA/GC) electrode is used for the oxidation of MOX, an increase in the peak current was observed and the oxidation peak potential shifted to more positive values. The peak current values of CV voltammograms recorded for the oxidation of MOX at the bare GC and the poly(4-ABSA/GC) electrodes at 50 mV s^{-1} scan rate in 0.2 M acetate buffer (pH 5.0) were 9.691 µA and 112.87 µA, respectively (Figs. 3a and 3b). Consequently, an increase of eleven times in the peak current on the modified electrode surface was obtained. Furthermore, the value of peak potential of the oxidation peak of MOX at modified GC electrode was shifted to smaller positive values. These behaviors were evaluated as evidence that the modified GC electrode exhibits an electrocatalytic effect for the oxidation of MOX.

Effect of pH

The effect of pH on the oxidation of MOX was studied in the range of pH from 2 to 10 by using different buffer solutions. Britten-Robinson (B-R), phosphate and acetate buffers were used to determine the type of support electrolyte and the value of optimum pH. The peak current values of the oxidation peak obtained from the CV voltammograms of the solutions of 1×10^{-4} M MOX diluted with different support electrolytes in the range from pH 2 to 10 are shown in Fig. 4.

As seen in Fig. 4, the oxidation peak current of MOX in 0.2 M acetate buffer reached the maximum value at pH 5.0. At the same time, the anodic peak potential shifts toward less positive values with increasing pH up to 5.0. Therefore, pH 5.0 was selected for further studies.

The nature of the oxidation peak of MOX

Fig. 5 shows the cyclic voltammograms of 0.2M acetate buffer (pH 5.0) containing 1×10^{-4} M MOX on the poly(4-ABSA/GC) electrode surface at the following scan rates: 50, 60, 70, 80, 90, 100, 200, 300, 400 and 500 mV s^{-1} .

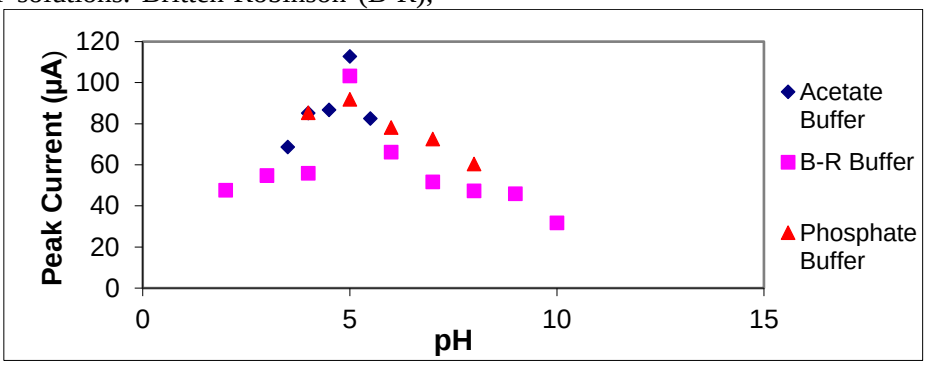

Fig. 4. The oxidation peak current values of 1×10^{-4} M MOX recorded in the range from pH 2.0 to 10.0 in 0.1 M phosphate, 0.04 M B-R and 0.2 M acetate buffers (scan rate: 50 mV s^{-1}).

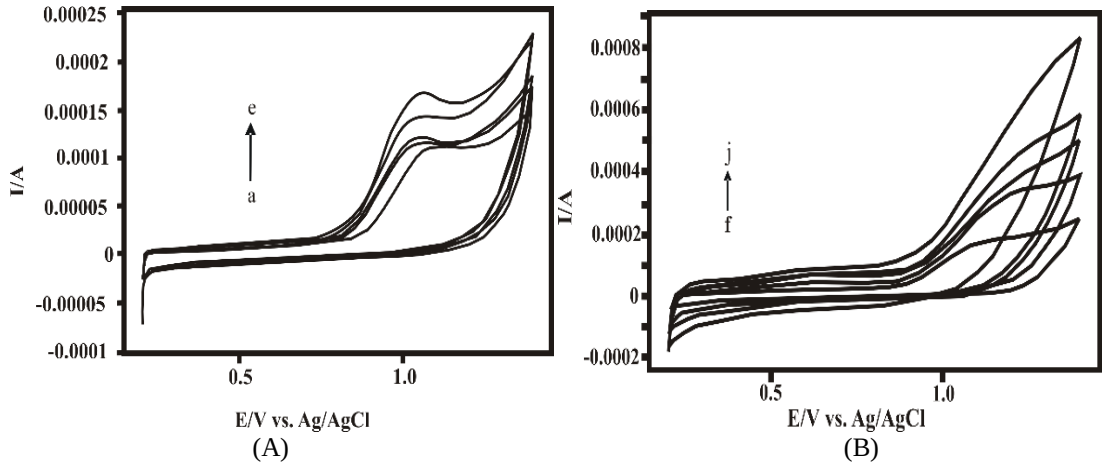

Fig. 5. Cyclic voltammograms recorded at the poly(4-ABSA/GC) electrode in 0.2 M acetate buffer (pH 5.0) containing 1×10^{-4} M MOX (scan rates: **(A)** a) 50, b) 60, c) 70, d) 80, e) 90 and **(B)** f) 100, g) 200, h) 300, i) 400, j) 500 mV s^{-1}).

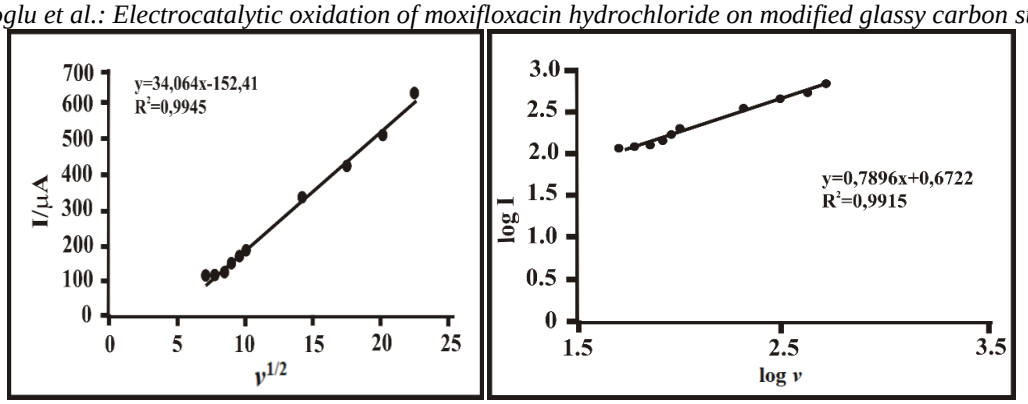

Fig. 6. (A) The peak current values plotted against $v^{1/2}$ and **(B)** the logarithm of peak current (log *I*) against the logarithm of scan rate (log *v*) of the oxidation peak obtained from the CV voltammograms recorded at the poly(4-ABSA/GC) electrode of 1×10^{-4} M MOX in 0.2 M acetate buffer (pH 5.0) (scan rates: a) 50, b) 60, c) 70, d) 80, e) 90, f) 100, g) 200, h) 300, i) 400, j) 500 mV s^{-1}).

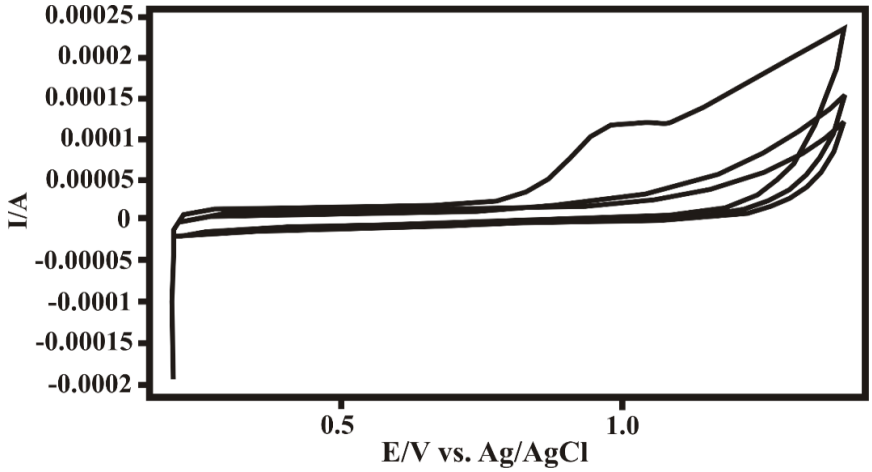

Fig. 7. The cyclic voltammogram of three cycles recorded in the potential range from 0.2 to 1.4 V of 1×10^{-4} M MOX in 0.2 M acetate buffer (pH 5.0) at the poly (4-ABSA/GC) electrode (scan rate: 50 mVs^{-1}).

A good linearity between the square root of scan rate and peak current was obtained in the range of 50-500 mV s^{-1}. The linear regression equation was Ip (μA) = 34.06 $\upsilon^{1/2}$ - 152.4 with correlation coefficient (r) = 0.994. The correlation coefficient is very close to 1.0. Consequently, it is understood that the oxidation process is diffusion-controlled [27].The plot of logarithm of peak current (log *I*) *versus* logarithm of scan rate (log *v*) has a slope of 0.789 which is greater than the theoretical value of 0.75. Since the slope is at about 0.789, it can be considered that the electrochemical oxidation reaction of MOX is diffusion-controlled but adsorption is also effective. Also, the CV voltammogram of three cycles of 1×10^{-4} M MOX in 0.2 M acetate buffer at the poly(4-ABSA/GC) electrode was recorded to evaluate the nature of the oxidation peak of MOX (Fig. 7).

As seen in Fig. 7, the oxidation peak of MOX appeared in the first cycle. However, this peak completely disappeared in the second and third cycles. It is estimated that the oxidation peak disappeared in the second and third cycles due to adsorption on the surface of the modified glassy carbon electrode of the MOX molecules or the ones of the oxidation products. This observation can be considered as another piece of evidence that the electrochemical oxidation reaction of MOX is diffusion-controlled but adsorption is also effective. Therefore, the modified glassy carbon electrodes were only used for one measurement. Consequently, the glassy carbon electrode surface was again cleaned and modified before each new experiment.

Selection of the electroanalytical technique to determine MOX

The DPV and CA techniques were used for the voltammetric determination of MOX. Fig. 8 displays the DPV voltammograms of various concentrations of MOX at the poly(4-ABSA/GC) electrode in 0.2 M acetate buffer (pH 5.0).

A plot of the peak current values as a function of the concentration was drawn. The plot was linear in

the concentration range from 1×10^{-6} to 9×10^{-6} M MOX. For the regression plot of the peak current *versus* MOX concentration, the slope was 1×10^{7} μAM^{-1}, the intercept was 159.6 μA and the correlation coefficient was $R^2 = 0.993$ (Fig. 9). Limit of detection (LOD) and limit of quantification (LOQ) values were calculated using the following equation [27]:

$$LOD = 3\ s/m,\ LOQ = 10\ s/m$$

where, s is the standard deviation of the peak current (for five runs) and m is the slope of the calibration curve. To determine LOD and LOQ values, the standard deviation of peak currents for five measurements recorded at 3×10^{-6} M, which is the concentration above the lowest concentration in the calibration graph, was determined to be 1.063. The LOD and LOQ were 3.189×10^{-7} M and 1.063×10^{-6} M, respectively, achieved at the poly(4-ABSA/GC) electrode.

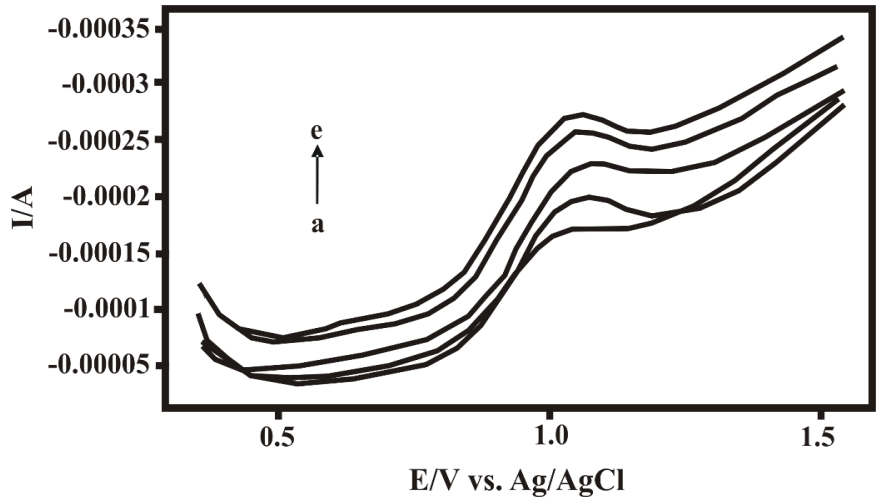

Fig. 8. DPV voltammograms for increasing concentrations of MOX: a) 1×10^{-6}, b) 3×10^{-6}, c) 5×10^{-6}, d) 7×10^{-6} and e) 9×10^{-6} M in the potential range from 0.2 V to 1.4 Vin 0.2 M acetate buffer (pH 5.0) on the poly(4-ABSA/GC) electrode surface.

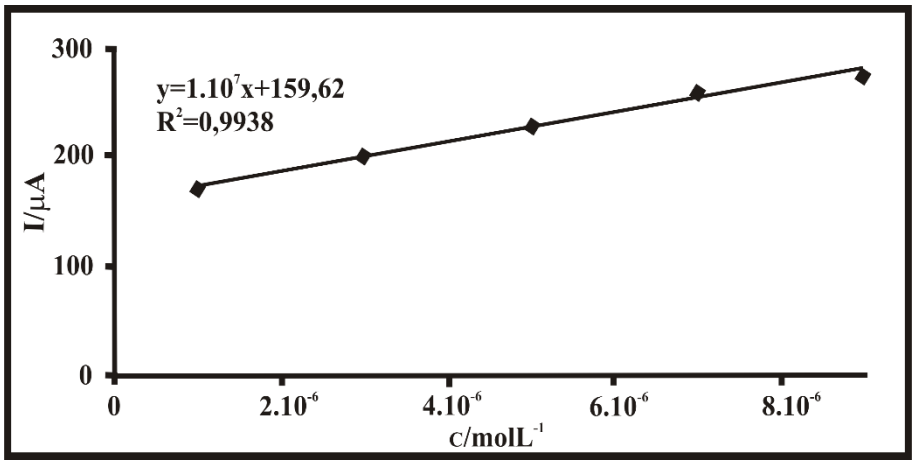

Fig. 9. Calibration plot for increasing concentrations of MOX obtained from DPV voltammograms.

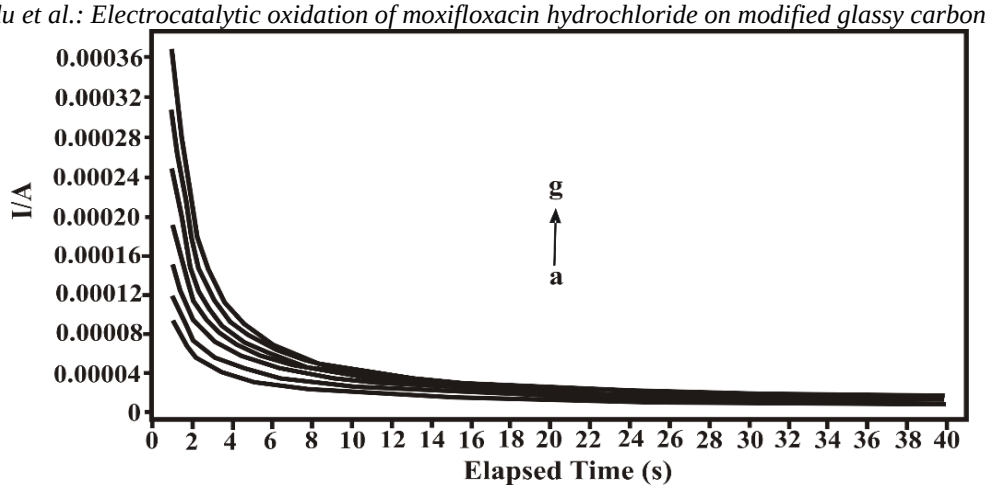

Fig. 10. Chronoamperometric response of the poly(4-ABSA/GC) electrode for increasing concentrations of MOX solutions of: a) 5×10^{-6} M, b) 9×10^{-6} M, c) 1×10^{-5} M, d) 3×10^{-5} M, e) 5×10^{-5} M, f) 7×10^{-5} M, g) 9×10^{-5} M in 0.2 M acetate buffer (pH 5.0) containing different concentrations of MOX for a potential step of 1.15 V *vs*. reference electrode. Variation of chronoamperometric currents at t= 40 s *vs*. concentration of MOX.

Also, the electrocatalytic oxidation of MOX at the poly(4-ABSA/GC) electrode was studied with the CA technique. The chronoamperograms obtained for a series of MOX solutions with various concentrations are illustrated in Fig. 10. An increase in concentration of MOX was accompanied by an increase in anodic currents obtained for a potential step of 1.15 V *versus* reference electrode.

The current values recorded from the chronoamperograms obtained for a series of MOX solutions were used to draw the calibration plot (Fig. 11).

The plot drawn with current values obtained from chronoamperometric response was linear in the concentration range from 5×10^{-6} to 9×10^{-5} M MOX. The LOD and LOQ values obtained from this calibration plot are 5.50×10^{-7} and 1.83×10^{-6} M, respectively.

When compared with the DPV and CA techniques used to determine the amount of MOX, it is understood that the detection limits obtained using the DPV technique have smaller values. Therefore, the DPV technique is preferred for determination of MOX.

Determination of MOX in pharmaceutical preparations

To determine the amount of MOX in the 400 mg Avelox tablets, a drug tablet of 0.7069 g was taken and powdered. A solution of 10 mL of 25.8 mg of the drug in powdered form was prepared in methanol. A volume of 30 μL of the stock solution was diluted to 10 mL with 0.2 M acetate buffer (pH 5.0). The DPV voltammogram of the drug tablet dosage form containing MOX is shown in Fig. 12.

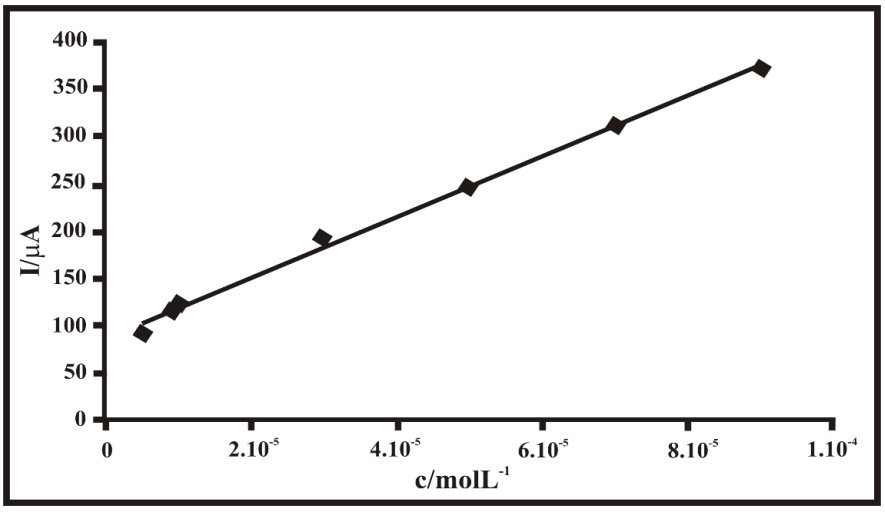

Fig. 11. Calibration plot obtained from chronoamperograms of MOX in 0.2 M acetate buffer (pH 5.0).

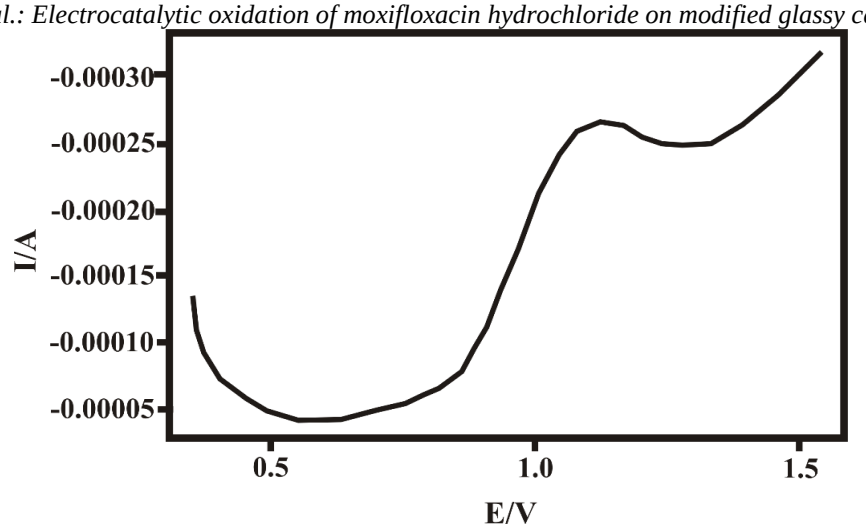

Fig. 12. The DPV voltammogram of the drug tablet sample containing MOX in 0.2 M acetate buffer in the potential range from 0.2 V to 1.4 V at poly(4-ABSA/GC) electrode.

Table 1. Application of the DPV technique for the assay of MOX in pharmaceutical preparations

Parameters	Results
Labeled MOX, mg	436.8
Amount found, mg	428.2
Number of measurements, N	5
Relative standard deviation (*RSD*), %)	0.280
Bias, %	1.96

As seen in Fig. 12, when the DPV voltammogram of the drug tablet sample containing MOX is examined, its characteristic oxidation peak is found to be at about 1.12 V and the peak current is 266.71 μA. Consequently, it is understood that there is no interference on the oxidation of moxifloxacin HCl in the drug tablet form at the poly (4-ABSA/ GC) electrode.

The amount of MOX in Avelox commercial tablets was calculated by reference to the appropriate calibration plots. The results obtained are given in Table 1.

The drug dosage form contains microcrystalline cellulose, sodium croscarmellose, lactose monohydrate, magnesium stearate, red iron (III) oxide, HPM cellulose 15 cp, polyethylene glycol 4000 and titanium dioxide as auxiliary substances together with MOX.

The amount of MOX in the sample was calculated by using the equation y=1×107x+159.62, obtained from the calibration graph of the DPV technique.

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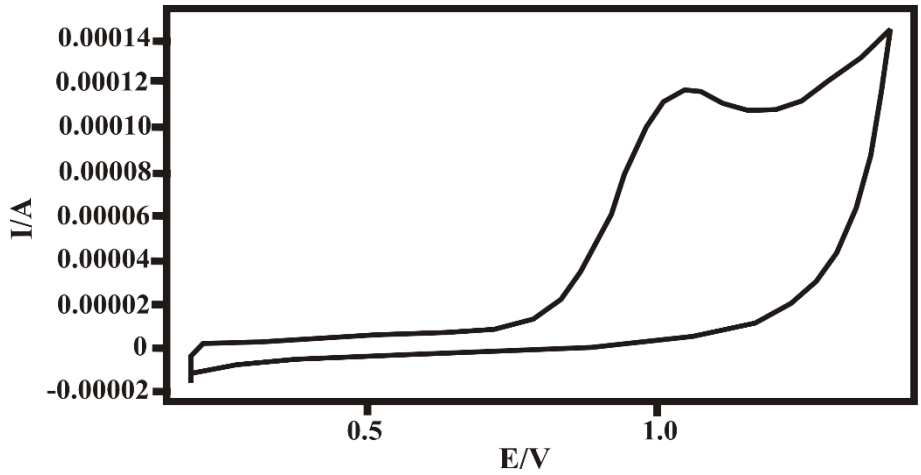

Fig. 13. The CV voltammogram of the drug tablet dosage form a sample containing MOX in 0.2 M acetate buffer in the potential range from 0.2 V to 1.4 V at poly(4-ABSA/GC) electrode.

According to the calculations made for the sample of 25.8 mg, the drug tablet contains MOX at the rate of 60.58% (w/w).

Also, the CV technique was used to reveal that there was no interference on the oxidation of MOX in the drug tablet dosage form. The CV voltammogram of the sample is shown in Fig. 13. As can be seen in Fig. 13, when the CV voltammogram of the sample is recorded, the oxidation peak of M OX is at about 1.05 V. There is no shift in the peak potential value. In addition, there is no change in the shape of the oxidation peak. Therefore, according to the CV voltammogram, it is understood that there is no interference. Consequently, the poly(4-ABSA/GC) electrode can be used for the selective and sensitive determination of the amount of MOX in tablet dosage forms.

CONCLUSIONS

Glassy carbon electrode coated with poly (4-aminobenzene sulfonic acid) film was used for electrocatalytic determination of MOX. The modified glassy carbon electrode showed good electrocatalytic activity for the oxidation of MOX. The modified electrode provides higher sensitivity and selectivity in the determination of MOX.

Differential pulse voltammetry technique can be used to the determination of MOX in the drug tablet form at the optimum conditions of GCE modified with 4-ABSA as the working electrode and 0.2 M acetate buffer (pH=5.0) as the supporting electrolyte.

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