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Comparative Study of Different Modified Potentiometric Sensors for Determination of Moxifloxacin HCl in Dosage Forms

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Abstract

In situ modified carbon paste, screen-printed and PVC electrodes were fabricated for the determination of moxifloxacin hydrochloride (MOXHC). The electrodes under study revealed linear response over wide concentration range of 1.0×10^{-6} - 1.0×10^{-2} mol L^{-1} of MOXHC at 25°C with a monovalent cationic slope. It was found that the slope is 57.2 ± 2.6, 59.2 ± 4.6 and 57.7 ± 2.7 mV $decade^{-1}$for IPVC electrodes modified with 7.5 mg NaTPB, PMA and PTA ion pairing agents, respectively, and 58.6 ± 1.7, 60.0 ± 2.0 and 59.0 ± 3.3 mV $decade^{-1}$ for ISPE modified with 22, 16 and 30 mg NaTPB, RN and PTA ion pairing agents, respectively, but 60 ± 2.3 mV $decade^{-1}$ for ICPE modified with 10 mg NaTPB. Moreover, the selectivity coefficient of the electrodes was determined by applying both matched potential and separate solution methods. The modified SPE sensor shows high selectivity and sensitivity for determination of MOXHC. The response of the electrodes was found to be pH independent in the range of 2-6 for ISPEs and IPVC electrodes and 3-7 for ICPE electrode. The electrodes under study have short response time. This potentiometric method can be used for determination of MOXHC in pharmaceutical preparation and the results obtained agreed with those obtained with HPLC official method. The proposed potentiometric method was validated according to the IUPAC recommendation.

Keywords: Moxifloxacin HCl; *in situ* Modified ion selective electrodes; Carbon paste; Screen-printed; PVC electrode; Pharmaceutical preparations

Introduction

Moxifloxacin hydrochloride (MOXHC) is the common name for 1-cyclopropyl-7-[(1S,6S)-2,8-diazabicyclo[4.3.0]non-8-yl]-6-fluoro-8-methoxy-4-oxo- quinoline-3-carboxylic acid hydrochloride of molecular weight 437.891 g mol^{-1} and molecular formula $C_{21}H_{25}FN_3O_4Cl$ [1]. It is fourth-generation synthetic fluoroquinolone antibacterial agent. Moxifloxacin (MOXH) (Figure 1) is a new 8-methoxyquinolone derivate of fluoroquinolones with enhanced activity in vitro against Gram-positives bacteria and maintenance of activity against Gram-negative bacteria. The drug is rapidly absorbed, reaching maximum plasma concentrations between 1 and 4 h after oral administration. Its half-life of 11-15 h allows a daily administration. MOXH is administered to patients in 400 mg daily doses, being that the final concentrations in serum and urine for the treated patients are of 2.00-5.00 and 30.00-60.00 µg mL^{-1}, respectively [1]. Several analytical methods were previously described for determination of MOXHC drug such as electro analytical [1], spectrophotometric [2,3] and chromatographic [4-10] methods.

Potentiometric measurements are based on measuring the relative potential difference between sensing electrode and reference electrode giving information on the sample composition when there is no current flowing between them and without perturbing the sample. In contrast to other analytical techniques, the potentiometric measurements do not consume the analytes, so they are especially attractive when low total amounts are to be measured. Moreover, the analytical signal is independent upon the electrode surface area giving amenability to miniaturization. Potentiometric sensors have analytical and economic advantages including ease of fabrication, simple monitoring instrumentation, fast response, application to turbid or colored solutions, high sensitivity, wide linear dynamic ranges, low cost, and possible interfacing with flow injection analysis systems (FIA) [11-13]. The potential of these electrodes is dependent on the activity (concentration) of analyte.

CPEs have advantages of easy to prepare, fast response, easily renewable modified surface, inexpensive, and can be coupled to simple instruments. However, their limited mechanical and physical stability and degradation in non polar electrolytic solvents, leading to a deterioration of the signal, limited their use to the research laboratory (84). Further approaches are frequently made by transferring the concept from CPEs to more robust sensors, such as thick films (SPEs). Critical issues that arise with all conventional ISEs are detection limit, linear range, selectivity, operational pH, temperature and pressure

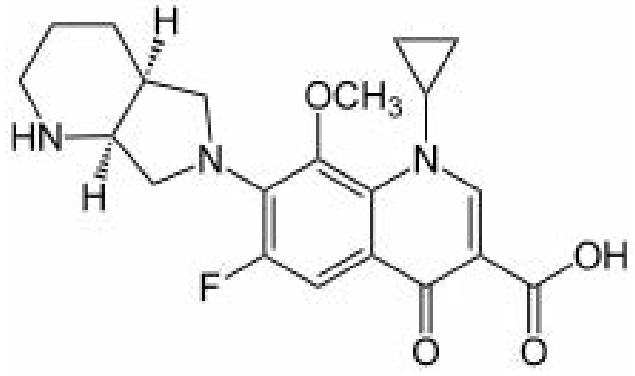

Figure 1: Structure of moxifloxacin hydrochloride.

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limits, and short life time due to leaching out of electroactive material. Moreover, they are incompatible to integrated systems. On the other hand, thick film technology includes screen printing technique which is especially suitable due to its simplicity, low cost, high reproducibility and efficiency of the large scale production (commercialization) [14-16].

At this study fabrication of modified carbon paste and in situ modified carbon paste, screen printed, PVC ion selective electrodes and the characteristics and analytical performance of them like influence of different plasticizers, ion pairing agent content, pH range, temperature and effect of the interfering cations have been investigated. The fabricated electrodes were used for determination of MOXHC in pure and pharmaceutical preparation. The parameters of method validation were optimized according to ICH guidelines.

Experimental

Reagents

All chemicals and reagents used were of analytical reagent grade and some of them were used as such without any further purification. They included moxifloxacin hydrochloride provided by EVA Company for Pharmaceutical Industry, Egypt. Relative high molecular weight polyvinyl chloride and graphite powder (synthetic 1-2 μm) were supplied from Aldrich. *o*-Nitrophenyloctylether (*o*-NPOE) and tricresylphosphate (TCP) were purchased from Fluka and Alfa Aesar, respectively. Dibutylphthalate (DBP), dioctylphthalate (DOP) and dioctylsebacate (DOS) were supplied from Merck. Ion pairing agents such as sodium tetraphenylborate (NaTPB) and ammonium reineckate (RN); $[NH_4(Cr(NH_3)_2(SCN)_4).H_2O]$ were supplied from Fluka. Phosphotungstic acid (PTA); $H_3[PW_{12}O_{40}]$ and phosphomolybdic acid (PMA); $H_3[PMo_{12}O_{40}]$, were purchased from BDH. Acetone, cyclohexanone and tetrahydrofuran were supplied from Aldrich Company, Egypt.

Apparatus

Laboratory potential measurements were performed using HANNA 211 pH meter. Silver-silver chloride double - junction reference electrode (Metrohm 6.0222.100) in conjugation with different drug ion selective electrodes was used. pH measurements were done using Jenway 3505 pH meter. Digital multimeter connected to a portable PC and Brand digital burette was used for the measurement of the drug under investigation. In the present work, modified and in situ modified screen printed, PVC and carbon paste electrodes were constructed as potentiometric sensors using homemade printing carbon ink as well as comparing the performance characteristics of such electrodes in determination of MOXHC in pure and pharmaceutical preparations.

Preparation of the working electrodes

Preparation of the screen printed electrodes: A manual screen printer was used to produce disposal SPEs. An array of 12 electrodes was printed on a flexible X-ray film by forcing the prepared conductive ink to penetrate through the mesh of a screen stencil. The screen printing electrodes involved several stages which were described in details below [17].

Selection of the screen template: A screen consisting of a heavy duty polyester fabric (I 003 M Sefar Pet 1000 with mesh count of 36) was pretensioned to ca 30x40 cm wooden frame. For the stainless steel template, steel sheet were pretensioned to a steel frame and contain grooves with the same electrode dimensions [18,19].

Preparation of the graphite ink suspension: The working screen printed electrodes were printed using homemade carbon ink which was prepared using 5-25 mg ion pairing agent (NaTPB, PMA, RN, or PTA) in 900 mg TCP and 2.5 g of 8% PVC solution. 1.5 g carbon powder was added under continuous mechanical mixing conditions until complete uniformity of the formed ink. After complete mixing of the ink components with a magnetic stirrer, the prepared ink was sonicated for 45 min to improve its homogeneity and remove air bubbles [18,19].

Printing of the screen printed electrodes (SPEs): A polyester sheet (sheet for X ray cleaned with conc. HNO_3 and washed several time with water and then cleaned with commercial thinner) was used as a substrate which was not affected by the curing temperature or the ink solvent and easily cutted by scissors. The well mixed graphite ink was poured onto the mesh and forced into the mesh with the aid of a 6 inch squeegee held at angle of approximately 60°C and mesh was held away from the polyester sheet. The squeegee was then pulled back across the template; this ensured the electrode templates were fully load with the ink. The wooden frame was pushed down onto the polyester sheet and the squeegee drawn across the template in a single swift action, which forced the ink through the mesh and onto the polyester sheet. The stencil frame was then released, revealing the electrodes printed onto the polyester sheet. The electrodes were cured at 60°C for dry and then cut out from the substrate. After finishing the printing process the stencil was cleaned with commercial thinner solution in order to remove the excess of ink within the template.

Preparation of carbon paste electrodes (CPEs): Carbon paste electrodes were prepared by intimate mixing different amounts (5-25 mg) of ion pairing agents with carbon powder (250 mg) and TCP (100 μL). Then this mixture was thoroughly mixed in the mortar until to achieve homogenization of this mixture. The resulting paste was then packed firmly into the hole of the electrode body [20]. The surface of the resulting carbon paste electrode was polished using a filter paper to obtain new working surface and rinsed carefully with double distilled water.

PVC electrodes construction: The membrane cocktails are prepared by dissolving the recognition element with a plasticizer and the polymeric matrix (PVC) in THF till homogeneous transparent solution is obtained, then poured in a Petri dish (5 cm diameter) and covered with a filter paper. Slow evaporation of THF at room temperature over 24 h leaves a flexible membrane of about 100 μm thickness. The master sheet is cut with a cork borer and mounted at the end of plastic tube filled with 10^{-3} mol L^{-1} drug solution and 0.1 mol L^{-1} KCl, as desired for establishing the potential of internal Ag/AgCl wire. To investigate the effect of the internal filling solution composition, different solutions of pure MOXHC (10^{-4} to 10^{-2} mol L^{-1}) mixed with KCl (0.1 mol L^{-1}) were tested. Results revealed that filling solution composition had no significant effect on the electrode potential response, except for the intercept. A mixture of 10^{-3} mol L^{-1} MOXHC/ 0.1 mol L^{-1} KCl was chosen as an internal filling solution and hence used in all subsequent studies throughout the work.

Potential measurements

The sample solutions were stirred and thermostated at room temperature. The response of the sensor for $MOXH^+$ was examined by measuring electromotive force (emf) of the following electrochemical cell: Ag | AgCl | satd. KCl || sample solution | MCPE; ICPE, IPVC or ISPE. The emf was plotted as a function of the logarithm of MOXHC concentration. Dilute MOXHC solutions (from 1.0×10^{-2} to 1.0×10^{-7}

mol L^{-1}) were prepared by serial dilution of 10^{-2} mol L^{-1} MOXHC stock solution. The detection limit was taken at the point of intersection of the extrapolated linear segments of the calibration curve.

Results and Discussion

To estimate the performance of the in situ modified screen printed, carbon paste and PVC electrodes; their basic analytical parameters were established including the electrode composition, slope characteristics, type of plasticizer, detection limit, response time, selectivity and dependence of the electrode potential on the solution pH and temperature.

Effect of the ion pairing agent content

In order to determine the suitable content of ion pairing agents (NaTPB, PMA, PTA, and RN) several SPE, CPE and PVC electrodes were prepared containing usually 5-25 mg of ion pairing agents. The results obtained are listed in Tables 1,2 and represented graphically in Figure 2. It is clear from these data that the electrodes have slope values of 57.2 ± 2.6, 59.2 ± 4.6 and 57.7 ± 2.7 mV decade^{-1} for IPVCs modified with 7.5 mg NaTPB, PMA and PTA ion pairing agents, respectively, and 58.6 ± 1.7, 60.0 ± 2.0 and 59.0 ± 3.3 mV decade^{-1} for ISPE modified with 22, 16 and 30 mg NaTPB, RN and PTA ion pairing agents, respectively. But, ICPE electrode modified with 10 mg NaTPB was found to have a slope of 60 ± 2.3 mV decade^{-1}.

NaTPB (mg)	Concentration range (mol L^{-1})	Slope (mV decade^{-1})	R
5	$1.0x10^{-6}$– $1.0x10^{-2}$	71.0 ± 1.8	0.999
7.5	$1.0x10^{-6}$– $1.0x10^{-2}$	67.0 ± 3.1	0.999
10	$1.0x10^{-6}$– $1.0x10^{-2}$	60.0 ± 2.3	0.999
12.5	$1.0x10^{-6}$– $1.0x10^{-2}$	55.0 ± 3.1	0.999
15	$1.0x10^{-6}$– $1.0x10^{-2}$	50.0 ± 1.0	0.999
20	$1.0x10^{-6}$– $1.0x10^{-2}$	45.7 ± 2.7	0.999
25	$1.0x10^{-6}$– $1.0x10^{-2}$	40.5 ± 2.4	0.998

Table 1: Effect of NaTPB content on the performance of ICPEs.

Effect of plasticizer type

Plasticizers are considered to have an important role in the behaviour of ISEs. They enhance the ionic mobility, improve the solubility of the sensing material and lower the overall bulk resistance of the electrode due to their polarity characteristics. Using of plasticizer facilitates the screen printing process and maintaining good electrochemical characteristics. The role of plasticizer type on the electrode performance was evaluated using electrodes plasticized with DBP, *o*-NPOE, TCP, DOS and DOP for CPEs, PVCs and SPEs, respectively. The results giving in Table 3 showed that the best performance is obtained with the electrodes prepared using TCP and *o*-NPOE plasticizers.

Effect of pH

The potentiometric response of the electrode was found to be sensitive to pH changes. Hence, the pH dependence of the potentials of the proposed sensor were investigated in the pH range of 1-12 for 1×10^{-2} and 1×10^{-4} mol L^{-1} MOXHC ion solutions, The pH of the test solution was adjusted by the addition of 0.1 mol L^{-1} NaOH or HCl. The results listed in Table 4 showed that the potential response remains constant over the pH range of 2-6 for ISPE and IPVC electrodes, but it was 3-7 for ICPE.

Effect of temperature

In order to determine the isothermal coefficient of the electrode (dE^o/dt), the standard electrode potentials (E^o) were determined from the calibration graph as the intercepts at p[MOXHC] = 0, of electrodes at different temperatures (10, 20, 30, 40, 50 and 60°C) and plotted versus (t-25), where (t) is the temperature of the experiment in degree

	IPVC			ISPE		
Concentration range (mol L^{-1})	Content (mg)	Slope (mV decade^{-1})	R	Content (mg)	Slope (mV decade^{-1})	R
	NaTPB			NaTPB		
$1.0x10^{-6}$– $1.0x10^{-2}$	5	47.0 ± 2.1	0.999	5	35.0±0.9	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	7.5	57.2 ± 2.6	0.999	7.5	38.2 ± 1.8	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	10	53.2 ± 1.8	0.999	10	48.0 ± 2.3	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	12.5	49.0 ± 2.5	0.999	12.5	50.0 ± 3.1	0.998
$1.0x10^{-6}$– $1.0x10^{-2}$	15	42.0 ± 1.7	0.999	16	54.3 ± 3.0	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	20	40.0 ± 1.3	0.999	22	58.6 ± 1.7	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	25	37.0 ± 1.8	0.999	30	52.1 ± 3.6	0.999
	PMA			RN		
$1.0x10^{-6}$– $1.0x10^{-2}$	5	51.0 ± 2.8	0.999	6	34.3 ± 1.6	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	7.5	59.2 ± 4.6	0.996	12	42.7 ± 2.7	0.998
$1.0x10^{-6}$– $1.0x10^{-2}$	10	54.7 ± 2.8	0.999	16	60.0 ± 2.0	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	12.5	53.0 ± 0.2	0.999	22	49.0 ± 2.0	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	15	50.0 ± 2.8	0.999	30	45.0 ± 3.1	0.998
$1.0x10^{-6}$– $1.0x10^{-2}$	20	49.0 ± 2.3	0.999			
$1.0x10^{-6}$– $1.0x10^{-2}$	25	52.0 ± 1.7	0.999			
$1.0x10^{-6}$– $1.0x10^{-2}$	PTA			PTA		
	5	51.6 ± 2.0	0.999	6	22.1 ± 0.9	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	7.5	57.7 ± 2.7	0.999	12	40.4 ± 1.7	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	10	53.0 ± 1.8	0.999	16	46.0 ± 1.8	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	12.5	49.0 ± 2.6	0.999	22	52.8 ± 2.7	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	15	45.0 ± 2.5	0.999	30	59.0 ± 3.3	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	20	43.1 ± 1.7	0.999	35	52.7 ± 1.6	0.999
$1.0x10^{-6}$– $1.0x10^{-2}$	25	40.0 ± 2.0	0.999			

Table 2: Effect of ion pairing agent type on the performance of IPVC and ISPE electrodes.

plasticizer type	Slope (mV decade^{-1})	R
o-NPOE	58.2 ± 1.30	0.998
TCP	58.2 ± 1.40	0.999
DBP	52.3 ± 1.60	0.997
DOS	54.8 ± 1.60	0.997
DOP	50.7 ± 1.70	0.998

Table 3: Effect of plasticizer type on the performance of ICPE modified with 10 mg NaTPB.

Electrode	Modifier	pH range	isothermal Coefficients(V/°C)
ISPE	22 mg NaTPB	2.0–6.0	0.267
ISPE	16 mg RN	2.0–6.0	0.319
ISPE	30 mg PTA	2.0–6.0	0.291
IPVC	7.5 mg TPB	2.0–6.0	0.279
IPVC	7.5 mg PMA	2.0–6.0	0.329
IPVC	7.5 mg PTA	2.0–6.0	0.226
ICPE	10 mgNaTPB	3.0–7.0	0.269

Table 4: pH working range and isothermal coefficients of the proposed electrodes.

Method	Interfering ion	$K^{pot}_{D,B}$ ICPE (10 mg NaTPB)	$K^{pot}D,B$ IPVC (7.5 mg NaTPB)	$K^{pot}_{D,B}$ IPVC (7.5 mg of PMA)	$K^{pot}_{D,B}$ IPVC (7.5 mg PTA)
MPM	Glucose	1.7 x10^{-4}	5.1 x10^{-4}	1.2 x10^{-4}	9.3 x10^{-6}
	Fructose	4.6 x10^{-4}	7.0 x10^{-4}	1.6 x10^{-4}	4.6 x10^{-5}
	Maltose	5.0 x10^{-4}	3.8 x10^{-4}	1.1 x10^{-4}	5.4 x10^{-5}
	Lactose	4.4 x10^{-4}	8.3 x10^{-4}	1.9 x10^{-4}	4.4 x10^{-5}
	Sucrose	3.6 x10^{-4}	9.7 x10^{-4}	2.8 x10^{-4}	6.3 x10^{-5}
	Starch	8.2 x10^{-5}	2.2 x10^{-4}	2.1 x10^{-4}	4.9 x10^{-6}
	Glycine	1.3 x10^{-4}	7.6 x10^{-4}	3.9 x10^{-4}	4.2 x10^{-5}
SSM	Na+	5.6 x10^{-5}	5.0 x10^{-6}	5.9 x10^{-6}	2.9 x10^{-6}
	Cd^{2+}	2.7 x10^{-4}	1.2 x10^{-4}	1.6 x10^{-4}	6.4 x10^{-5}
	K+	3.8 x10^{-5}	3.9 x10^{-6}	4.7 x10^{-6}	1.8 x10^{-6}
	Mg^{2+}	2.6 x10^{-4}	1.1 x10^{-4}	1.4 x10^{-4}	4.7 x10^{-5}
	Zn^{2+}	3.2 x10^{-4}	1.4 x10^{-4}	1.7 x10^{-4}	6.7 x10^{-5}
	Ni^{2+}	1.7 x10^{-4}	1.5 x10^{-4}	1.8 x10^{-4}	8.5 x10^{-5}
	Mn^{2+}	2.9 x10^{-4}	1.0 x10^{-4}	1.3 x10^{-4}	5.3 x10^{-5}
	Ba^{2+}	2.1 x10^{-4}	2.8 x10^{-4}	2.0 x10^{-4}	4.5 x10^{-5}
	Fe^{3+}	1.2 x10^{-4}	2.7 x10^{-4}	3.6 x10^{-4}	1.3 x10^{-4}
	Pb^{2+}	1.1 x10^{-4}	1.5 x10^{-4}	1.5 x10^{-4}	7.3 x10^{-5}
	Al^{3+}	8.9 x10^{-4}	1.9 x10^{-4}	3.4 x10^{-4}	1.8 x10^{-4}
	Cr^{3+}	1.1 x10^{-4}	2.7 x10^{-4}	3.9 x10^{-4}	3.3 x10^{-4}
	Cu^{2+}	5.6 x10^{-5}	7.3 x10^{-4}	1.1 x10^{-4}	7.9 x10^{-5}

Table 5: Selectivity coefficients values for ICPE and IPVC electrodes.

centigrade and according to the following equation [21] :

$$E^{\circ}_{cell} = E^{\circ}_{cell(25^{\circ}C)} + \left[\left(dE^{\circ} \right)_{cell} / dt \right] + (t - 25)$$

A straight line was obtained and the slope of this line represents the isothermal coefficient of the electrodes which were found to be 0.267, 0.319 and 0.291 V/°C for ISPE modified with NaTPB, RN and PTA, respectively, and 0.279, 0.329, 0.226 V/°C for IPVC modified with NaTPB, PMA and PTA but it was 0.269 V/°C for IPCE modified with NaTPB. The obtained values of the isothermal coefficient which listed in Table 4 reveal that the electrodes under investigation had high thermal stability within the used range of temperature. The investigated electrodes can be used up to 60°C without noticeable deviation from the Nernstian behaviour.

Selectivity and interference studies

Potentiometric selectivity coefficient refers to the ability of the ISE to differentiate a particular primary ion from other interfering ions [22-24]. The selectivity behaviour is obviously one of the important characteristics of SPE, CPE and PVC sensors in which reliable measurement of the target drug is determined to be possible or not. The potentiometric selectivity coefficients ($K^{pot}_{D,B}$) were determined according to IUPAC recommendations using the separate solutions (SSM) and matched potential (MPM) methods. In matched potential method (MPM), the selectivity coefficient is defined as the activity ratio of the primary ion and interfering ion which give the same potential change in a reference solution. This method does not require Nernstian responses to the activity (concentration) of either primary or interfering ions. It is a suitable method for determination of selectivity coefficients of the neutral compounds. The selectivity coefficients (log $K^{pot}_{D,B}$) of the SPE, CPE and PVC were determined employing separate solution method (SSM) with the rearranged Nicolsky equation [25,26]:

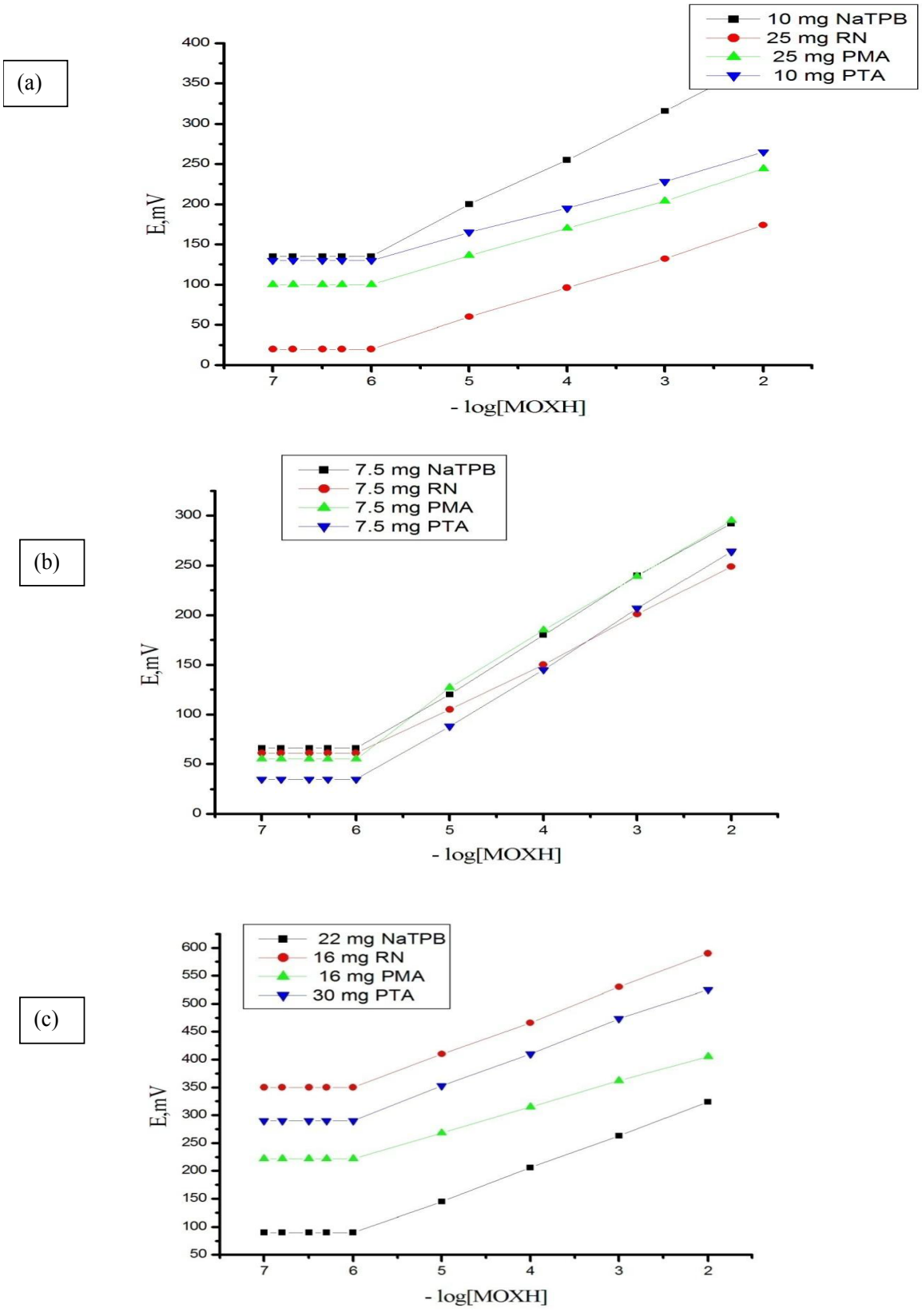

Figure 2: Effect of ion pairing agent type on the performance of (a) ICPEs; (b) IPVC and (c) ISPE.

Method	Interfering ion	$K^{pot}_{D,B}$ ISPE (22 mg NaTPB)	KpotD,B ISPE (30 mg PTA)	$K^{pot}_{D,B}$ ISPE (16 mg RN)
MPM	Glucose	4.9 x10^{-4}	8.3 x10^{-3}	3.6 x10^{-3}
	Fructose	4.2 x10^{-4}	7.3 x10^{-3}	8.8 x10^{-3}
	Maltose	2.9 x10^{-4}	5.8 x10^{-3}	6.2 x10^{-3}
	Lactose	2.7 x10^{-4}	5.6 x10^{-3}	1.3 x10^{-3}
	Sucrose	8.9 x10^{-4}	6.5 x10^{-3}	3.2 x10^{-3}
	Starch	8.2 x10^{-4}	5.0 x10^{-3}	2.9 x10^{-3}
	Glycine	9.6 x10^{-4}	4.4 x10^{-3}	7.6 x10^{-4}
SSM	Na+	4.1 x10^{-5}	3.9 x10^{-5}	8.8 x10^{-5}
	Cd^{2+}	2.7 x10^{-4}	1.2 x10^{-3}	9.8 x10^{-3}
	K^{+}	7.2 x10^{-5}	5.6 x10^{-5}	1.1 x10^{-4}
	Mg^{2+}	4.8 x10^{-3}	1.6 x10^{-3}	2.1 x10^{-3}
	Zn^{2+}	5.6 x10^{-3}	7.0 x10^{-4}	1.6 x10^{-3}
	Ni^{2+}	1.6 x10^{-3}	8.5 x10^{-4}	2.4 x10^{-3}
	Mn^{2+}	1.9 x10^{-3}	8.2 x10^{-4}	3.4 x10^{-3}
	Ba^{2+}	2.5 x10^{-3}	9.2 x10^{-4}	2.2 x10^{-3}
	Fe^{3+}	1.2 x10^{-4}	1.8 x10^{-4}	1.4 x10^{-4}
	Pb^{2+}	2.4 x10^{-3}	1.9 x10^{-4}	1.2 x10^{-3}
	Al^{3+}	1.1 x10^{-4}	1.5 x10^{-4}	1.2 x10^{-4}
	Cr^{3+}	1.1 x10^{-4}	1.3 x10^{-4}	1.0 x10^{-4}
	Cu^{2+}	1.4 x10^{-3}	2.3 x10^{-4}	1.5 x10^{-3}

Table 6: Selectivity coefficients values for ISPE electrodes.

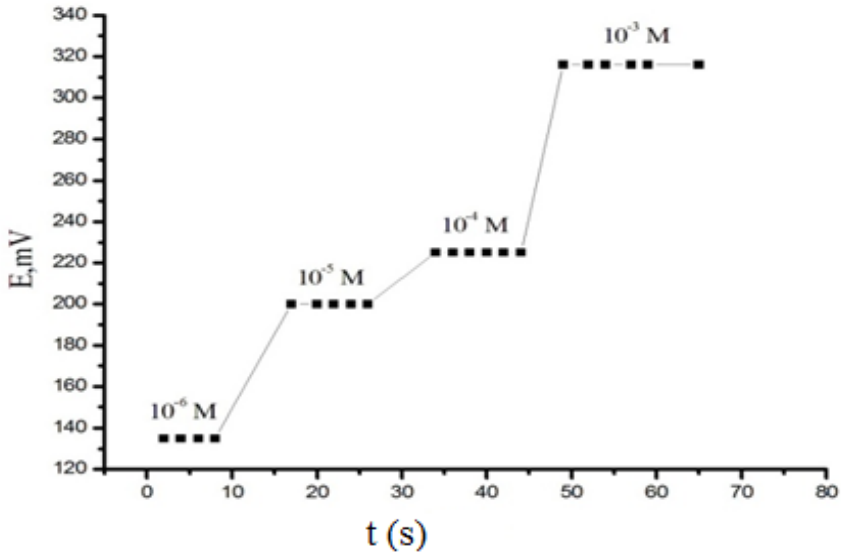

Figure 3: The dynamic response time of ICPE modified with 10 mg NaTPB ion pairing agent.

$$\log K^{pot}_{D,B} = \frac{(E_1 - E_2)}{S} + \left(1 + \frac{z_1}{z_2}\right)\log a$$

where, E_1 is the potential measured in 1.0x10^{-3} mol L^{-1} MOXHC (D), E_2 the potential measured in 1.0x10^{-3} mol L^{-1} of the interfering compound (B), z_1 and z_2 are the charges of the MOXHC (D) and interfering species (B), respectively, and S is slope of the electrode calibration plot. The results obtained are summarized in Tables 5,6.

The results obtained showed no significant interference and this reflects a very high selectivity of the electrodes under investigation towards MOXHC. The results also indicated that no serious interference from glucose, maltose, fructose, starch and lactose. The inorganic cations did not interfere due to the differences in their ionic size and hence their mobilities, polarities, and permeabilities as compared to those of $MOXH^+$ cation.

Response time

The response time is important factor which characterize ISEs. It can be defined as the time taken by the electrodes to reach steady potential values of 90% of the final equilibrium values, after successive immersions in a series of solutions, each having a 10-fold concentration difference [27-31]. The dynamic response time of the sensors under study was determined for the concentration range from 1.0 x10^{-6} to

1.0 x 10^{-3} mol L^{-1}. The response time of the electrodes were found to be 5.0, 5.3 and 4.6 s for ISPE modified with NaTPB, RN and PTA ion pairing agents, respectively, and 7.6, 7.0 and 5.6 s for IPVC modified with NaTPB, PMA and PTA, respectively, and 7.3 s for ICPE modified with NaTPB. So the best electrodes which have lower response time are SPEs (Figures 3-5).

Lifetime

The lifetime of the investigated sensors; ICPEs, IPVCs and ISPEs, was studied by periodically constructing the calibration graphs under optimum conditions on different days using the investigated sensors. it was clear that life time were found to be 88, 91 and 81 days for ISPE modified with NaTPB, RN and PTA, respectively, 13, 17 and 15 days for IPVC modified with NaTPB, PMA and PTA, respectively, and 47 days for ICPE modified with NaTPB. Figures 6-8 showed that there is no significant change in slopes of the calibration graphs. After this period, the slope of the calibration graph decreased. A shiny new surface is obtained every time for measurement using CPE by squeezing out small portion of the paste and polishing it on filter paper. After preparation of SPEs, they were kept at 4 °C and directly used for potentiometric measurements.

Analytical application

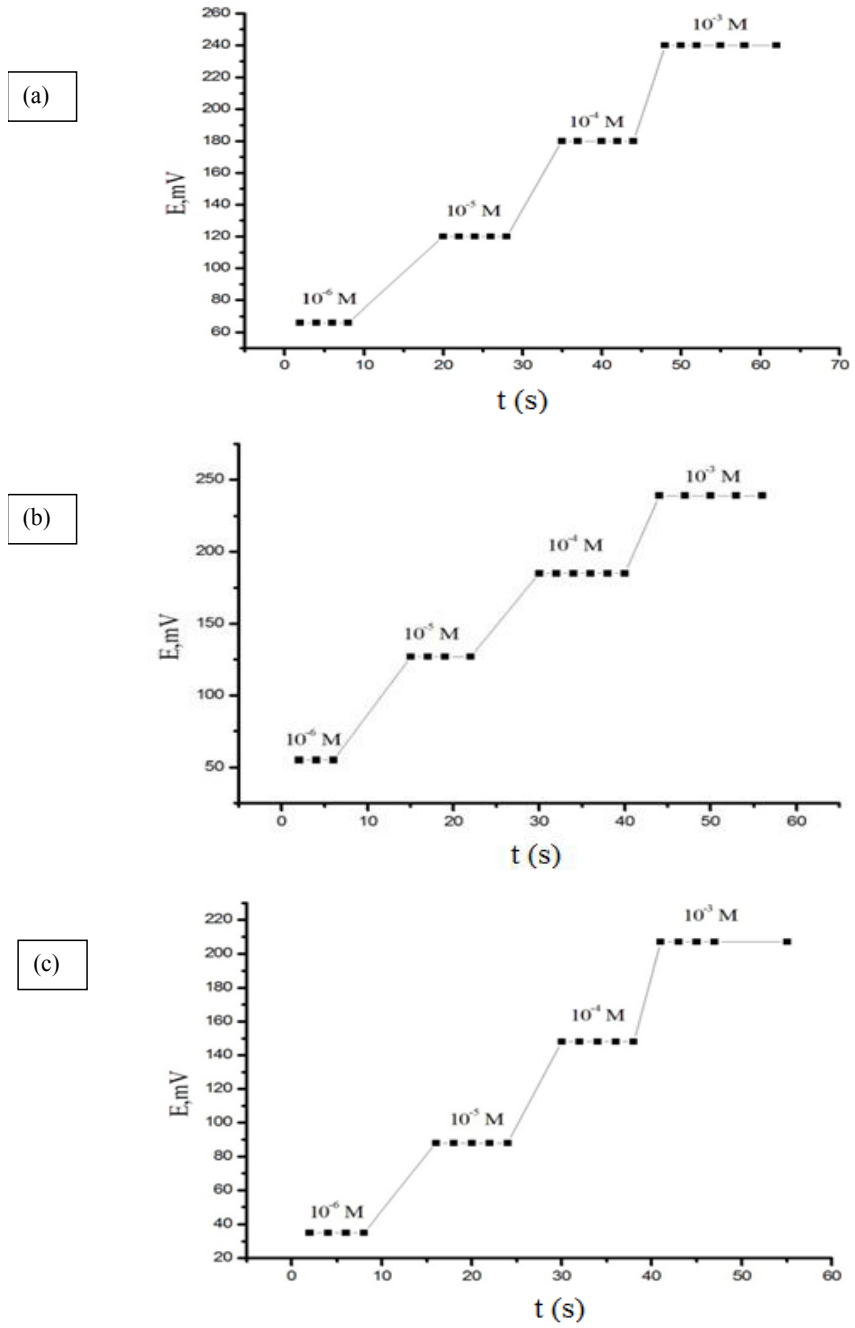

Figure 4: The dynamic response time of IPVC modified with (a) 7.5 mg NaTPB; (b) 7.5 mg PMA and (c) 7.5 mg PTA ion pairing agents.

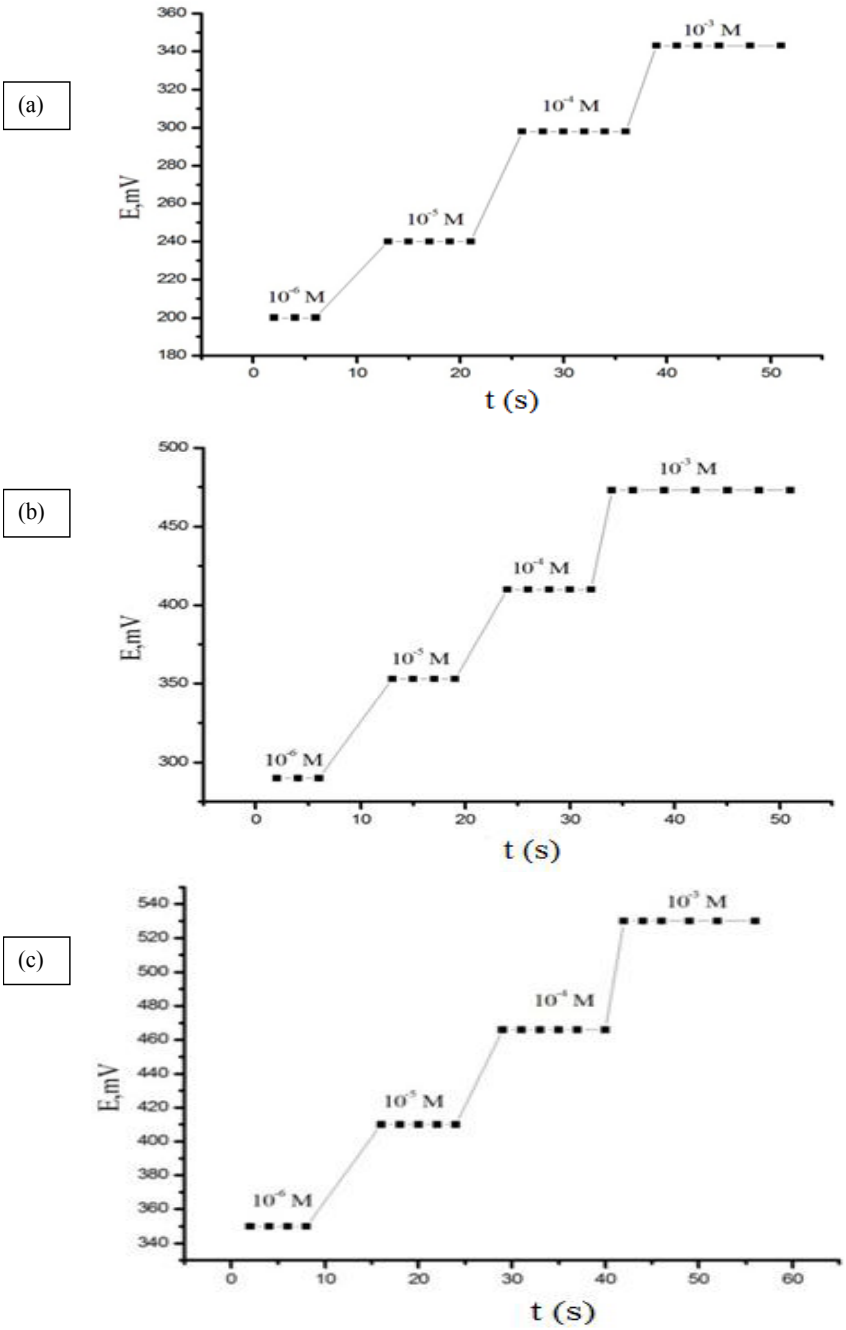

Figure 5: The dynamic response time of ISPE modified with (a) 22 mg NaTPB; (b) 30 mg PTA and (c) 16 mg RN ion pairing agents.

The proposed electrodes were applied for the potentiometric determination of MOXHC drug in pure and pharmaceutical preparations. The results obtained were compared with the official method and the data obtained were listed in Table 7.

Method validation

Electro analytical method validation is the process used to confirm that the determination procedure employed for a specific test is suitable for its intended use like other analytical methods [32]. Validation parameters of accuracy, precision, linearity, specificity and limit of detection and quantification were achieved using a standard MOXHC stock solution. Inter- and intra-day accuracy and precision were carried out and the data obtained were listed in Table 8. The low values of standard deviation and relative standard deviation indicate the high accuracy and precision of the proposed potentiometric method.

Conclusion

The proposed in situ modified SPE, CPE and PVC electrodes might be useful detectors and interesting alternative methods for the determination of [$MOXH^+$] in different real samples. The fabricated

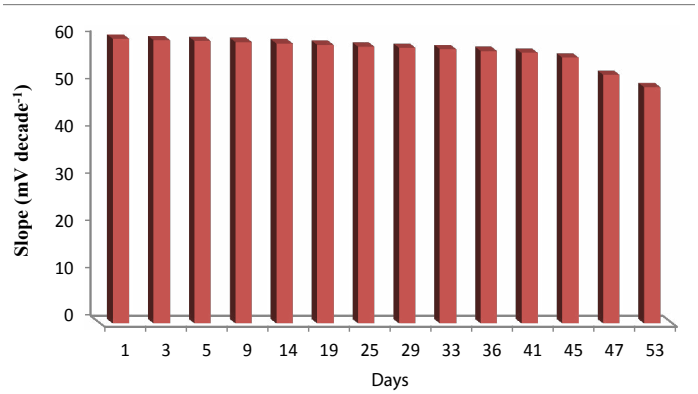

Figure 6: Life time of the paste for ICPE modified with 10 mg NaTPB ion paring agent.

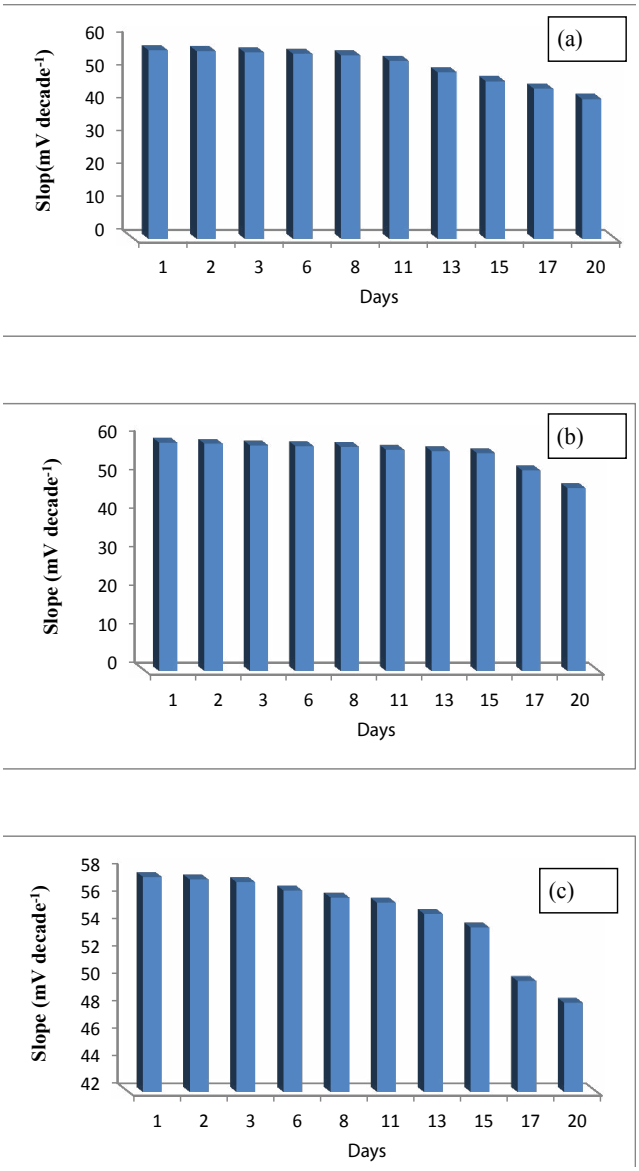

Figure 7: Life time of IPVC modified with (a) 7.5 mg NaTPB, (b) 7.5 mg PMA and (c) 7.5 mg PTA ion paring agents.

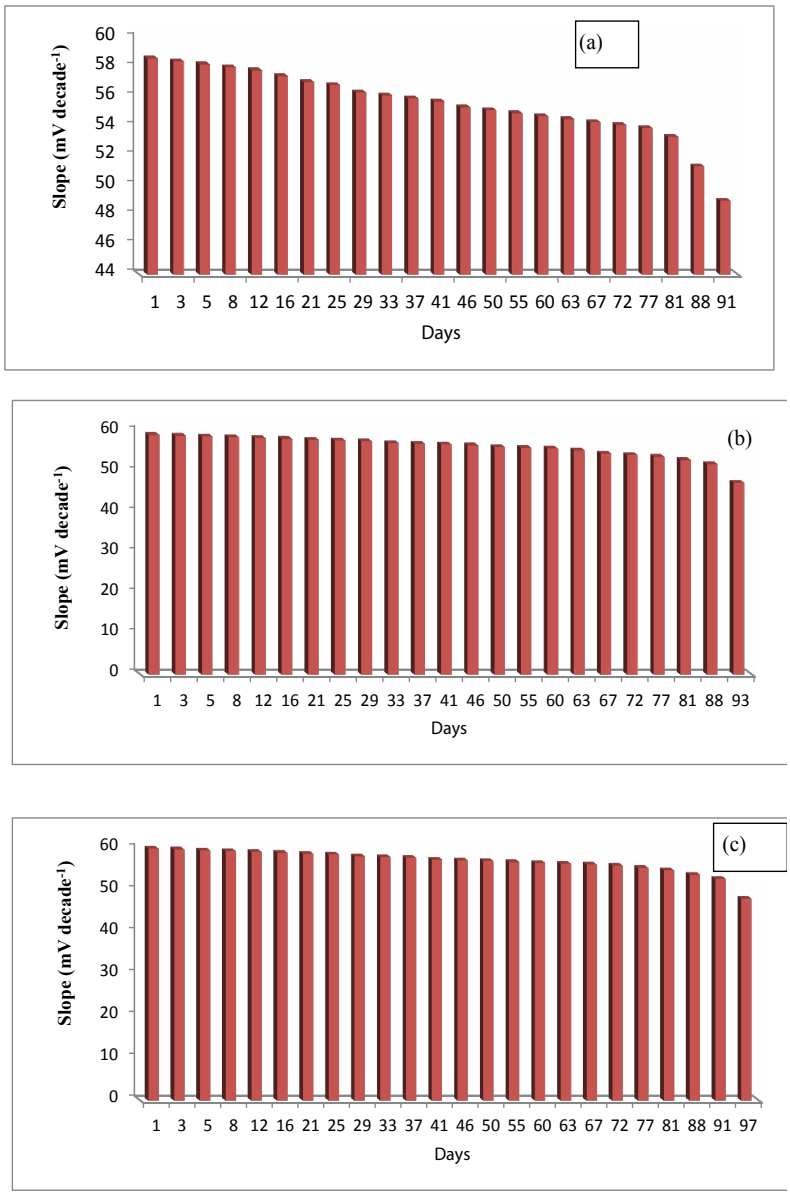

Figure 8: Life time of ISPE modified with (a) 22 mg NaTPB; (b) 30 mg PTA and (c) 16 mg RN ion paring agents.

electrodes showed high sensitivity, reasonable selectivity, fast static response, long-term stability and applicability over a wide pH range with minimal sample pre-treatment. The presented potentiometric methods for the determination of MOXH hydrochloride with the prescribed electrodes are simple, sensitive, highly specific and advantageous over the previously described procedures for MOXHC determinations in pure form and pharmaceutical formulation (Table 9).

Electrode type	[MOXHC][a] taken$_{-1}$ mg mL	SD (RSD%)		Recovery %		[MOXHC] found mg mL^{-1}		Standard official method [c]			
		SAM[b]	Calibration	SAM[b]	Calibration	calibration	SAM[b]	RSD% (n = 5)	Recovery %))	[MOXHC] found$_{-1}$ mg mL	[MOXHC] taken$_{-1}$ mg mL
ISPE (22 mg NaTPB)	0.306	0.005 (1.909)	0.005 (1.79)	94.28	96.40	0.288	0.295	0.243	99.60	2.180	2.189
	2.189	0.004 (0.188)	0.004 (0.213)	99.76	99.37	2.183	2.175				
ISPE (16 mg RN)	0.306	0.002 (1.002)	0.006 (2.169)	97.30	97.41	0.297	0.297				
	2.189	0.004 (0.198)	0.004 (0.186)	99.40	99.20	2.176	2.171				
ISPE (30 mg PTA)	0.306	0.005 (1.802)	0.006 (2.095)	97.05	94.41	0.297	0.289				
	2.189	0.005 (0.228)	0.004 (0.212)	99.74	99.93	2.183	2.187				
IPVC 7.5 mg NaTPB	0.306	0.004 (1.417)	0.002 (0.981)	96.89	98.03	0.296	0.300				
	2.189	0.006 (0.295)	0.008 (0.369)	99.93	100.11	2.187	2.191				
IPVC (7.5 mg PMA)	0.306	0.003 (1.161)	0.004 (1.589)	98.44	95.50	0.301	0.292				
	2.189	0.005 (0.249)	0.007 (0.339)	99.74	99.36	2.183	2.175				
IPVC (7.5 mg PTA)	0.306	0.005 (1.813)	0.004 (1.384)	95.91	95.17	0.293	0.291				
	2.189	0.007 (0.360)	0.006 (0.304)	99.47	99.24	2.177	2.172				
ICPE (10 mg NaTPB)	0.306	0.007 (2.372)	0.004 (1.443)	98.20	96.07	0.300	0.294				
	2.189	0.003 (0.169)	0.004 (0.187)	99.88	100.01	2.186	2.189				

[a]**Average of five replicate (n = 5)** [b]**Standard addition method** [c]**Standard official method**

Table 7: Potentiometric determination of MOXHC in pure and pharmaceutical preparation by calibration and SAM methods using modified ICPE, ISPE and IPVC sensors.

Drug	Electrode type	[MOXH] Taken$_{i,1}$ mg mL	Intra-day				Inter-day			
			Found$_{i,1}$ mg mL	Recovery%	SD	RSD%	Found$_{i,1}$ mg mL	Recovery%	SD	RSD%
Pure MOXH	ISPE 22 mg NaTPB	0.306	0.303	99.26	0.004	1.354	0.300	98.03	0.005	1.865
		2.189	2.178	99.52	0.008	0.370	2.194	100.23	0.003	0.172
	ISPE 16 mg RN	0.306	0.291	99.17	0.003	1.326	0.296	96.97	0.006	2.047
		2.189	2.186	99.88	0.005	0.265	2.180	99.61	0.005	0.244
	ISPE 30 mg PTA	0.306	0.294	96.16	0.007	2.518	0.300	98.12	0.005	1.749
		2.189	2.189	100.02	0.002	0.131	2.191	100.10	0.004	0.198
	IPVC 7.5 mg NaTPB	0.306	0.296	96.89	0.007	2.470	0.291	98.34	0.005	1.843
		2.189	2.170	99.15	0.005	0.267	2.180	99.62	0.005	0.237
	IPVC 7.5 mg PMA	0.306	0.290	98.00	0.014	4.955	0.288	97.36	0.003	1.337
		2.189	2.180	99.58	0.004	0.194	2.171	99.18	0.003	0.152
	IPVC 7.5 mg PTA	0.306	0.294	97.24	0.003	1.055	0.298	97.38	0.006	2.340
		2.189	2.182	99.71	0.006	0.285	2.179	9.50	0.007	0.333
	ICPE 10 mg NaTPB	0.306	0.302	98.85	0.006	2.028	0.303	99.26	0.005	1.869
		2.189	2.181	99.66	0.004	0.212	2.176	99.41	0.002	0.137
Idlox tablet	ISPE 22 mgNaTPB	0.306	0.305	99.91	0.005	1.738	0.293	97.99	0.008	2.826
		2.189	2.177	99.47	0.006	0.276	2.177	99.47	0.004	0.193
	ISPE 16 mg RN	0.306	0.294	96.32	0.007	2.514	0.298	97.46	0.005	1.981
		2.189	2.168	99.06	0.003	0.170	2.189	100.03	0.004	0.187
	ISPE 30 mg PTA	0.306	0.301	98.61	0.003	1.159	0.296	96.97	0.003	1.179
		2.189	2.165	98.92	0.005	0.254	2.183	99.72	0.005	0.259
	IPVC 7.5 mg NaTPB	0.306	0.297	97.05	0.003	1.198	0.300	98.12	0.008	2.804
		2.189	2.181	99.63	0.007	0.332	2.185	99.85	0.003	0.151
	IPVC 7.5 mg PMA	0.306	0.305	99.91	0.004	1.495	0.303	99.10	0.003	1.301
		2.189	2.180	99.61	0.003	0.142	2.181	99.63	0.005	0.251
	IPVC 7.5 mg PTA	0.306	0.290	95.01	0.003	1.064	0.292	95.58	0.007	2.409
		2.189	2.168	99.05	0.006	0.302	2.174	99.32	0.004	0.210

	ICPE 10 mg NaTPB	0.306	0.298	97.54	0.002	0.886	0.298	97.38	0.002	0.727
		2.189	2.170	99.15	0.007	0.345	2.187	99.93	0.006	0.275
Moxiflox tablet	ISPE 22 mg NaTPB	0.306	0.297	97.14	0.007	2.447	0.305	99.83	0.003	1.085
		2.189	2.166	98.94	0.004	0.229	2.176	99.40	0.008	0.409
	ISPE 16 mg RN	0.306	0.296	96.81	0.004	1.388	0.289	98.52	0.001	0.590
		2.189	2.188	99.97	0.006	0.290	2.182	99.71	0.009	0.432
	ISPE 30 mg PTA	0.306	0.291	95.26	0.002	0.863	0.300	98.12	0.007	2.541
		2.189	2.188	99.95	0.005	0.271	2.171	99.18	0.004	0.220
	IPVC 7.5 mg NaTPB	0.306	0.302	98.77	0.002	0.733	0.306	100.16	0.001	0.421
		2.189	2.173	99.28	0.003	0.152	2.170	99.15	0.008	0.380
	IPVC 7.5 mg PMA	0.306	0.305	99.83	0.002	0.779	0.292	98.50	0.006	2.206
		2.189	2.179	99.54	0.004	0.227	2.177	99.44	0.006	0.285
	IPVC 7.5 mg PTA	0.306	0.296	96.70	0.001	0.616	0.297	97.22	0.005	1.702
		2.189	2.177	99.48	0.009	0.445	2.187	99.93	0.007	0.322
	ICPE 10 mg NaTPB	0.306	0.290	97.77	0.002	0.744	0.308	100.73	0.001	0.614
		2.189	2.179	99.56	0.006	0.300	2.172	99.22	0.002	0.118

Table 8: Inter- and intra-days precision for determination of MOXHC in moxiflox tablet using ICPE, ISPE and IPVC sensors.

Electrode	Modifier	Slope mV decade^{-1}	pH range	Response time (Sec)	Life time s)day(	LOD (mol L^{-1})	Linear range (mol L^{-1})	LOQ (mol L^{-1})
ISPE	22 mg NaTPB	58.6 ± 1.7	2.0–6.0	5.0	88	1.0×10^{-6}	1.0×10^{-6} –1.0×10^{-2}	3.3×10^{-6}
ISPE	16 mg RN	60.0 ± 2.0	2.0–6.0	5.3	91	1.0×10^{-6}	1.0×10^{-6} –1.0×10^{-2}	3.3×10^{-6}
ISPE	30 mg PTA	59.0 ± 3.3	2.0–6.0	4.6	81	1.0×10^{-6}	1.0×10^{-6} –1.0×10^{-2}	3.3×10^{-6}
IPVC	7.5 mg TPB	57.2 ± 2.6	2.0–6.0	7.6	13	1.0×10^{-6}	1.0×10^{-6} –1.0×10^{-2}	3.3×10^{-6}
IPVC	7.5 mg PMA	59.2 ± 4.6	2.0–6.0	7.0	17	1.0×10^{-6}	1.0×10^{-6} –1.0×10^{-2}	3.3×10^{-6}
IPVC	7.5 mg PTA	57.7 ± 2.7	2.0–6.0	5.6	15	1.0×10^{-6}	1.0×10^{-6} –1.0×10^{-2}	3.3×10^{-6}
ICPE	10 mg NaTPB	60.0 ± 2.3	3.0–7.0	7.3	47	1.0×10^{-6}	1.0×10^{-6} –1.0×10^{-2}	3.3×10^{-6}

Table 9: Critical response characteristics of ICPEs, ISPE and IPVCs sensors.

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