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Determination of antihypertensive drug moexipril hydrochloride based on the enhancement effect of sodium dodecyl sulfate at carbon paste electrode

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ABSTRACT

Herein, an electrochemical differential pulse voltammetric method was developed for the determination of moexipril hydrochloride based on the enhancement effect of sodium dodecyl sulfate. The oxidation process has been carried out in Britton-Robinson buffer. Moexipril hydrochloride exhibits a well-defined irreversible oxidation peak over the entire pH range (2–11). The peak current varied linearly over the range from 4.0×10^{-7} to 5.2×10^{-6} mol L^{-1}. The limits of detection and quantification were 6.87×10^{-8} mol L^{-1} and 2.29×10^{-7} mol L^{-1}, respectively. The recovery was found in the range from 99.65% to 100.76%. The relative standard deviation was found in the range from 0.429% to 0.845%. The proposed method possesses high sensitivity, accuracy and rapid response. Finally, this method was successfully used to determine moexipril hydrochloride in tablets.

1. Introduction

Drug analysis, an important branch of analytical chemistry, plays important role in drug quality control. Therefore, the development of sensitive, simple, rapid and reliable method for the determination of active ingredient is of great importance and interest.

Moexipril hydrochloride (MOEX), (3S)-2-[(2S)-2-{[(1S)-1-(ethoxycarbonyl)-3phenylpropyl] amino}-1-oxopropyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid hydrochloride (Fig. 1) is a new potent orally active non-sulfhydryl angiotensin-converting enzyme (ACE) inhibitor for the treatment of hypertension and congestive heart failure, post myocardial infarction, high coronary disease risk, diabetes mellitus, chronic renal failure and/or cerebrovascular disease [1]. MOEX improves cardiac function and reduces mortality. It also relieves symptoms and increases exercise tolerance. The drug prevents inactive angiotensin I from being converted to angiotensin II, which causes vasoconstriction and retention of sodium and water. Thus, major effects of the drug are dilation of veins and arteries, reduced preload and after-load, reduced workload of the heart and increased perfusion of body organs and tissues [2].

A review of the literature revealed that few methods have been reported for the determination of MOEX, gas chromatographic-mass spectrometric method [3], spectrophotometric methods [4], high performance liquid chromatographic (HPLC) method with derivative spectrophotometry [5] and stability indicating reversed phase liquid chromatographic (RPLC) method [6].

Electrochemical methods have proved to be sensitive, accurate and reliable for the determination of organic molecules that undergo oxidation or reduction reactions, including drugs and related molecules in pharmaceutical dosage forms and biological fluids [7–13].

Carbon based electrodes are currently in widespread use in electroanalytical chemistry, because of their broad potential window, low cost, rich surface chemistry, low background current and chemical inertness. Carbon paste electrode (CPE) has some special characteristics and benefits such as the ease of surface renewal, individual polarizability and easy to apply modifications. The disadvantage of CPE is the tendency of the organic binder to dissolve in solutions containing an appreciable fraction of organic solvent [14].

The term surfactant is a blend of “surface active agent”. Surfactants are usually amphiphilic organic compounds (normally possessing a hydrophobic tail and a hydrophilic head), which allow them to change the interfacial properties of liquids in which they are present. Surfactants are commonly classified into four categories, according to the formal charge present in their hydrophilic head: anionic (negatively charged), cationic (positively charged), nonionic (uncharged) and amphoteric (presents both positive and negative charges at an intermediate pH) [15]. Surfactant was widely used in electroanalytical chemistry to improve the sensitivity and selectivity [16–18]. Fig. 2 shows surfactant aggregates such as bilayers, cylinders, or surface micelles adsorbed on electrode surface in solution with surfactant concentration above the critical micelle concentration [19].

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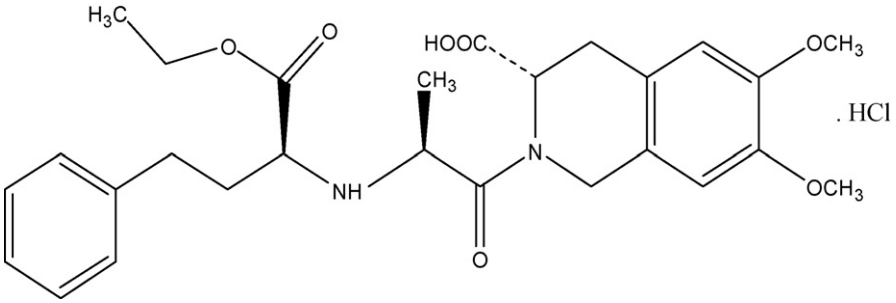

Fig. 1. Chemical structure of moxipril hydrochloride.

The literature survey revealed that no attempts have been made to study the voltammetric behavior of MOEX as an oxidation process and thus in continuation to our previous work [20–23], the aim of this study is to establish and to optimize the experimental conditions for the determination of MOEX in pure and pharmaceutical forms by using cyclic voltammetry and differential pulse voltammetry (DPV) techniques utilizing the enhancement effect of sodium dodecyl sulfate (SDS) as an anionic surfactant.

2. Experimental

2.1. Apparatus

Voltammetric measurements were carried out using a computer-driven AEW2 analytical electrochemical workstation with ECProg3 electrochemistry software (Sycopel, England) in combination with a C-2 stand with a three-electrode configuration: a carbon paste working electrode (BAS model MF-2010), an Ag/AgCl/3 mol L^{-1} NaCl reference electrode (BAS model MF-2063) and a platinum wire counter electrode (BAS model MW-1032). Origin 7.0 software was used for the transformation of the initial signal. A cyberscan 500 (EUTECH Instruments, USA) digital pH-meter with a glass combination electrode served to carry out the pH measurements.

2.2. Chemicals and reagents

Moexipril hydrochloride working standard powder was kindly supplied by Minapharm pharmaceutical company (Egypt) and was used without further purification. Primox tablets containing 15 mg MOEX per tablet, manufactured by Minapharm under license from Schwarz Pharma (Germany). Stock solution of MOEX (1.0×10^{-3} mol L^{-1}) was prepared by dissolving an appropriate amount of MOEX in methanol which was obtained from El-Nasr pharmaceutical company (Egypt). The stock solution was stored in a refrigerator. Britton-Robinson (BR) buffer was prepared by mixing the acid mixture containing phosphoric acid (0.04 mol L^{-1}), acetic acid (0.04 mol L^{-1}) and boric acid (0.04 mol L^{-1}). Buffer solutions were adjusted by adding the necessary amount of 2.0 mol L^{-1} NaOH solution in order to obtain the appropriate pH value. Graphite powder and paraffin oil were supplied from Aldrich and Sigma, respectively. The surfactant (SDS) was purchased from Aldrich was prepared as a stock solution of 1.0×10^{-2} mol L^{-1} using double distilled water and sonicated for 30 min. All chemicals were of analytical grade and used without further purification.

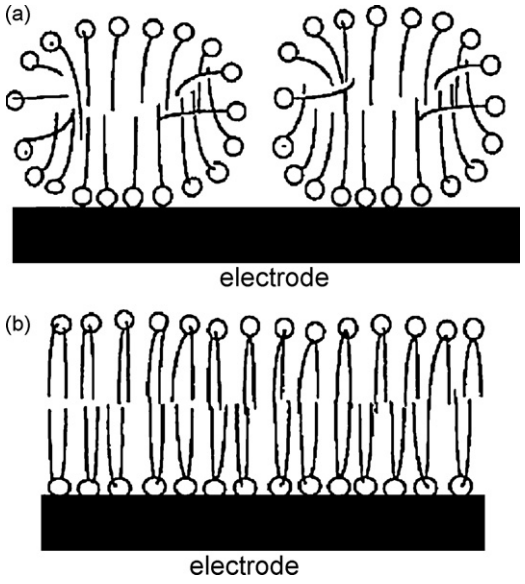

Fig. 2. Conceptual drawings of surfactant aggregates on electrode surfaces in micellar solutions: (a) side view of surface micelles or cylinders; (b) side view of a bilayer.

2.3. Preparation of the working electrode

The paste was prepared by mixing 0.5 g graphite powder and 0.3 mL paraffin oil in a mortar with a pestle. The carbon paste was packed into the hole of the electrode body and smoothed on a filter paper until it had a shiny appearance. Unless otherwise stated, the paste was carefully removed and another new CPE was remade after each measurement.

2.4. Assignment of the optimum conditions for the determination of moexipril hydrochloride

2.4.1. Effect of pH

To obtain the optimum pH, an appropriate amount of MOEX stock solution (1.0×10^{-3} mol L^{-1}) was placed in the electrolytic cell containing 5 mL of BR buffer and the cyclic voltammogram was recorded. The experiment was repeated by using buffer solutions of different pH values and the optimum pH was obtained.

2.4.2. Effect of SDS concentration

The influence of SDS concentration on the peak current (I_p) of MOEX was carried out by immersing the working electrode in BR buffer solution of the optimum pH containing an appropriate amount of 1.0×10^{-3} mol L^{-1} MOEX solution. The cyclic voltammograms were recorded at different concentrations of SDS and followed by the plot of the peak current (I_p) vs. the concentration of SDS to obtain the optimum concentration of SDS.

2.4.3. Effect of scan rate

To study the effect of scan rate (υ) on the peak current (I_p) of MOEX, the working electrode was immersed in the optimum buffer solution containing an appropriate amount of 1.0×10^{-3} mol L^{-1} MOEX solution and the cyclic voltammograms were recorded at different scan rates over the scan range from

10 to 250 mV s^{-1}. Plot $\log I_p$ vs. $\log \upsilon$ to know the nature of the process, diffusion controlled process or adsorption controlled process.

2.4.4. Effect of instrumental parameters

The optimum instrumental conditions for the determination of MOEX by using DPV method were chosen from the study of the variation of the peak current with pulse amplitude, pulse width and scan rate. During the study, each parameter was changed while the others were kept constant: pulse amplitude over the range from 25 to 100 mV, pulse width from 30 to 90 ms and scan rate from 10 to 50 mV s^{-1}.

2.5. General procedure for the determination of moexipril hydrochloride in the pure form

Three electrodes were immersed in 5 mL of BR buffer solution of the optimum pH containing an appropriate amount of SDS solution. Since dissolved oxygen did not interfere with the anodic voltammetry, no deaeration was performed. Aliquots of the drug solution (1.0×10^{-3} mol L^{-1}) were introduced into the electrolytic cell and voltammetric analyses were carried out and the voltammograms were recorded. The peak current was evaluated as the difference between each voltammogram and the background electrolyte voltammogram. All measurements were carried out at the room temperature.

2.6. Determination of moexipril hydrochloride in primox tablets

Five tablets of primox were weighed and the average mass per tablet was determined, then these tablets were powdered. A portion of the finely powder needed to obtain 1.0×10^{-3} mol L^{-1} MOEX solution was accurately weighed and transferred into 100 mL volumetric flask which contains 70 mL of methanol. The flask was sonicated for about 25 min and made up the volume with the same solvent. The solution was then filtered to separate out the insoluble excipients, rejecting the first portion of the filtrate. Aliquots of the drug solution were introduced into the electrolytic cell and the general procedure was carried out.

3. Results and discussion

3.1. Electrochemical behaviors of MOEX

To elucidate the electrode reaction of MOEX, the cyclic voltammograms at CPE were recorded at different pH values and at different scan rates. As an example, Fig. 3 shows the cyclic voltammograms of 4.0×10^{-5} mol L^{-1} MOEX solution in BR buffer of pH 7.0 in the absence and presence of 1.0×10^{-4} mol L^{-1} SDS at a scan rate of 100 mV s^{-1}. Each voltammogram exhibits one well-defined anodic peak, with no peak on the reverse scan, suggesting the irreversible nature of the electrode reaction. It is obvious from the figure that the oxidation peak current of MOEX increases greatly in the presence of SDS suggesting that SDS can significantly improve the determining sensitivity of MOEX and make the electron transfer of MOEX more easily.

3.2. Effect of pH

MOEX exhibits two pKa values of 3.05 and 5.40 [24]. The pH value of buffer solution heavily affects the existing form of MOEX and further influences its oxidation peak current. The oxidation peak current of 4.0×10^{-5} mol L^{-1} MOEX solution in the presence of 1.0×10^{-4} mol L^{-1} SDS over the pH range from 2 to 11 were examined using cyclic voltammetry. Fig. 4 shows the plot of the peak current (I_p) vs. pH. It is obvious from the figure that the peak current reaches its maximum values at pH 3.0 and 7.0, we note that the peak current at pH 7.0 is greater than that obtained at pH 3.0 and thus neutral medium is the suitable medium for the determination of MOEX by using DPV technique.

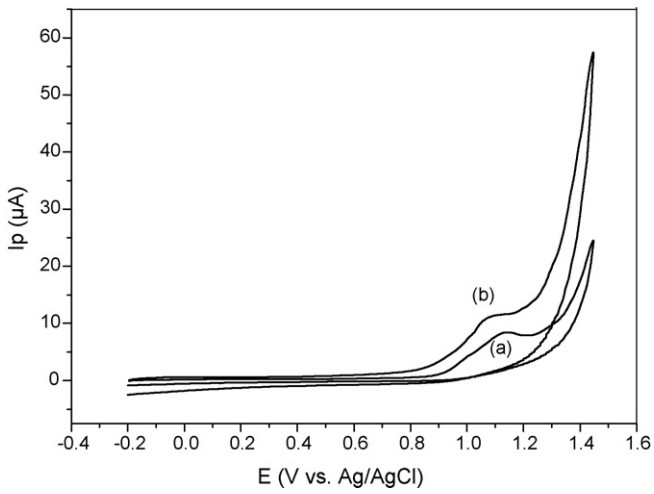

Fig. 3. Cyclic voltammograms of 4.0×10^{-5} mol L^{-1} MOEX solution in BR buffer of pH 7.0 at CPE in the absence (a) and presence of 1.0×10^{-4} mol L^{-1} SDS (b). Scan rate 100 mV s^{-1}.

3.3. Effect of SDS concentration

Although SDS can improve the oxidation peak current of MOEX, the peak current enhancement is closely related to the concentration of SDS. The relationship between the oxidation peak current of MOEX and the concentration of SDS was illustrated in Fig. 5. As gradual improving the concentration of SDS, the oxidation peak current firstly increases gradually, and then changes slightly. However, the oxidation peak current of MOEX decreases conversely when SDS concentration is higher than 1.2×10^{-4} mol L^{-1}. This may be caused by the fact that the electrostatic interaction between the negative-charged head group of SDS and cationic MOEX in solution phase drastically influences the oxidation signal by activity change of MOEX. In this paper, the concentration of SDS is chosen as 1.0×10^{-4} mol L^{-1}.

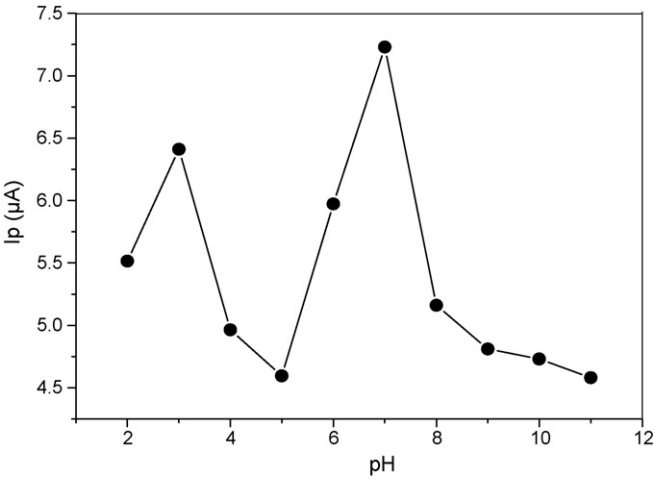

Fig. 4. Effect of pH on peak current of 4.0×10^{-5} mol L^{-1} MOEX solution in BR buffer at CPE in the presence of 1.0×10^{-4} mol L^{-1} SDS. Scan rate 100 mV s^{-1}.

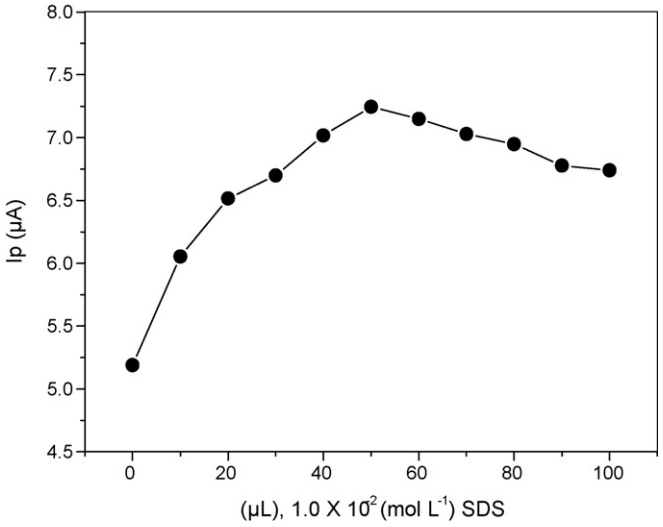

Fig. 5. Effect of the concentration of SDS on the oxidation peak current of 4.0×10^{-5} mol L^{-1} MOEX solution at CPE in BR Buffer of pH 7.0. Scan rate 100 mV s^{-1}.

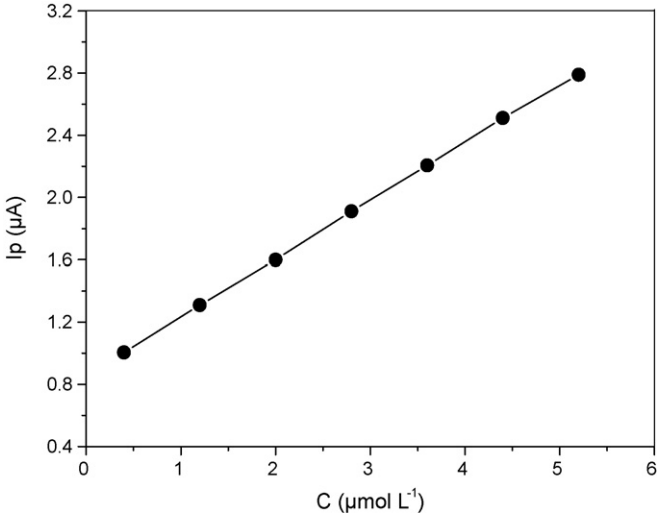

Fig. 7. Calibration curve of MOEX at CPE by using DPV method, pulse amplitude 50 mV and scan rate 20 mV s^{-1}.

3.4. Effect of scan rate

The effect of scan rate (υ) on the peak current (I_p) of MOEX was shown in Fig. 6. Linear relationship was observed between $\log I_p$ and $\log \upsilon$ over the scan range from 10 to 250 mV s^{-1} and corresponds to the following equation: $\log I_p = -0.044 + 0.48 \log \upsilon$. The slope of 0.48 is close to the theoretically expected value of 0.50 for a diffusion controlled process [25].

3.5. Effect of instrumental parameters

It was found that the peak current was increased with the increasing pulse amplitude and scan rate, while it decreased with the increasing pulse width. To obtain relatively high and narrow peaks the values of 50 mV, 30 ms and 20 mV s^{-1} were finally chosen for pulse amplitude, pulse width and scan rate, respectively.

Fig. 7.

3.6. Determination of moexipril hydrochloride in the pure form

On the basis of the electrochemical oxidation of MOEX at CPE, analytical method was developed involving DPV method for the determination of the drug under investigation. Linear relation between the peak current (I_p) and MOEX concentration (C) was found in the range from 4.0×10^{-7} to 5×10^{-6} mol L^{-1}. The calibration plot was described by the following equation:

$$I_p\,(\mu A) = 0.373C(\mu \text{mol L}^{-1}) + 0.860 \quad r^2(\text{Correlation coefficient}) = 0.9999$$

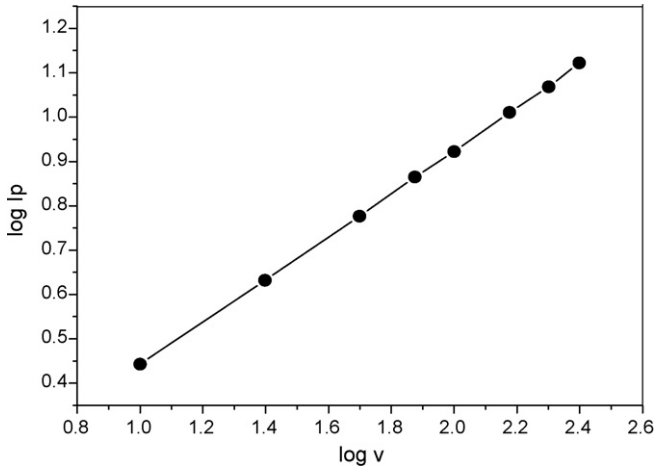

Fig. 6. Anodic peak current response of 4.0×10^{-5} mol L^{-1} MOEX solution in the presence of 1.0×10^{-4} mol L^{-1} SDS at CPE as a function of scan rate (υ) in BR Buffer of pH 7.0.

Three replicate calibration curves were obtained over the range from 4.0×10^{-7} to 5.2×10^{-6} mol L^{-1}. The limits of detection (LOD) and quantification (LOQ) were calculated by using the following equations: LOD = 3 SD/m and LOQ = 10 SD/m, where "SD" is the standard deviation of the intercept of the calibration curve and "m" is the slope of the calibration curve [26]. The LOD and LOQ were 6.87×10^{-8} mol L^{-1} and 2.29×10^{-7} mol L^{-1}, respectively.

Accuracy and precision of the proposed method were determined by replicate analyses of five different concentrations of MOEX, the results were given as shown in Table 1. The recovery was found in the range from 99.65% to 100.76% and the relative standard deviation (RSD) was in the range from 0.429% to 0.845%.

The proposed method is more sensitive than that of stability indicating reversed phase liquid chromatographic (RPLC) method 9.35×10^{-6} to 9.35×10^{-5} mol L^{-1} [6], HPLC method 9.35×10^{-7} to 2.24×10^{-5} mol L^{-1} [5], derivative spectrophotometric method 1.87×10^{-6} to 2.06×10^{-5} mol L^{-1} [5] and two spectrophotometric methods: 9.35×10^{-6} to 8.41×10^{-5} mol L^{-1} and 1.87×10^{-6} to 1.12×10^{-4} mol L^{-1} [4].

Table 1
Analytical parameters for the determination of MOEX.

Parameter	DPV method
Linearity range (mol L^{-1})	4.0×10^{-7}–5.2×10^{-6}
Calibration curve equation	I_p (μA) = 0.373C (μmol L^{-1}) + 0.860
Correlation coefficient (r^2)	0.9999
LOD (mol L^{-1})	6.87×10^{-8}
LOQ (mol L^{-1})	2.29×10^{-7}
RSD[a] (%)	0.429–0.845
Recovery (%)	99.65–100.76

[a] Five different concentration of MOEX; number of replicates (n) = 5.

Table 2
Determination of MOEX in primox tablets compared with the reference method [6].

Claimed (mg/tab)	Reference method [6] Recovery (%) ± SD[a]	DPV method Recovery (%) ± SD[a]
15	98.88 ± 0.80	99.96 ± 0.66
	F-test[b]	1.51
	t-test[b]	0.35

[a] Averaged from five determinations.
[b] Tabulated *F* and *t* values at 95% confidence level = 6.39 and 2.776, respectively [26].

3.7. Determination of moexipril hydrochloride in primox tablets

The proposed voltammetric method was successfully applied to determine moexipril hydrochloride (MOEX) in dosage form (Primox tablets) indicating that there is no interference from some common excipients used in pharmaceutical preparations such as lactose, magnesium oxide, gelatin, magnesium stearate and hydroxypropyl cellulose. The linearity range was from 4.0×10^{-7} to 5.2×10^{-6} mol L^{-1} with mean recovery of 99.98% and mean relative standard deviation of 0.77%. The results were compared with those obtained with the approved reference method [6].

The results obtained were compared statistically with those from published method [6] by using Student's *t*-test (for accuracy) and the variance ratio *F*-test (for precision). The results in Table 2 show that the *t* and *F* values were smaller than the critical values, indicating that the student *t*-test and variance ratio *F*-test excluded any significant differences between the proposed voltammetric method and the published method with respect to accuracy and precision.

4. Conclusion

SDS can be used to improve the sensitivity of determination of MOEX using CPE due to the electrostatic interaction between negative-charged head group of SDS and cationic MOEX. The proposed DPV method can be used successfully to determine MOEX in pure and pharmaceutical forms. It is a good alternative for the analytical determination of MOEX because it is simple, low cost, fast, sensitive, accurate and precise. Furthermore, the proposed procedure showed clear advantages such as low detection limit, short period of real time of drug analysis and no time consuming extraction steps were required prior to the analysis.

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