Int. J. Electrochem. Sci., 10 **(2015)** 2439 - 2454

International Journal of
ELECTROCHEMICAL
SCIENCE
www.electrochemsci.org

Improved Determination of Mebeverine Hydrochloride in Urine, Serum and Pharmaceutical Preparations Utilizing a Modified Carbon Paste Electrode

Tamer Awad Ali[1,*], *Gehad G. Mohamed*[2], *M. M. Omar*[2], *Veronia N. Abdrabou*[2]

[1] Egyptian Petroleum Research Institute (EPRI), 11727, Cairo, Egypt.
[2] Chemistry Department, Faculty of Science, Cairo University, 12613, Giza, Egypt.
[*]E-mail: dr_tamerawad@yahoo.com

Received: 21 November 2014 / *Accepted:* 22 December 2014 / *Published:* 19 January 2015

A simple, rapid and sensitive method for the determination of mebeverine hydrochloride (MBHCl) in urine, serum and pharmaceutical preparations using modified carbon paste electrodes was developed. The electrochemical sensors showed a linear dynamic range of 3.0×10^{-7} – 1.0×10^{-2} and 1.0×10^{-7} – 1.0×10^{-2} mol L^{-1} with detection limit of 3.0×10^{-7} and 1×10^{-7} mol L^{-1} for modified carbon paste (MCPEs; sensors I and II), respectively. The slopes of the calibration graphs are 56.78±0.85 and 58.80±0.46 mV $decade^{-1}$ for MCPEs with tricresylphosphate (TCP) (sensor I) and *o*-nitrophenyloctylether (*o*-NPOE) (sensor II) as plasticizers, respectively. The response time was relatively quick in the whole concentration range (8 and 7 s), respectively. The electrodes can be used at least 65 and 73 days without observing any deviations in a pH range of 2.0–8.0 and 1.5–8.0 for electrodes I and II, respectively. The fabricated electrodes displayed good selectivity for MBHCl with respect to number of common foreign inorganic cations, sugar species, and glycine as the fillers that may be added to the pharmaceutical preparation. Fortunately, such materials mostly do not interfere. The sensors were successfully applied for the determination of MBHCl in its tablets, urine and serum. The results obtained using these potentiometric electrodes were comparable with those obtained using official method.

Keywords: Mebeverine ion-selective electrodes; Modified carbon paste sensors; Pharmaceutical preparations; Urine and Serum.

1. INTRODUCTION

Mebeverine hydrochloride (MBHCl) or (3,4-dimethoxybenzoic acid 4-[ethyl-(2-[4-methoxyphenyl] -1-methylethyl) -amino] butyl ester) (Fig. 1) has an antispasmodic action on smooth muscle. It is used in the treatment of abdominal pain and spasm associated with gastrointestinal

disorders such as mucous colitis [1-3]. The most common method used in determination of MBHCl is the chromatographic method which is high senstive method but very expensive, time consuming and need special technical training. They include high performance liquid chromatography [4-6], online micellar electrokinetic chromatography [7,8], high performance thin layer chromatography[9], supercritical-fluid chromatography–mass spectrometry [7], and online reversed-phase liquid chromatography–gas chromatography [10]. Other alternatives includ spectrophotometry [11,12] and first-derivative UV-spectrophotometry [9,13,14].

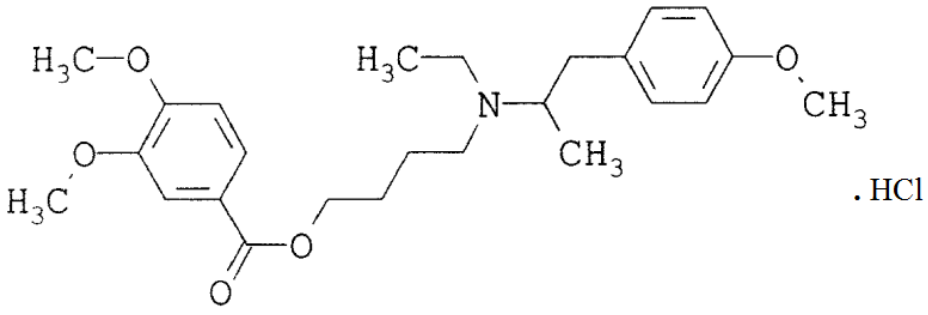


Figure 1. Structural formula of Mebeverine hydrochloride drug (MB)

The development and application of ion-selective electrodes are widely used in pharmaceutical analysis [15,16]. Numerous ion selective electrodes (ISEs) have been constructed in order to determine a number of pharmacologically active substances present in pharmaceutical preparations. The inherent advantages of ISEs: simple design, construction and manipulation, reasonable selectivity, fast response time, low cost, adequate detection limits, the ability to measure the activity of various drugs directly and selectively, wide analytical ranges, and adequate precision and accuracy [17-20], all the mentioned factors before make the ISE potentiometric method very attractive for pharmaceutical analysis.

Over the past five decades, carbon paste, i.e., a mixture of carbon (graphite) powder and a binder (pasting liquid), has become one of the most popular electrode materials used for the laboratory preparation of various electrodes, sensors, and detectors. Modified carbon paste electrodes (MCPEs), possess important advantages such as very low Ohmic resistance, very short response time in addition to the ease of fabrication and regeneration as well as long functional lifetime [21-26].

Therefore, MCPEs have found direct application in a variety of analytical situations, such as amperometry [27], voltammetry [28,29], and potentiometry [25,26,30-32]. These advantages draw the attention of researchers in recent years [33,34], although the exact behavior of carbon paste electrodes is not fully understood. In spite of successful progress in the design of highly selective electrodes for various ions, there has not been any report on the development of selective and sensitive mebeverine sensors.

The results presented in this paper showed that the modified carbon paste electrodes developed for MBHCl determination based on β-cyclodextrin (β-CD) ionophore has wide working concentration range, good Nernstian slope, low detection limit, high selectivity over a wide variety of other cations

and wider pH range than previous reported methods [35,36]. The fabricated potentiometric sensors were applied for the determination of MBHCl in pure and in tablets, urine and serum.

2. EXPERIMENTAL

2.1. Apparatus.

Laboratory potential measurements were performed using Jenway 3505 pH-meter. Silver-silver chloride double-junction reference electrode (Metrohm 6.0726.100) in conjugation with different ion selective electrode was used. pH measurements were done using Thermo-Orion, model Orion 3 stars, USA. Prior to analysis, all glassware used were washed carefully with distilled water and dried in oven before use.

2.2. Reagents and Chemicals

Analytical grade reagents are used in this study. Tricresylphosphate (TCP) from Alfa Aesar was used for the preparation of the sensors. Other types of plasticizers, namely dioctylphthalate (DOP), dibutylphthalate (DBP), *o*-nitrophenyloctylether (*o*-NPOE) and dioctylsebacate (DOS) were purchased from Sigma, Merck, Fluka and Merck, respectively. Graphite powder (synthetic 1–2μm) was supplied from Aldrich and β-cyclodextrin (β-CD) was purchased from Merck. Mebeverine hydrochloride was provided by Rameda Company, 6th October City, Giza, Egypt. Glucose, urea, sucrose, starch, maltose, lactose, fructose, glycine, chloride salts of chromium, calcium, ferric, sodium, potassium, zinc, cobalt, nickel, barium and copper were used as interfering ions. Bidistilled water was used throughout all experiments.

2.2.1. Pharmaceutical samples

Coloverine (sample 1; Chemipharm Company, 6th October City, Giza, Egypt, each tablet contains 135 mg/tablet), Duspatalin (sample 2; Abbott International Egypt, New Cairo, Cairo, Egypt, each tablet contains 135 mg/tablet), Colona (sample 3; Rameda Company, 6th October City, Giza, Egypt, each tablet contains 135 mg/tablet), and Colospasmin (sample 4; Epico Company, 10th Ramadan, El Sharkeya, Egypt, each tablet contains 135 mg/tablet).

2.3. Procedures

2.3.1. Preparation of modified carbon paste electrode (MCPE)

A 500 mg pure graphite powder and 2.5-12.5 mg of β-CD ionophore are transferred to mortar and mixed well with plasticizer (0.2 mL of DOP, TCP, DBP, DOS or *o*-NPOE). The modified paste is filled in electrode body and kept in distillated water for 24 h before use [15,16,20-24]. A fresh surface

was obtained by gently pushing the stainless-steel screw forward and polishing the new carbon-paste surface with filter paper to obtain a shiny new surface.

2.3.2. Calibration of the new MCPE

The new MCPE was calibrated by immersion in conjunction with a reference electrode in a 25-mL beaker containing 2.0 mL acetate buffer solution of pH 4. Then 10 ml aliquot of MBHCl solution of concentration ranging from 1×10^{-7} to 1×10^{-2} mol L^{-1} were added with continuous stirring and the potential was recorded after stabilization to ±0.1 mV. A calibration graph was then constructed by plotting the recorded potentials as a function of -log [MBHCl)]. The calibration graphs will be used for subsequent determination of unknown MBHCl concentration [24,25,31].

2.4. Analytical method for pharmaceutical formulation

Ten mebeverine hydrochloride tablets were weighed accurately, crushed and mixed in a mortar, and the weight equivalent to one tablet is dissolved in 50 mL of distilled water under stirring condition. The solution was transferred into a 50-mL volumetric flask, and then completed to the mark with the same solvent. 5 mL of this solution was taken and transferred into another 50-mL volumetric flask, completed to volume with the distilled water. The MBHCl modified carbon paste ion selective electrodes and the reference electrode were immersed into the test solution. The content of MBHCl in the tablets was determined by using the direct potentiometric method.

2.4.1. Potentiometric determination

In batch measurements, the standard addition method was applied [15,21,37]. In this method the proposed electrode was immersed into a sample of 25 ml with unknown concentration (1×10^{-7}–1×10^{-4} mol L^{-1}) drug solution and the equilibrium potential of E_u was recorded, then 0.1 ml of 1×10^{-3} mol L^{-1} of standard drug solution was added into the testing solution and the equilibrium potential of E_s was obtained. From the potential change $\Delta E = (E_u - E_s)$ one can determine the concentration of the testing sample using the equation:

$$C_x = (C_s \times V_s)/[(V_x + V_s) \times 10^{\Delta E/S} - V_x)]$$

where C_x and V_x are the concentration and the volume of the unknown, respectively. Cs and Vs are the concentration and the volume of the standard, respectively, S is the slope of the calibration graph, and E is the change in millivolt due to the addition of the standard.

2.4.2. Determination of MBHCl in biological fluids

Different quantities of MBHCl was added to 2 ml serum or 4 ml urine and they were transferred to a 100 ml volumetric flask, completed with water and small volumes (0.1–2 ml) of 0.01 mol L^{-1} HCl to the mark to give solutions of pH ranging from 3 to 5.5 and concentrations of 1.0×10^{-4}

to 5.0 × 10^{-3} mol L^{-1} of MBHCl. These solutions are subjected to the potentiometric determination using direct, calibration and standard additions method for MBHCl determination [16].

3. RESULTS AND DISCUSSION

3.1. Composition and characteristics of the sensors.

It is well known that the response characteristics for a given electrode depend significantly on the kind and paste composition. In preliminary experiments, the paste optimization of MB-CMCPE was performed by the selection of an optimum ratio of β-cyclodextrin (CD) ionophore. For this purpose, five electrodes were prepared containing different amounts of β-CD ionophore (2.5, 5, 7.5, 10 and 12.5 mg) and the results obtained were given in Table 1. The results showed that on using paste of optimum compositions (10 mg, sensor II), a slope of 57.71±0.59 mV $decade^{-1}$ over a relatively wide range of MBH^+ concentration (1× 10^{-7}- 1×10^{-2} mol L^{-1}) was obtained, and the value of the correlation coefficient (r^2) was higher than that obtained with other pastes. Other pastes exhibit slopes of 33.69, 45.41, 54.46 and 52.13 mV $decade^{-1}$ for 2.5, 5, 7.5 and 12 mg of β-CD, respectively, but the linearity ranges of the calibration curves are shorter and the correlation coefficients are worse (0.983–0.997). In all subsequent studies, electrode (o-NPOE, sensor II) made of paste containing of 10 mg of β-CD ionophore was used.

Using the optimized paste composition, the potentiometric response of the sensor was studied for MBH^+ within the concentration range of 1.0×10^{-7}-1.0×10^{-2} mol L^{-1} at 25 °C and the data obtained were represented graphically in Fig. 2. The results showed that the sensors have Nernstian response of 56.78±0.85 and 57.71±0.59 mV $decade^{-1}$ and linear concentration range from 3.0×10^{-7}-1.0×10^{-2} and 1.0×10^{-7}-1.0×10^{-2} mol L^{-1} for MCPEs with tricresylphosphate (TCP) (sensor I) and *o*-nitrophenyloctylether (*o*-NPOE) (sensor II) as plasticizers, respectively. Experiments were repeated several times to check the reproducibility of the results. EMFs were plotted against log of activities of MBH^+ and calibration curves were drawn for five sets of experiments and a standard deviation of ±0.098-0.136 mV was observed. The detection limit of the sensors was determined according to IUPAC recommendations from the intersection of two extrapolated linear portions of the curve [15,22,23] and was found to be 3.0×10^{-7} and 1.0×10^{-7} mol L^{-1} for sensor (I) and sensor (II), respectively.

Table 1. Effect of ionophore content β-CD on the performance characteristics of MB-MCPEs using *o*-NPOE plasticizer.

β-CD ionophore Content (mg)	Concentration range (mol L^{-1})	Slope (mV $decade^{-1}$)	Recovery %	Total potential change, mV
2.5	1.0 ×10^{-6} - 1.0×10^{-2}	33.69±1.53	98.30	135
5	1.0 ×10^{-6} - 1.0×10^{-2}	45.41±1.22	98.89	225
7.5	1.0 ×10^{-7} - 1.0×10^{-2}	54.46±1.06	99.70	272
10	1.0 ×10^{-7} - 1.0×10^{-2}	57.71±0.59	99.94	289
12.5	1.0 ×10^{-6}- 1.0×10^{-2}	52.13±0.98	99.48	261

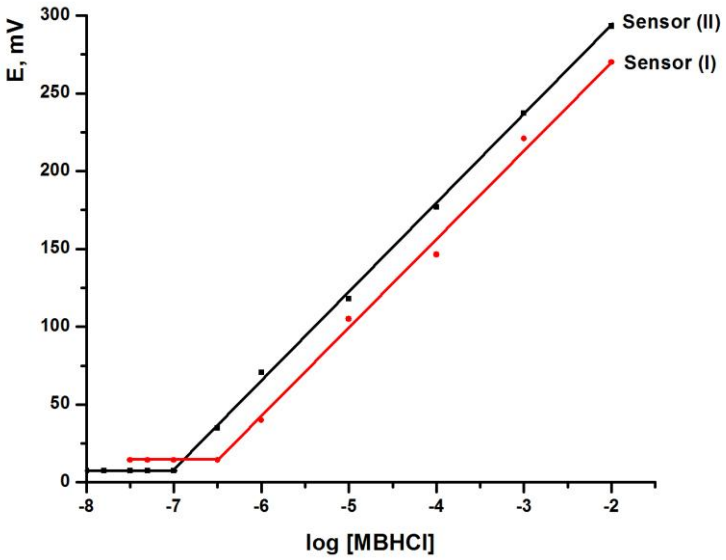


Figure 2. Calibration curve for MBHCl-modified carbon paste electrodes.

3.2. Effect of soaking

The performance characteristics of the MB-MCPEs were studied as a function of soaking time. For this purpose, the electrodes were soaked in 1.0×10^{-3} mol L^{-1} solution of MBHCl and the calibration graphs (p[MBHCl] versus E_{elec} (mV)) were plotted after without, 5, 10, 15 min and 0.5, 1.0, 2.0, 6.0, 12 and 24 h. The optimum soaking time was found to be without and 15 min, when the slopes of the calibration curves were 56.78 and 58.80 mV $decade^{-1}$, at 25 °C for sensor (I) and sensor (II), respectively (Fig. 3). Soaking for longer time than 15 min is not recommended to avoid leaching of the electroactive species (although very little) into the bathing solution. The electrodes should be kept dry in an opaque closed vessel and stored in a refrigerator while not in use. The reproducibility of repeated measurements on the same solutions was ±1 mV.

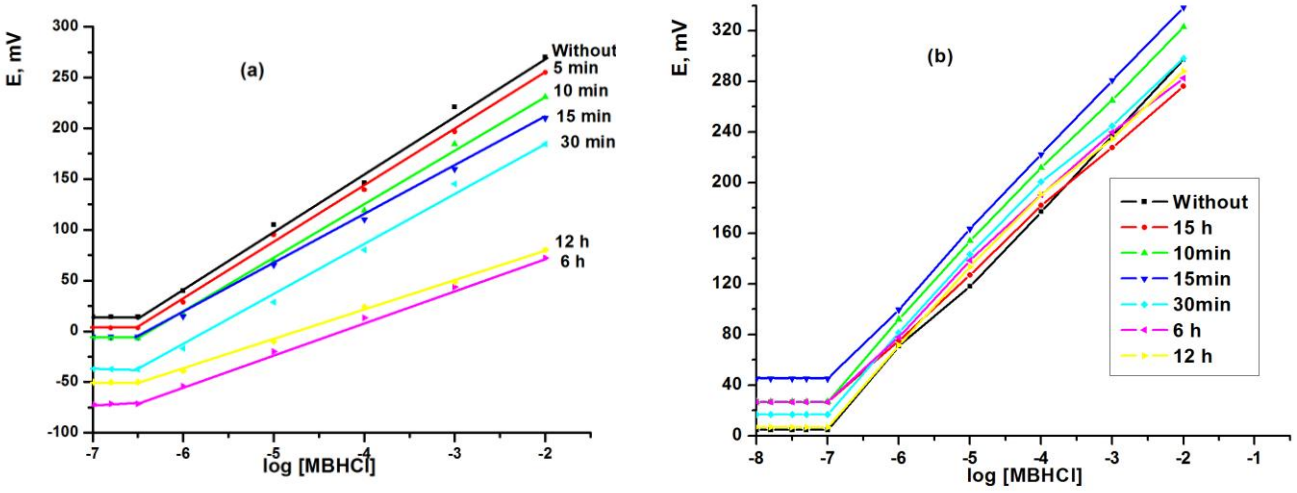


Figure 3. Effect of soaking time on the performance of MCPEs (a) (sensor I) and (b) (sensor II).

3.3. Response time

For any sensor, the response time is an important factor that must be investigated. For electrochemical sensors, this parameter is evaluated by measuring the average time required to achieve a potential within ± 0.1 mV of the final steady-state potential upon successive immersion of a series of interested ions, each having a 10-fold difference in concentration. The average static response times 8 and 7 s for sensor (I) and sensor (II), respectively, were obtained when contacting different MBH^+ solutions from 1.0×10^{-6} to 1.0×10^{-3} mol L^{-1}, (Fig. 4). Experimental conditions such as stirring or the flow rate, the ionic concentration and composition of the test solution, the concentration and composition of the solution to which the electrode was exposed before performing the experiment measurement, any previous usage or preconditioning of the electrode, and the testing temperature can all affect the experimental response time of a sensor [23,31,32,34]. For the proposed modified MBH^+ sensors, the response time over the whole concentration range was less than 110 s.

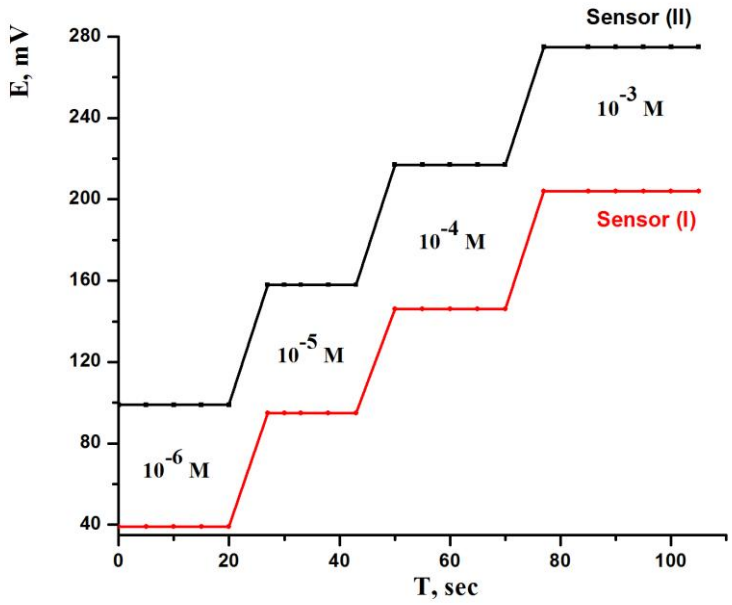


Figure 4. Dynamic response time of MB-MCPEs [Sensors (I) and (II)].

3.4. Lifetime and reproducibility

The lifetimes of electrodes (I and II) were investigated by performing the calibration periodically with standard solutions and calculating the response slopes. It was indicated that the electrodes (I and II) can be used continuously for about 65 and 73 days for sensors I and II, respectively, without considerable decrease in its slope values (Fig. 5). This kind of the paste electrodes do not require any preconditioning in the solutions of corresponded drugs or maintenance before use. The paste of electrodes were washed with water after each application and stored in a desicator under atmospheric condition and kept far from the light.

3.5. Effect of pH

The effect of pH of the MBHCl test solution on the electrode potential is graphically represented in Fig. 6. The pH of the initial solution is altered by the addition of very small volumes of HCl and/or NaOH (0.1–1.0 M each). Data presented in Fig. 6 indicates that the pH has a negligible effect within the pH range of 2 - 8.0 and 1.5 - 8.0 for sensors I and II, respectively. In this range, the electrode can be safely used for MBH^+ determination. During the operative life of the electrode (73 days), no significant change in the potential pH behaviour is observed. The decrease in mV readings at pH < 1 may be due to interference of hydronium ion. At higher pH values (pH > 8.0), the hydroxyl of the MB is formed in the test solution and consequently, the concentration of protonated species gradually decreased. As a result, lower e.m.f. readings were recorded as shown in Fig 6.

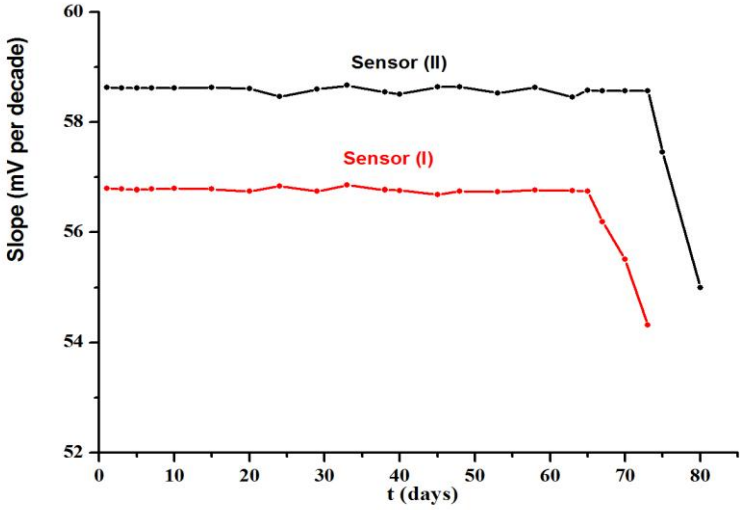
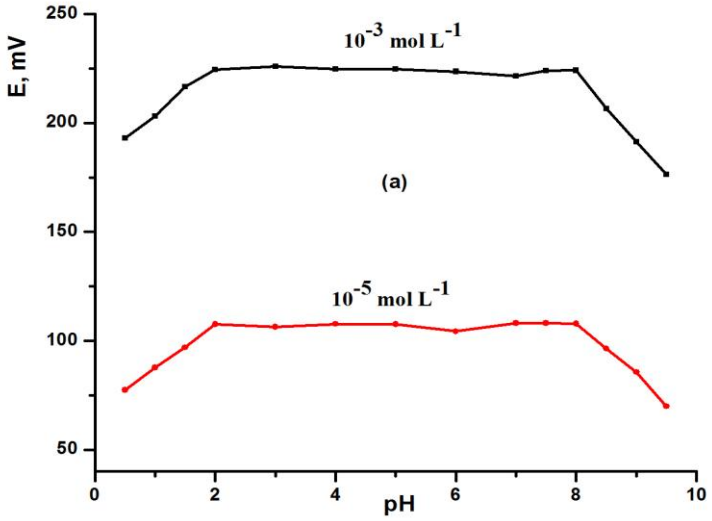


Figure 5. Life time of MBHCl-MCPEs [Sensors (I) and (II)]



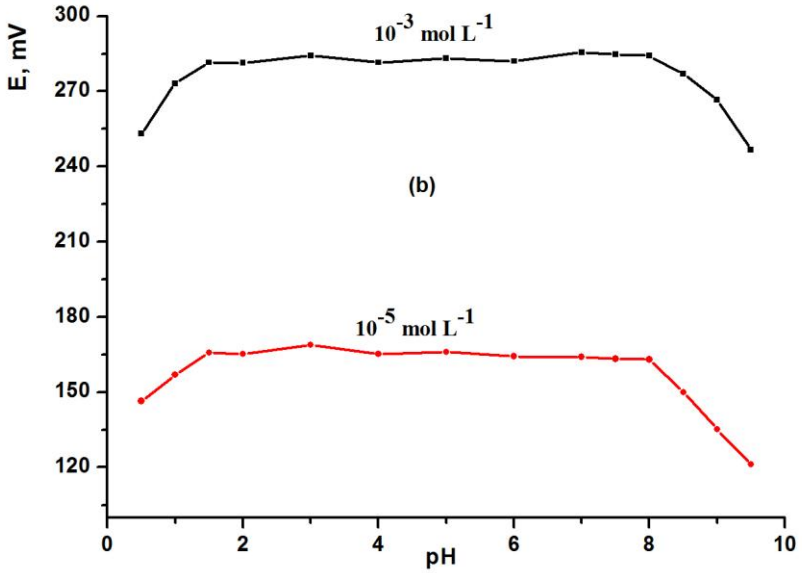


Figure 6. Effect of pH of the test solution on MCPEs [(a) Sensor (I) and (b) Sensor (II)]

3.6. Effect of temperature

To study the thermal stability of the modified CPE sensors, calibration graphs (electrode potential (E_{cell}) versus p[MBHCl]) were constructed at different test solution temperatures (20, 30, 40, 50 and 60 ˚C). The standard cell potentials (E°_{cell}) were determined at different temperatures from the respective calibration plots as the intercepts of these plots at p[MBHCl] = 0 and were plotted versus (t−25), where t was the temperature of the test solution in °C. A straight line plot is obtained according to Antropov's equation [16,20,31,32] and the slope of this line represents the isothermal coefficient of the electrodes which was found to be 0.00098 and 0.00091 V/°C for sensors I and II, respectively, Figure 7. The obtained value of the isothermal coefficient indicates that the electrodes under investigation had high thermal stability within the used range of temperature. Calibration graphs were recorded, as previously described, at test solution temperatures 25, 30, 40, 50 and 60°C for the MCPE electrodes. It is clear that the electrodes exhibit a good Nernstian behaviour in the temperature range 20-60 °C. This means that the electrodes are thermally stable and responds linearly with MBHCl concentrations. Nevertheless, all slope values were slightly lower than the ones calculated from the Nernstian equation, because the exchange process responsible for the paste potential is slightly restricted, due to the partial covalent character of the bond in the ion associate and the rigidity of the electrodes surface on which the gel layer is formed. The latter reason also explains the good resistance of the electrode surface to temperature changes over the investigated range.

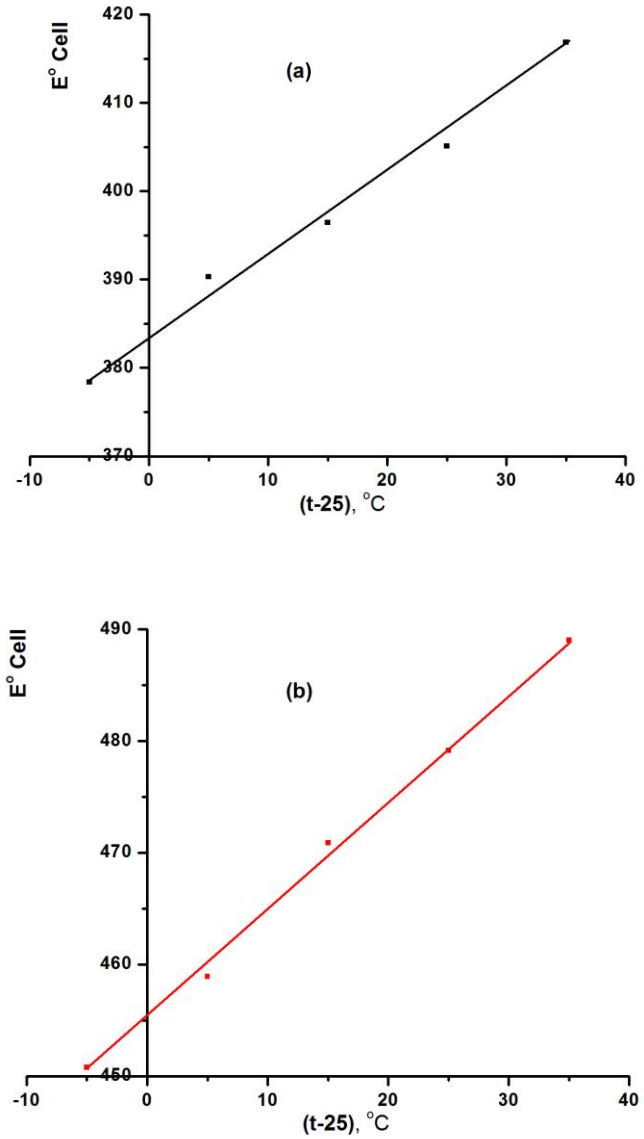


Figure 7. Effect of temperature on the performance of MCPEs [(a) Sensor (I) and (b) Sensor (II)].

3.7. Effect of foreign ions

The separate solution method (SSM) is recommended by IUPAC to determine the selectivity coefficient of the ISE [19,20,34]. SSM is based on Nickolsky–Eisenman equation (1):

$$\text{Log}\,(K^{pot}_{MBH^+,M}) = ((E_M - E_{MBH^+})/S) + (1-(Z_{MBH^+}/Z_M))\,(\log a_{MBH^+}) \quad \text{Equation (1)}$$

where E_M and E_{MBH^+} are the potentials measured in 1×10^{-3} mol L^{-1} solutions of the interfering ions and MBH^+ cation, *S is* the calibration slope, Z_{MBH^+} and Z_M are the charges of MBH^+ cation and the interfering ions and *a* is the concentration of the ions used (1×10^{-3} mol L^{-1}). According to the "matched potential method (MPM)", the selectivity coefficient is defined as the activity ratio of the primary ion (MBH^+) and the interfering ion (M) that gives the same potential change in a reference solution [21,22,24,31]. The selectivity coefficient, $K^{MPM}_{MBH^+,M}$ is determined as

$$K^{MPM}_{MBH^+, M} = \Delta A / a_M , \qquad \Delta A = a'_{MBH^+} - a_{MBH^+} \qquad \text{Equation (2)}$$

where a_{MBH^+} is the initial primary ion activity and $\acute{a}_{MBH^+}$ is the new activity of MBH^+ cation after addition of an aliquot of interfering ions, and a_M is the activity of interfering ions (M^{n+}) after the respective addition. The concentration of MBH^+ cation used, as primary ion in this study was 1.0×10^{-3} mol L^{-1}. The resulting values of the selectivity coefficients are summarized and compared in Table 2. However, in case of univalent interferences, the values obtained by the SSM are considerably larger than those by the MPM. As it is evident from Table 2, most of the interfering ions showed low values of selectivity coefficients, indicating no significant interference in the performance of the paste electrode assembly.

Table 2. Potentiometric selectivity coefficients of some interfering ions using MCPEs (Sensors I and II).

Interfering ions	$-\log K^{MPM}_{MBH^+, M}$ sensor (I)	sensor (II)	Interfering ions	$-\log K^{SSM}_{MBH^+, M}$ sensor (I)	sensor (II)
Maltose	4.26	4.87	Cr^{3+}	3.73	3.92
Lactose	4.69	4.81	Fe^{3+}	2.74	3.12
Glucose	3.29	3.64	Ca^{2+}	3.22	3.53
Sucrose	4.45	4.83	Cu^{2+}	2.47	3.04
Glycine	4.96	5.01	Zn^{2+}	4.52	4.68
Fructose	4.72	5.89	K^+	4.43	4.22
Starch	3.35	3.27	Na^+	3.32	3.96
Urea	3.11	3.72	Ba^{2+}	4.67	4.98
Ni^{2+}	2.56	2.84	Co^{2+}	3.02	3.22

3.8. Analytical application

The designed sensors were utilized to determine mebeverine hydrochloride in pharmaceutical preparations (Coloverine, Duspatalin, Colona and Colospasmin tablets) using the proposed potentiometric method. The results obtained were compared to the British Pharmacopiea [15,16] and the data obtained are summarized in Table (3). There were no significant differences between the calculated and comparative values indicating that the electrodes can be used for potentiometric determinations of MBHCl in such samples. Statistical evaluation of the results of analysis of pure MBHCl by the proposed electrodes and the British Pharmacopiea [15,16] showed that there is no significant difference between the proposed and reported method in terms of F- and t-test values (Table 3). The percentage recovery values, relative standard deviation and standard deviation found to be 98.80-99.71, 0.994-1.15 and 0.006-0.043 for electrode (I) and 99.2-100.3, 0.85-1.04 and 0.003-0.037

for electrode (II), respectively. The low values of standard deviation and relative standard deviation in comparison with the official method reflects the high accuracy and precision of the proposed potentiometric method.

Table 3. Potentiometric determination of MBHCl in pharmaceutical formulations using MCPEs (Sensors (I) and (II)).

Samples[b]	[MBHCl] Taken mg mL^{-1}	Value						British Pharmacopiea		
		Sensor (I)			Sensor (II)					
		Found mg mL^{-1}	Recovery (%)	RSD[a] (%)	Found mg mL^{-1}	Recovery (%)	RSD[a] (%)	Found mg mL^{-1}	Recovery (%)	RSD[a] (%)
(1)	0.25	0.247	98.80	1.15	0.248	99.20	1.03	0.246	98.40	1.75
(2)	0.30	0.297	99.00	1.07	0.299	99.67	0.98	0.296	98.67	1.84
(3)	0.25	0.248	99.20	1.01	0.249	99.60	1.04	0.247	98.80	2.01
(4)	0.35	0.349	99.71	0.994	0.351	100.3	0.85	0.347	99.14	1.08
SD		0.006 - 0.043			0.003-0.037			0.002-0.021		
F-test[#]		0.83-2.01			0.36-1.84					
t-test[#]		1.01-2.21			0.52-2.05					

[a] number of replicates is 4.

[#] Tabulated F value at 95% confidence limit = 6.388 for n = 4).

[#] Tabulated t value at 95% confidence limit = 2.77 for n = 4).

[b] Samples (1-4) are described in details in the experimental part.

3.6.1. Application to serum and urine

Table 4. Determination of MBHCl in spiked urine and human serum using MCPEs (Sensors (I) and (II).

Sample	Statistical parameters	(Sensor I)			(Sensor II)		
		Direct Method	Calibration graphs	Standard addition method	Direct method	Calibration graphs	Standard addition method
Urine	Mean recovery (%)	98.92	98.99	98.20	99.10	99.40	99.00
	N	4	4	4	4	4	4
	Variance	0.92	0.81	0.74	0.96	0.78	0.91
	RSD (%)	1.21	1.03	1.45	1.02	0.92	1.27
Serum	Mean recovery (%)	98.96	99.00	98.80	99.10	99.60	98.95
	N	4	4	4	4	4	4
	Variance	0.78	0.69	0.65	0.58	0.43	0.60
	RSD (%)	1.01	1.14	1.21	0.87	0.74	0.81

The proposed potentiometric method was applied to determine MBHCl in biological fluids such as human serum and urine. The results obtained are summarized in Table 4. The accuracy of the proposed sensors (I and II) was investigated by the determination of MBHCl in spiked urine and serum samples prepared from serial concentrations of MBHCl reference standards. The results summarized in Table 4, showed that the proposed potentiometric method is accurate and precision for the determination of MBHCl in urine and serum samples without interferences from the coformulated adjuvants as indicated by the percentage recovery values [16].

3.7. Precision and accuracy

In order to determine the precision of the proposed method, solutions containing concentrations of MBHCl were prepared and analyzed in four replicates and the analytical results are summarized in Table (5). The low values of the relative standard deviation (%RSD) also indicate the high precision and the good accuracy of the proposed method. RSD (%) and SD values were obtained within the same day to evaluate repeatability (intra-day precision) and over five days to evaluate intermediate precision (inter-day precision).

3.9. Comparison study

In Table 6, some important characteristics of the proposed electrodes are compared with the corresponding values previously reported for MB-selective electrodes based on different modifiers [35,36,38]. It is evident from this table that in many cases, the performances of the proposed electrode show superior behaviour if compared with the previously reported MBHCl sensors.

Table 5. Evaluation of intra- and inter-days precision and accuracy of MCPEs (Sensors (I) and (II)).

Electrode type	Sample No.	[MBHCl] Taken, (mg/mL)	Intra day				Inter day			
			[MBHCl] Found, (mg/mL)	Recovery * (%)	SD	RSD%	[MBHCl] Found, (mg/mL)	Recovery *(%)	SD	RSD%
Sensor (I)	Pure [MBHCl]	0.25	0.249	99.60	0.001	0.846	0.248	99.20	0.011	1.033
		0.30	0.298	99.33	0.003	0.957	0.297	99.00	0.015	1.045
	Sample 2	0.25	0.247	98.80	0.035	1.003	0.249	98.00	0.052	1.326
		0.30	0.295	98.33	0.046	1.024	0.295	98.00	0.057	1.368
	Sample 4	0.25	0.247	98.80	0.037	1.012	0.248	98.40	0.027	1.115
		0.30	0.299	99.66	0.006	1.008	0.297	99.00	0.012	1.014
Sensor (II)	Pure [MBHCl]	0.35	0.350	100.0	0.004	0.837	0.249	99.71	0.009	0.984
		0.40	0.401	100.3	0.007	0.585	0.400	100.0	0.005	0.742
	Sample 2	0.35	0.346	98.85	0.074	1.002	0.248	98.57	0.092	1.043
		0.40	0.403	100.8	0.009	1.004	0.401	100.3	0.004	0.753
	Sample 4	0.35	0.349	99.71	0.010	1.011	0.347	99.14	0.026	1.051
		0.40	0.399	99.75	0.015	1.031	0.397	99.25	0.018	1.008

Table 6. Comparing some of the MB-MCPEs characteristics with some of the previously reported MB-ISEs.

References	Slope (mV decade^{-1})	Response time (s)	pH	Life time (days)	Linear range (mol L^{-1})	DL (mol L^{-1})
Proposed sensors (sensor I)	56.78	8	1.5-8.0	63	3.0×10^{-7}–1.0×10^{-2}	3.0×10^{-7}
(sensor II)	58.80	7	1.5-8.0	75	1.0×10^{-7}–1.0×10^{-2}	1.0×10^{-7}
[35]	57.8	<10	1.5 - 7.2	30	5.0×10^{-7}-1.0×10^{-2}	1.2×10^{-7}
[36] Electrode (A)	56.0	5-8	1.0 - 6.5	55	4.0×10^{-6}-1.0×10^{-2}	3.1×10^{-6}
[36] Electrode (B)	59.0	5-8	1.0 - 6.5	50	4.0×10^{-6}-1.0×10^{-2}	4.0×10^{-6}
[36] Electrode (C)	55.0	8-10	1.0 - 6.5	29	7.9×10^{-6}–1.0×10^{-2}	8.0×10^{-6}
[36] Electrode (D)	56.0	5-8	1.0 - 6.5	22	2.0×10^{-5}-1.0×10^{-2}	2.0×10^{-5}
[39]	-	20	4-7.5	-	-	0.043 (µg/mL)

4. CONCLUSION

The proposed modified carbon paste electrodes based on β-cyclodextrin (CD) as ionophore are interesting alternative method for the determination of [MBH^+] in different pharmaceutical preparations, urine and serum. The present electrodes show high sensitivity, reasonable selectivity, fast static response, long-term stability and applicability over a wide pH range with minimal sample pretreatment. The presented method for the determination of mebeverine hydrochloride with the prescribed electrodes are simple, sensitive, highly specific and advantageous over the previously described procedures for MBHCl determinations in pure and in pharmaceutical preparations. It ensures a good accuracy for the MBHCl assay due to the possibility to control the ion activity continuously and also a fast assay of MBHCl in tablets, urine and serum samples. The accuracy of the method is indicated by excellent recovery and low standard deviation and relative standard deviation.

References

1. E. Baloğlu, S.Y. Karavana, I.Y. Hyusein, T. Köse, *AAPS Pharm Sci Tech* 11 (2010) 181.
2. S.E. Reme, D. Stahl, T. Kennedy, R. Jones, S. Darnley, T. Chalder, *Psychological Medicine* 41 (2011) 2669.
3. S.E. Reme, T. Kennedy, R. Jones, S. Darnley, T. Chalder, *Journal of Psychosomatic Research* 68 (2010) 385.
4. R. Youssef, Acta Chromatographica 26 (2014) 67.
5. E. Souri, A. Negahban Aghdami, N. Adib, *Research in Pharmaceutical Sciences* 9 (2014) 199.
6. H.M. Heneedak, I. Salama, S. Mostafa, M. El-Sadek, *Current Analytical Chemistry* 10 (2014) 565.
7. J. Kristinsson, I. Snorradottir, M. Johansson, *Pharmacology and Toxicology* 74 (1994) 174.

8. A.M. Al-Sabagh, K.I. Kabel, M.R. Noor El-Din, E.A. Elsharaky, *Egyptian Journal of Petroleum* 21 (2012) 81.
9. A.F.M. El Walily, A. El Gindy, M.F. Bedair, *Journal of Pharmaceutical and Biomedical Analysis* 21 (1999) 535.
10. I.A. Naguib, M. Abdelkawy, *European Journal of Medicinal Chemistry* 45 (2010) 3719.
11. S.M.S. Derayea, *Analytical Methods* 6 (2014) 2270.
12. T. Rajesh, N. Lakshmi Prasanna, A. Ashok Kumar, *International Journal of Pharmacy and Pharmaceutical Sciences* 6 (2014) 96.
13. S.A. Shama, A.S. Amin, *Spectrochimica Acta - Part A: Molecular and Biomolecular Spectroscopy* 60 (2004) 1769.
14. K. Rajitha, N. Lakshmi Prasanna, G. Vasundhara, R. Naveen Kumar, A. Ashok Kumar, *International Journal of Pharmacy and Pharmaceutical Sciences* 6 (2014) 345.
15. E.Y.Z. Frag, T.A. Ali, G.G. Mohamed, Y.H.H. Awad, *International Journal of Electrochemical Science* 7 (2012) 4443.
16. T.A. Ali, G.G. Mohamed, A.M. Al-Sabagh, M.A. Migahed, Fenxi Huaxue/ *Chinese Journal of Analytical Chemistry* 42 (2014) 565.
17. E. Khaled, G.G. Mohamed, T. Awad, *Sensors and Actuators, B: Chemical* 135 (2008) 74.
18. G.G. Mohamed, T.A. Ali, M.F. El-Shahat, M.A. Migahed, A.M. Al-Sabagh, *Drug Testing and Analysis* 4 (2012) 1009.
19. G.G. Mohamed, T.A. Ali, M.F. El-Shahat, A.M. Al-Sabagh, M.A. Migahed, E. Khaled, *Analytica Chimica Acta* 673 (2010) 79.
20. G.G. Mohamed, M.F. El-Shahat, A.M. Al-Sabagh, M.A. Migahed, T.A. Ali, *Analyst* 136 (2011) 1488.
21. T.A. Ali, A.M. Eldidamony, G.G. Mohamed, D.M. Elatfy, *International Journal of Electrochemical Science* 9 (2014) 2420.
22. T.A. Ali, A.L. Saber, G.G. Mohamed, T.M. Bawazeer, *International Journal of Electrochemical Science* 9 (2014) 4932.
23. T.A. Ali, G.G. Mohamed, *Sensors and Actuators B: Chemical* 202 (2014) 699.
24. T.A. Ali, G.G. Mohamed, M.M.I. El-Dessouky, S.M. Abou El Ella, R.T.F. Mohamed, *International Journal of Electrochemical Science* 8 (2013) 1469.
25. T.A. Ali, G.G. Mohamed, M.M.I. El-Dessouky, S.M. Abou El-Ella, R.T.F. Mohamed, *Journal of Solution Chemistry* 42 (2013) 1336.
26. T.A. Ali, R.F. Aglan, G.G. Mohamed, M.A. Mourad, *International Journal of Electrochemical Science* 9 (2014) 1812.
27. T.K. Malongo, S. Patris, P. Macours, F. Cotton, J. Nsangu, J.-M. Kauffmann, *Talanta* 76 (2008) 540.
28. Y. Umezawa, P. Bühlmann, K. Umezawa, K. Tohda, S. Amemiya, Potentiometric Selectivity Coefficients of Ion-Selective Electrodes. Part I. Inorganic Cations (Technical Report), Pure and Applied Chemistry, 2000, p. 1851.
29. A. Mokhtari, H. Karimi-Maleh, A.A. Ensafi, H. Beitollahi, *Sensors and Actuators B: Chemical* 169 (2012) 96.
30. T.A. Ali, A.A. Farag, G.G. Mohamed, *Journal of Industrial and Engineering Chemistry* 20 (2014) 2394.
31. T.A. Ali, G.G. Mohamed, E.M.S. Azzam, A.A. Abd-Elaal, *Sensors and Actuators, B: Chemical* 191 (2014) 192.
32. T.A. Ali, E.M.S. Azzam, M.A. Hegazy, A.F.M. El-Farargy, A.A. Abd-elaal, *Journal of Industrial and Engineering Chemistry* 20 (2014) 3320.
33. M.K. Halbert, R.P. Baldwin, *Analytical Chemistry* 57 (1985) 591.
34. G.G. Mohamed, T.A. Ali, M.F. El-Shahat, A.M. Al-Sabagh, M.A. Migahed, *Electroanalysis* 22 (2010) 2587.

35. H. Ibrahim, Y.M. Issa, H.M. Abu-Shawish, *Journal of Pharmaceutical and Biomedical Analysis* 44 (2007) 8.
36. H. Ibrahim, Y.M. Issa, H.M. Abu-Shawish, *Journal of Pharmaceutical and Biomedical Analysis* 36 (2005) 1053.
37. J.L.F.C. Lima, M.C.B.S.M. Montenegro, M.G.F. Sales, *Journal of Pharmaceutical and Biomedical Analysis* 18 (1998) 93.
38. H.A.J.A. Lawati, Z.M.A. Dahmani, G.B. Varma, F.O. Suliman, *Luminescence* 29 (2014) 275.