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Reduction Behavior of Moxifloxacin Hydrocholaride and Its Analysis in Spiked Human Urine and Dosage Form by Voltammetry

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ABSTRACT

A voltammetric method was developed to analyze moxifloxacin hydrochloride (MoxHCl) in pharmaceutical preparations and spiked human urine. The experimental measurements were completed using different buffer systems (pH 0.50- 12.05) on Glassy Carbon Electrode (GCE) with differential pulse voltammetry (DPV) and Cyclic Voltammetry (CV) methods. The effect of pH on the peak current and potential were determined. Britton-Robinson (BR) buffer (pH 7.00) was used for analysis. The peak was established to be diffusion-controlled based on the nature of electrode. Calibration plots were prepared for the concentration range from 3×10^{-4} M to 1.1×10^{-3} M with DPV. Limits of detection (LOD) and quantification (LOQ) were calculated as 5.1×10^{-5} M and 2.30×10^{-4} M, respectively. The validation of the applied methods was completed. Electroreduction mechanism was proposed.

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INTRODUCTION

Moxifloxacin HCl (Fig. 1) is a kind of broad-spectrum antimicrobial fluoroquinolone [1]. It is used in the treatment of bacterial sinusitis [2,3].

MoxHCl was analyzed with high-performance liquid chromatography. [4-6] In the literature, several electroanalytical techniques based on oxidative behavior of MoxHCl are also reported. Studies with modified electrodes [1,7], glassy carbon electrode [8,9] and carbon paste electrode[10] were reported. There are studies in the literature about the reduction behaviour of moxifloxacin and the determination by electrochemical reduction method [11-13]. In this study, electroreduction of MoxHCl was investigated with CV and DPV on a GCE, also the effects of supporting electrolyte, pH and scan rate on the electroreduction of this substance were investigated. It was shown that the method could be applied in pharmaceutical preparations and human urine.

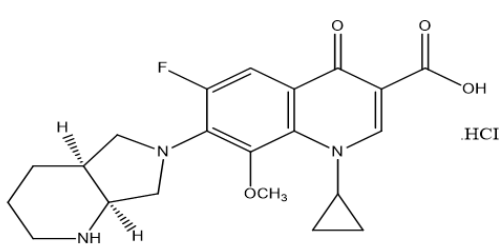

Figure 1. Chemical formula of MoxifloxacinHCl.

EXPERIMENTAL

Apparatus

In this work, current and potential values were measured with 757-VA Trace-Analyzer (Metrohm).Three electrodes were used; a working electrode (GCE), counter (platinum-wire) and reference electrode (silver/silver chloride in 3 M potassium chloride). The working electrode was cleaned using alumina and rinsed with ethanol and deionized water. Voltammograms were taken after argon gas was passed through a buffer and the analysis solution. A 744 pH-meter (Metrohm, Herisau, Switzerland) was used for pH measurements.

Reagents and Materials

MoxHCl was obtained from Bayer, Istanbul, Turkey. Stock solutions of 1.00×10^{-1} M of MoxHCl were created with deionized water. Diluted solutions were prepared from this stock solution. 0.5 M H_2SO_4, 0.067 M phosphate, 0.2 M acetate and 0.04 M BR buffers were used as supporting electrolytes. Deionized-water was obtained from Sartorius Arium model deionized water Systems. Chemicals used were high purity. The calibration curve was formed from 3.0×10^{-4} M to 1.1×10^{-3} M using the DPV technique.

Analysis of Spiked Pharmaceutical Samples

Ten Avelox tablets were prepared containing $1x10^{-1}$ M MoxHCl in deionized water. This solution was centrifuged for about 15 minutes at 5000 rpm. After that, the diluted supernatant was taken and measured. The content of the active drug was determined with the calibration curve.

Analysis in Urine Spiked Samples

A sample taken freshly from a villager was adjusted 2:8 using deionized-water. Then 8.0 mL of 0.065 M phosphate buffer (pH 6.50) was inserted into the cell and measured for blank. After that, 500 µL of urine sample was inserted and urine and blank were measured. To get a 4×10^{-4} M, 40µL (2 mL Urine + 7 mL deionized Water + 1.0 mL of 1.0 M MoxHCl) was placed into the cell and measured. 30 µL of 1.0×10^{-1} M MoxHCl was used for measurement. The calibration curve was obtained from these measurements.

RESULTS AND DISCUSSION

Electrochemical Reduction Properties of MoxHCl

The best analytical signal was obtained at pH 6.50 in 0.065 M phosphate solution and this was selected for drug analysis (Fig. 2).

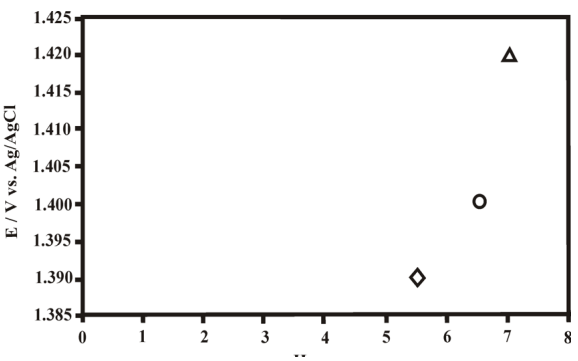

Figure 2. Change of pH at the DPV peak potential in 5×10^{-5} M MoxHCl (◊) acetate, (0.02 M), (o) phosphate (0.067 M) and (Δ) BR (0.04 M) buffers.

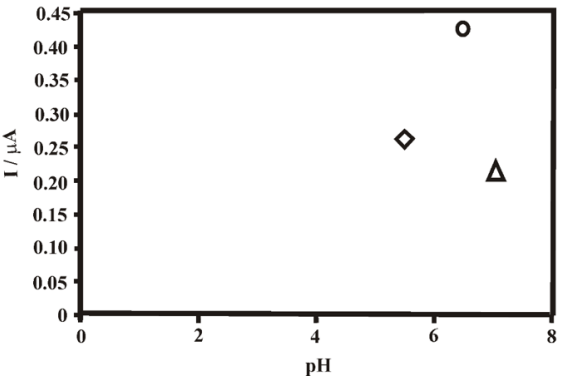

Figure 3. Change of the DPV peak current in 5×10^{-5}M MoxHCl in (◊) acetate, (0.02 M), (o) phosphate (0.067 M) and (Δ) BR (0.04 M) buffers.

The increase in pH linearly shifted the peak potential to more negative values. This indicates participation of proton transfer at the electrode reaction (Fig. 3).

The effects of scan rate from 50 to1000 mVs^{-1} on the potential and current of peak MoxHCl were investigated. The CV of MoxHCl at pH 6.50 in 0.065 M phosphate buffer is given in Fig. 4.

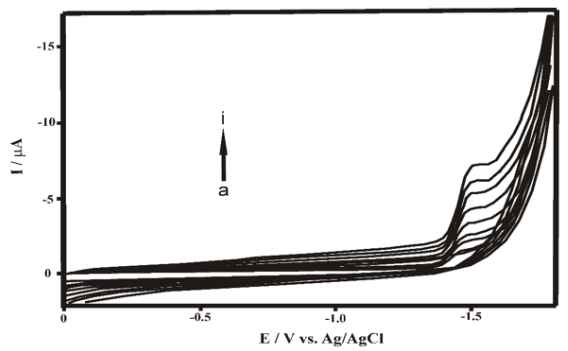

Figure 4. Cyclic voltammograms of 1×10^{-4} M MoxHCl in 0.067 M phosphate buffer (pH 6.50) on the GCE. Scan rate, v, mVs^{-1}, a) blank, b) 50, c) 100, d) 150, e) 250, f) 400, g) 600, h) 750, and ı) 1000.

The R value of peak current and square root of the scan rate is 0.999 ($I_p/\mu A=0.0471\nu^{1/2}$-0.2105). Slope (0.06797) of the curve of log I versus log ν showed that the reduction mechanism is diffusion-controlled [14-16].

The cyclic voltammogram of MoxHCl exhibited one cathodic peak and potential value changed to more negative values with the rising scan rate, indicating that the reaction is irreversible [16].

Validation of the Applied Voltammetric Technique

The concentration was established in the range from 3×10^{-4} M to 1.1×10^{-3} M with DPV (Fig. 5).The equation of

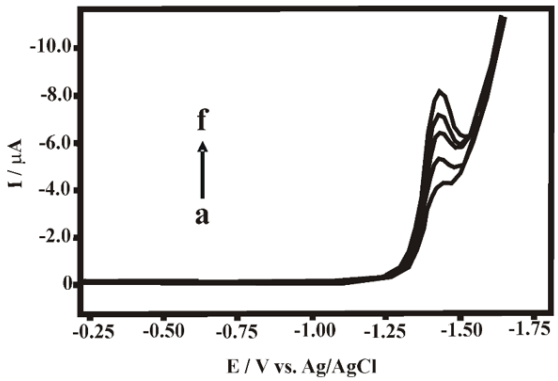

Figure 5. Calibration voltammograms for different concentrations of MoxHCl in 0.067 M phosphate buffer (pH 6.50) on the GCE with DPV a) blank b) 3.0×10^{-4} c) 5.0×10^{-4} d) 7.0×10^{-4} e) 9.0×10^{-4} and f) 1.10×10^{-3} M MoxHCl.

the calibration curve was I_p/µA=2830 C(M)+0.446 with, R (Correlation Coefficient, 0.99); (Repeated experiment: 4). The validation parameters of applied method are given in Table 1 and Table 2.

Table 1. Parameters of analytical MoxHCl determined in phosphate buffer (pH 6.50) using the DPV technique.

Parameters	*Results*
Measured potential,V	*-1.4*
Linear concentration range, M	*3×10^{-4}- 1.1×10^{-3}*
Slope, µAM	*2830*
SD of slope	*4.15*
Intercept, nA	*0.446*
SD of intercept	*5.87*
Correlation coefficient, R	*0.99*
LOD, M	*5.51×10^{-5}*
LOQ, M	*2.30×10^{-4}*
Reproducibility of peak current, RSD %	*1.078 for 9×10^{-4} M*
Reproducibility of peak potential, RSD %	*0.505 for 9×10^{-4} M*

Analysis of MoxHCl in Pharmaceutical Preparations with Voltammetry Techniques

MoxHCl was determined in Avelox form and results are given in Table 2.

Analysis of Spiked Human Urine

The analysis of MoxHCl in a urine sample was completed

Table 2. Results for assay of MoxHCl in pharmaceutical preparation.

Parameters	*Results*
MoxHCl, mg	*436.5*
Amount found, mg	*442.05*
Relative Standard deviation, RSD%	*2.38*
Bias %	*1.27*
MoxHCl spiked, mg	*1.3*
Found, mg	*1.24*
Average recovery, %	*95*
Relative standard deviation of recovery, RSD %	*2.46*
Bias %	*5*

(Fig. 6). The values of these analyses are given in Table 3.

Table 3. Quantitative determination of MoxHCl in spiked human urine samples with recovery results.

Parameters	*Results*
MoxHCl, M	*4×10^{-4}*
MoxHCl found, M	*3.91×10^{-4}*
Number of measurements, N	*10*
Average recovery, %	*97.75*
RSD %	*0.90*
Bias %	*2.25*

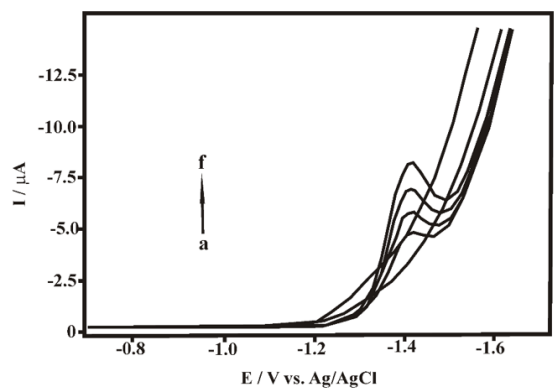

Figure 6. DP voltammograms of MoxHCl in spiked human urine a) Blank, 0.067 M phosphate buffer (pH6.50) b) a + 600 µL urine (1:9); c) 4.0×10^{-4} MoxHCl with urine d) 2.0×10^{-4} e) 4.0×10^{-4} and f) 6.0×10^{-4}M MoxHCl.

Electroreduction Mechanism of MoxHCl

Electroreduction mechanisms of MoxHCl were proposed as below:

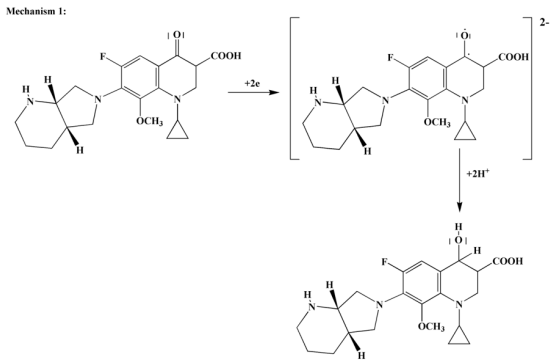

Figure 7. Proposed electroreduction mechanism of MoxHCl.

CONCLUSION

In summary, MoxHCl was determined in phosphate buffer (pH 6.50) in pharmaceutical preparations using DPV. The advantage of the voltammetric technique is that it can be applied fast, at low cost and directly to the analysis form of the drug without interference.

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