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Potentiometric determination of oxybutynin hydrochloride in pharmaceutical formulations at modified carbon paste electrodes

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New potentiometric sensitive and selective modified carbon paste (MCPE) electrodes based on ion pair formation between phosphotungestic acid (PTA), sodium tetraphenyl borate (NaTPB), phosphomolybdic acid (PMA) or ammonium reineckate (RN) and oxybutynin hydrochloride (Ox.HCl) has been developed. The proposed electrodes have Nernstian slope values of 58.50±0.71, 58.71±1.20, 54.80±1.30 and 59.20±0.70 mV decade^{-1} for electrodes modified with 20, 10, 5 and 10 mg of Ox-TPB (electrode I), Ox-RN (electrode II), Ox-PMA (electrode III) and Ox-PTA (electrode IV) ion pairs, respectively. It is found that the dynamic drug concentration range at 25 °C is 1.0×10^{-5}–1.0×10^{-2} mol L^{-1}. The response of MCPEs is pH independent in the range 2.0–6.0 with a fast response time of 10 s for electrode I and 12 s for electrodes II-IV. These electrodes have good Nernstian response in the temperature range 10–60 °C with slope (isothermal coefficient) equal 0.791×10^{-3}, 0.769×10^{-3}, 0.629×10^{-3} and 1.277×10^{-3} V/°C for electrodes I, II , III and IV respectively. These small values indicate the high thermal stability of the electrodes. The MCPEs have shown a relatively long life time of 36 days. A pure and pharmaceutical formulation of Ox.HCl has quantified using calibration and standard addition methods and the obtained results agreed with that of the official HPLC method. Validation parameters have been optimized according to ICH recommendations. Limits of detection and quantification are calculated under the optimized conditions. For the analytical applications, pharmaceutical dose form has performed. Various interferents have been used to investigate the interference in the analytical application and found that the proposed method would be well adopted for real sample analysis.

Keywords: Modified carbon paste (MCPE), Ion pairing agents, Oxybutynin HCl, Pharmaceutical formulation

The active substance in oxybutynin tablets is oxybutynin hydrochloride[1] (Ox.HC1) (4-diethylamino-2-butynylphenylcyclohexylglycolate hydrochloride). The empirical formula of oxybutynin chloride is $C_{22}H_{31}NO_3$ HCl. The structural formula appears in Fig. 1. Oxybutynin chloride is a white crystalline solid. It is readily soluble in water and acids, but relatively insoluble in alkalis. This is one of a group of medicines called anticholinergics or antispasmodics. It increases the volume of the bladder by relaxing the muscle of the bladder wall, and helps to control the release of urine. It is used to treat loss of control in passing water (urinary incontinence), urgency and frequency in patients unable to control their bladder, for neurogenic bladder disorders (lack of bladder control caused by problems with the nervous system or spinal cord), and night time bedwetting, when other treatments have not worked. It can also be used to treat hyperhidrosis (excessive sweating) and it is found that people who treat with oxybutynin HCl reported greater improvements compared with those treated with placebo. So, it can be used to treat damage to the brain neurons and birth defects in spinal tracks.

Oxybutynin chloride exerts a direct antispasmodic effect on smooth muscle and inhibits the muscarinic action of acetylcholine on smooth muscle, i.e. no blocking effects occur at skeletal neuromuscular junctions or autonomic ganglia (antinicotinic effects). In patients with conditions characterized by involuntary bladder contractions, cystometric studies have demonstrated that oxybutynin chloride increases bladder (vesical) capacity, diminishes the frequency of uninhibited contractions of the detrusor muscle, and delays the initial desire to void.

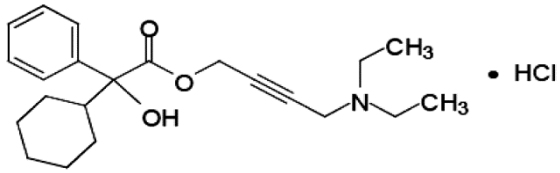

Fig. 1 — Chemical structure of Ox.HCl drug.

For quantitative determination of Ox.HCl few methods have been performed for its analysis such as polarography[2], spectrophotometry[3,4], HPLC[5] and polymeric matrix membrane[6,7]. Though these reported methods are well established, they have drawbacks such as elaborate sample preparation, costly equipment, long analysis time, the need for specialized expertise, expensive laborious equipment and specific proficiency, which makes them incompatible for routine investigation.[8,9]

Ion-selective electrodes (ISEs) are now widely used for the direct potentiometric determination of ion concentrations in different samples by different electrochemical methods.[10-16] Their advantages are simple design, low cost, adequate selectivity, low detection limit, high accuracy, wide concentration range and applicability to coloured and turbid solution. In the area of chemically modified electrodes, carbon paste electrodes (CPEs) have attracted a wide range of analyst in recent years. CPEs have unique advantages such as easiness in the preparation, various ligands depending on the application can be easily mixed during the paste preparation, cheaper, and low back ground current interferences during analysis.[17] CPE is a mixture of conducting graphite powder and a pasting liquid (plasticizer). These electrodes are simple to make and an easily renewable. It belongs to a special group of heterogeneous carbon electrodes. They have been widely preferred as sensing material due to their high repoducibility, possibility of modification by a variety of modifiers, attainment of stable voltammograms, and use of less expensive materials.[18,19] These electrodes are used widely for voltammetric measurements. However, carbon paste-based sensors[20,21] are also used in coulometry (both amperometry and potentiometry). Carbon paste, glassy carbon paste and glassy carbon, electrodes when modified are termed as chemically modified electrodes. These chemically modified electrodes have been employed for the analysis of inorganic and organic species. Many of the studies of modified electrodes were undertaken simply because electrochemists were curious about the behavior of a new species attached to the surface of an electrode compared to these species in solution.[22,23]

In the present work, modified carbon paste electrodes (MCPEs) have been constructed and their performance characteristics were studied. The electrodes were modified based on the interaction of the ion pairing agents namely NaTPB, RN, PTA and PMA with the Ox.HCl drug to form the ion-pairs. Effect of content of ion pairs, plasticizer, pH, temperature, selectivity and life time were properly studied. The electrodes were used successfully as sensors for determination Ox.HCl in pure form and pharmaceutical preparation. Method validation parameters were studied. The method was precise and accurate as indicated from the percent recovery, standard and relative standard deviation values. It was observed that, low limit of detection, easiness in fabrication of electrodes, low cost material used in electrodes and application of the electrodes even in the presence of various interferents makes these electrodes suitable for determination of Ox.HCl analyte in pharmaceutical preparations.

Materials and Methods

Reagents and solutions

All chemicals and reagents used were of analytical reagent grade. In all experiments, double distilled water was used. o-Nitrophenyloctylether (o-NPOE) was supplied from Fluka while dioctylphthalate (DOP), dibutylphthalate (DBP) and dioctyl sebecate (DOS) were supplied from BHD. Tricresylphosphate (TCP), polyvinylchloride (PVC) with relative high molecular weight) and graphite powder were supplied from Aldrich. Sodium tetraphenylborate (NaTBP; $Na[B(Ph)_4]$) and ammonium reineckate (RN; $NH_4[Cr(NH_3)_2(SCN)_4].H_2O$), phosphotungstic acid (PTA; $H_3[PW_{12}O_{40}]$) and phosphomolybdic acid (PMA; $H_3[PMo_{12}O_{40}]$) were purchased from Aldrich (USA).

Lactose, fructose, maltose, sucrose, starch, $CoCl_2.6H_2O$, $NiCl_2.6H_2O$, $MnCl_2.4H_2O$, NaCl, $CrCl_3.6H_2O$, $CuCl_2.2H_2O$ were used as interfering materials and they were purchased from El-Nasr Company, Egypt. Uripan tablets (5 mg Ox.HCl per tablet) were produced by ADWIA Pharmaceutical Company, El-Obour City, Cairo, Egypt.

NaTPB solution (1.0×10^{-2} mol L^{-1}) was prepared by dissolving an accurate weighed amount of it in warm water, adjusted to pH 9 by adding sodium hydroxide and completed to the desired volume with distilled water. The resulting solution was standardized potentiometrically against standard (1.0×10^{-2} mol L^{-1}) thallium(I) acetate solution.

Aqueous solutions of PTA, PMA and RN were prepared using the analytical grade chemicals and the exact concentrations of these solutions were determined by the appropriate recommended

methods[24–26] and lower concentrated solutions were prepared by the appropriate dilutions.

1.0×10^{-3} mol L^{-1} solution each of sucrose, fructose, maltose, lactose, starch and chloride salts of sodium, cobalt, manganese, nickel, chromium and copper was prepared by dissolving the proper weights into 100 mL double distilled water. All solutions must be protected from light by keeping them in dark-colored quickfit bottles during the whole work.

Stock Ox.HCl solution (1.0×10^{-2} mol L^{-1}) was prepared by dissolving the proper weight of the drug (394 mg) into smaller amount of double distilled water then stirring till the drug completely dissolved. The resulting solution was then made up to 100 mL with double distilled water in a measuring flask.

To prepare 1.0×10^{-2} mol L^{-1} of Uripan (pharmaceutical preparation), 39 tablets were taken, grounded well, dissolved in small amount of distilled water with stirring then filtered to get rid of insoluble materials and transferred quantitatively to 100 mL volumetric flask. Then content was estimated via potentiometry using the proposed electrodes. The method was repeated several times to check the accuracy and reproducibility of the proposed method.

Apparatus

Laboratory potential measurements were performed using HANNA pH/mV meter model 211 (Romania). Silver-silver chloride double junction reference electrode (Metrohm 6.0222.100) in conjugation with different drug ion selective electrodes was used.

Modified carbon paste electrode preparation

The MCPEs were prepared by mixing 250 mg carbon powder and 100 µL TCP with different amounts (2–25 mg) of ion pairs of Ox-PMA, Ox-PTA, Ox-RN and Ox-NaTPB, then all were homogenized in the mortar. The resulting paste was packed into the electrode[27,28] body (Teflon holder), then the surface of electrodes was polished by filter paper to get new working surface and rinsed in distilled water.

Results and Discussion

Electrochemical behavior of Ox.HCl with utilized electrodes

To obtain the electrochemical behavior, calibration was carried out by immersing the electrode in conjunction with the double junction Ag/AgCl reference electrode in solutions of Ox.HCl in the concentration range of 1.0×10^{-7}–1.0×10^{-2} mol L^{-1}. They were allowed to equilibrate by stirring and then recording the e.m.f. readings occurred. The electrodes showed a linear response over the concentration range 1.0×10^{-5}–1.0×10^{-2} mol L^{-1}. Different MCPEs were prepared with different types and content of ion pairs of Ox-PTA, Ox-RN, Ox-PMA, Ox-TPB and plasticized with TCP. It was clear from Table 1 that electrodes modified with 20, 10, 5 and 10 mg of Ox-TPB (electrode I), Ox-RN (electrode II), Ox-PMA (electrode III) and Ox-PTA (electrode IV) ion pairs showed the best Nernstian slope of 58.50±0.71, 58.71±1.20, 54.80±1.30 and 59.20±0.70 mV $decade^{-1}$, respectively.

Effect of plasticizer

The plasticizer molecules diffuse into the polymer and weaken the polymer–polymer interactions (van der Waals' forces) according to the lubricating theory of plasticization.[29] The plasticizer molecules reduce polymer–polymer interactive forces and prevent the formation of a rigid network as they act as shields. This lowers the glass transition temperature of PVC and allows the polymer chains to move rapidly past each other, resulting in increased flexibility, softness, and elongation. The mechanistic explanation of plasticization considers the interactions of the plasticizer with the PVC resin macromolecules. It assumes that the plasticizer molecules are not permanently bound to the PVC resin molecules but are free to self-associate and to associate with the polymer molecules at certain sites such as amorphous

Table 1 — Effect of types and content of ion pairs on MCPEs performance

Ion pairs	MCPE		
	Content (mg)	Slope (mV $decade^{-1}$)	R^2
	5	44.90±4.32	0.9911
Ox-TPB	10	45.50 ± 2.50	0.9982
	15	37.06±3.72	0.9881
	20	**58.50±0.71**	**0.9994**
	25	39.28±4.31	0.9986
	2	41.40±3.30	0.9973
Ox-PMA	**5**	**54.80±1.30**	**0.9981**
	10	47.25±2.21	0.9985
	15	44.67 ±2.90	0.9971
	20	43.21± 3.11	0.9988
	5	38.71±4.10	0.9877
Ox-RN	**10**	**58.71±1.20**	**0.9999**
	15	46.58±2.10	0.9894
	20	45.61±2.90	0.9962
	5	49.41±0.21	0.9991
Ox-PTA	**10**	**59.20±0.70**	**0.9994**
	15	39.30 ±2.15	0.9986
	20	44.70±1.15	0.9977

R^2: Correlation coefficent

sites. As these interactions are weak, there is a dynamic exchange process whereby, as one plasticizer molecule becomes attached at a site or center, it is readily dislodged and replaced by another. Different plasticizers yield different plasticization effects because of the differences in the strengths of the plasticizer–polymer and plasticizer–plasticizer interactions. At low plasticizer levels, the plasticizer–PVC interactions are the dominant interactions, while at high plasticizer interactions, plasticizer–plasticizer concentrations can become more significant. The polar portion of the molecule must be able to bind reversibly with the PVC polymer, thus softening the PVC, while the non-polar portion of the molecule allows the PVC interaction to be controlled so it is not so powerful a solvator as to destroy the PVC crystallinity. Plasticizers have a strong affinity for PVC polymers, but do not undergo a chemical reaction that causes bonding, or grafting, to the polymer.[29]

It is found that the electrode plasticized with TCP is the best one as it gives the highest Nernstian slope (59.5 ±0.20) in comparison with the other plasticizers where their slope‘s values were 63.50±0.5, 48.91±0.2, 65.50±1.5 and 27.20±1.4 mV decade^{-1} for DBP, DOP, o-NPOE and DOS plasticizers, respectively.

The pH effect

Aforementioned observation is advantageous, since the prime objective of this work was to analyze Ox.HCl in pharmaceutical preparations. Further, a detailed effect of pH on the response of electrodes (I-IV) at different pH were evaluated. The effect of pH on the performance of electrodes (I-IV) was studied over the pH range of 2–9 by immersing electrodes in 1.0×10^{-3} and 1.0×10^{-5} mol L^{-1} of Ox.HCl solutions. It is clear from Fig. 2 that the electrodes (I-IV) have stable potential readings in the pH range 2.0–6.0. The change at higher pHs could be the result of hydroxide precipitate formation, while in the low pH range, competitive proton binding is probably behind the decreased potential values.[30]

Life time

The performance of the MCPE potentiometric sensors (electrodes I-IV) was studied. The electrodes (I – IV) were calibrated on different days. Fig. 3 showed that lifetime of past of the MCPEs (electrodes I – IV) were 36, 26, 30 and 30 days. These electrodes surface needed to be refreshed by scratch and rinsed in distilled water to remove the memory effect.

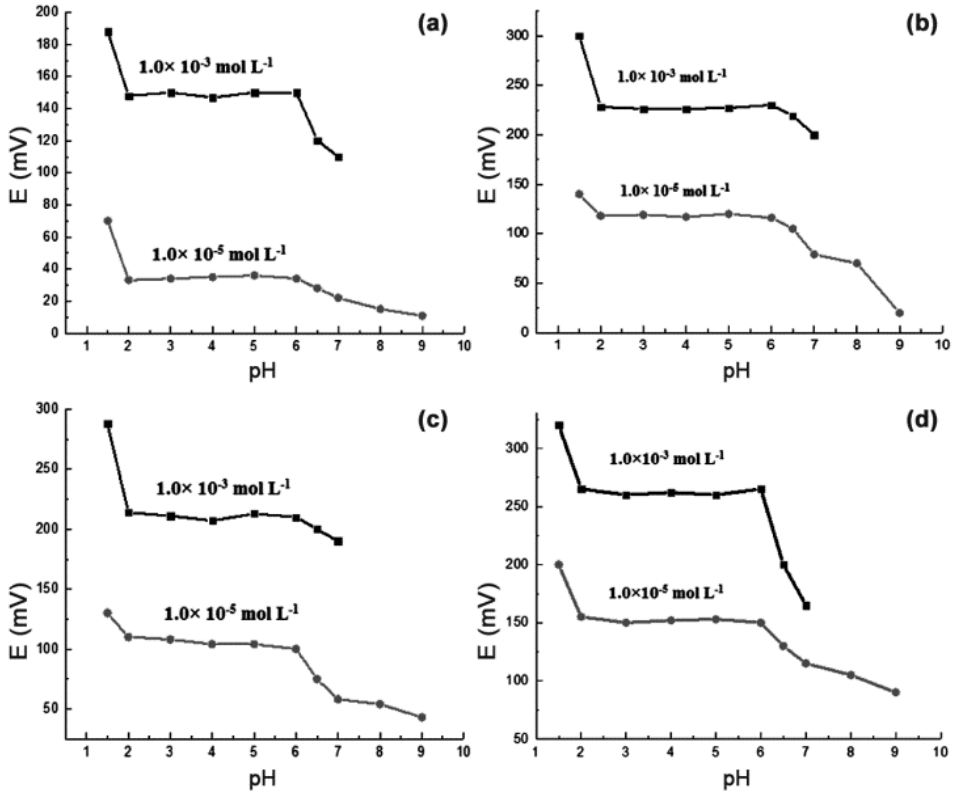

Fig. 2 □ Effect of pH on performance of MCPEs: (a) electrode I, (b) electrode II, (c) electrode III and (d) electrode IV.

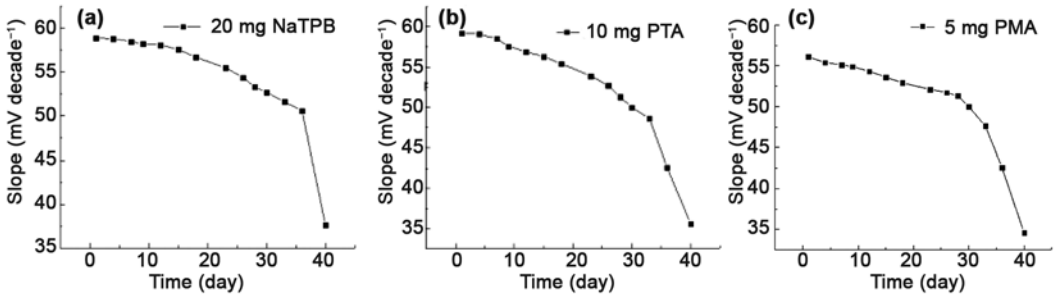

Fig. 3 — Effect of life time on the performance of some MCPEs: (a) electrode I, (b) electrode III and (c) electrode IV.

Table 2 — Potentiometric selectivity coefficient values of Ox.HCl using MCPEs (Electrodes I-IV)

Interfering compound	$K^{pot}_{D,B}$ MCPEs							
	Electrode I		Electrode II		Electrode III		Electrode IV	
	SSM	MPM	SSM	MPM	SSM	MPM	SSM	MPM
Mn^{2+}	5.37×10^{-3}		7.70×10^{-3}		1.89×10^{-3}		6.67×10^{-3}	
Ni^{2+}	8.29×10^{-3}		1.39×10^{-3}		3.11×10^{-4}		4.18×10^{-3}	
Na^{+}	2.15×10^{-4}		1.11×10^{-2}		5.98×10^{-5}		5.57×10^{-4}	
Cu^{2+}	7.37×10^{-3}		1.50×10^{-3}		1.47×10^{-3}		4.02×10^{-3}	
Co^{2+}	6.54×10^{-3}		1.69×10^{-3}		1.05×10^{-3}		5.49×10^{-3}	
Cr^{3+}	1.63×10^{-3}		4.94×10^{-3}		1.43×10^{-4}		1.19×10^{-3}	
Fructose		2.42×10^{-4}		7.50×10^{-5}		4.85×10^{-5}		3.58×10^{-3}
Maltose		1.39×10^{-4}		1.05×10^{-5}		1.62×10^{-5}		7.26×10^{-4}
Sucrose		1.45×10^{-4}		2.08×10^{-4}		5.06×10^{-5}		3.18×10^{-3}
Starch		3.45×10^{-4}		2.32×10^{-5}		5.98×10^{-5}		8.82×10^{-4}
Lactose		2.42×10^{-4}		1.06×10^{-5}		2.48×10^{-5}		6.17×10^{-3}

Selectivity coefficients

The influence of some inorganic cations and sugars on the electrodes were investigated as shown in Table 2. The selectivity coefficients values of the MCPEs reflect a very high selectivity of the proposed electrodes toward the Ox.HCl over the interfering species. The inorganic cations do not interfere owing to the differences in ionic size, and consequently their mobilities and permeability. In the case of sugars, the high selectivity is mainly attributed to the difference in polarity and lipophilic character of their molecules relative to Ox.HCl.

Effect of temperature

The effect of temperature on the performance of the potentiometric electrodes was evaluated from (10–60) °C and the isothermal coefficient ($dE°/dT$) will be determined for each electrode according to the following equation:[31]

$$E^0_{cell} = E^0(25) + \left(dE^0/_{dT}\right)(t-25)$$

Wher E^0 (25) is the standard electrode potential at 25 °C This effect is done by measuring the potential of the investigated electrode at different temperature (10–60 °C) for different concentrations then (t-25) was ploted against E^0_{cell}. It is obvious that the electrode gave a good Nernstian response in the temperature range 10–60 °C. The slope of the straight–line obtained represented the isothermal coefficient of MCPEs ($dE°/dT$) which were found to be 0.791×10^{-3}, 0.769×10^{-3}, 0.629×10^{-3} and 1.277×10^{-3} V/°C for electrodes I, II, III and IV, respectively as summarized in Table 3. The small value of isothermal coefficient indicates the high thermal stability of the electrodes.

The drug is stable up to 100 °C and amount of loss on drying at 100–105 °C is ≤ 3% according to the reported of manufacturing company.

Response time

The average time required for the electrode to reach a steady potential response within ±1 mV of the final equilibrium value. It is clear from Fig. 4 that these electrodes have a fast response time which is 10 s for electrode I and 12 s for electrodes II-IV, which reflect the incorporation of best content of ion pairs and good solvent mediator.

Application on pharmaceutical and comparison with official method

The designed sensors were utilized to determine Ox.HCl in pharmaceutical preparations (Uripan tablet)

Table 3 — Comparison between response characteristics of MCPEs (Electrodes I-IV)

	MCPEs			
Parameters	I	II	III	IV
Slope (mV decade^{-1})	58.50±0.71	58.71±1.20	54.80±1.30	59.20±0.70
Intercept	328.8	414.2	323.4	390.5
Correlation coefficient (R^2)	0.999	0.999	0.999	0.999
Linear range (mol L^{-1})	1.0×10^{-2}–1.0×10^{-5}	1.0×10^{-2}–1.0×10^{-5}	1.0×10^{-2}–1.0×10^{-5}	1.0×10^{-2}–1.0×10^{-5}
Detection limit (mol L^{-1})	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}	1.0×10^{-5}
Quantification limit (mol L^{-1})	3.33×10^{-5}	3.33×10^{-5}	3.33×10^{-5}	3.33×10^{-5}
Responce time (s)	12.0	10.0	10.0	10.0
Working pH	2.0–6.0	2.0–6.0	2.0–6.0	2.0–6.0
Lifetime (day)	36	26	30	30
Isothermal coefficient (V/°C)	0.791×10^{-3}	0.769×10^{-3}	0.629×10^{-3}	1.277×10^{-3}
Recovery (%)	97.92–101.86	97.92–102.50	98.01–102.48	98.22–102.51
SD	0.003–0.165	0.003–0.165	0.002–0.160	0.003–0.127
RSD (%)	1.02–4.05	1.01–4.05	0.99–4.31	1.07–4.05

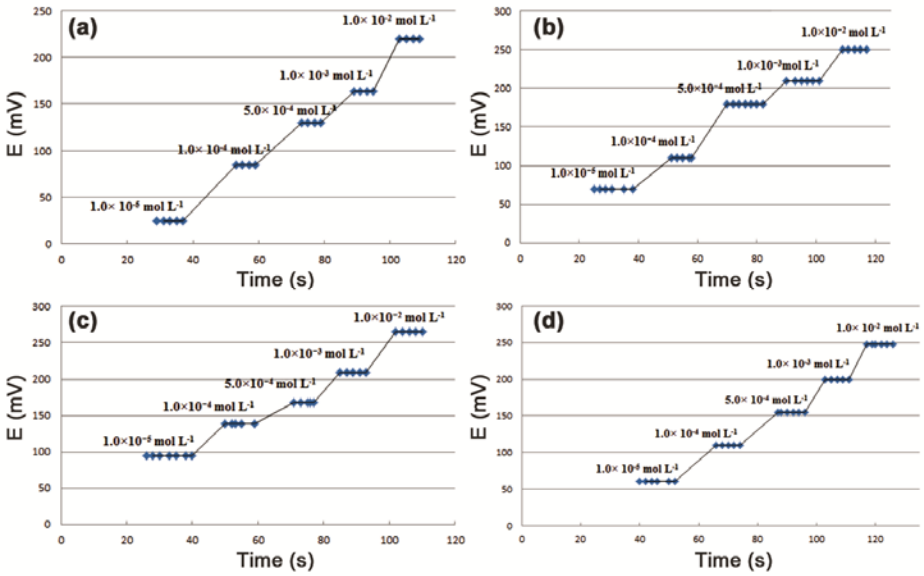

Fig. 4 — Dynamic response time of the MCPEs: (a) electrode I, (b) electrode II, (c) electrode III and (d) electrode IV.

using the potentiometric calibration and standard addition methods. The results obtained were compared to the official method[32] and the data obtained were summarized in Table 4. Statistical evaluation of the results of analysis of pure Ox.HCl by the proposed electrodes and the official method showed that there is no significant difference between the proposed and reported method.

Method validation

The analytical method[33-35] was validated according to the international conference for Harmonization (ICH) guidelines under the optimized experimental conditions: linearity, accuracy, precision, specificity, limit of detection (LOD) and limit of quantification (LOQ) were achieved for standard Ox.HCl solution. Limit of detection (LOD) and limit of quantification (LOQ) were calculated using the following equations LOD = 3S/m and LOQ = 10S/m where S is the standard deviation of the peak currents of the blank (five runs), and m is the slope of the calibration curve.

LOD is the lowest quantity of the investigated compound in sample that can be detected but not necessarily quantified with an acceptable uncertainty. It was the concentration of measured ion at the point of intersection between the extrapolated linear segment of the calibration curve representing the normal slope of electrode and horizontal line representing the voltage when the concentration has small changes and not produced any detectable change in the response. LOD for official method equal 80–120 ppm of target concentration. In this case, the LOD was 1.0×10^{-5} mol L^{-1} as shown in

Table 4 — Potentiometric determination of Ox.HCl in Uripan tablets using MCPE

Electrode Type	[Ox.HCl]	Calibration method in Uripan					Standard addition method				
	Taken (mg mL^{-1})	Found (mg mL^{-1})	Recovery (%)± SD	RSD (%)	F-test	t-test	Found (mg mL^{-1})	Recovery (%)± SD	RSD (%)	F-test	t-test
I	3.939	3.863	98.07±0.087	2.24	0.27	0.39	3.969	100.76±0.118	2.97	0.15	1.51
	0.394	0.393	99.74±0.007	1.73	0.18	2.00	0.394	100.00±0.011	2.70	0.07	1.09
	0.197	0.197	100.00±0.006	3.05	-	-	0.195	98.98± 0.005	2.65	-	-
II	3.939	3.940	100.03±0.051	1.29	0.77	2.30	3.919	99.49 ±0.039	1.01	1.33	2.00
	0.394	0.389	98.75±0.006	1.61	0.25	2.20	0.388	98.47± 0.008	1.94	0.14	2.39
	0.197	0.195	98.28±0.003	1.40	-	-	0.194	98.47± 0.002	1.03	-	-
III	3.939	3.919	99.50±0.039	0.99	1.33	2.00	3.879	98.48±0.040	1.02	1.27	0.50
	0.394	0.390	99.06±0.010	2.62	0.09	2.07	0.397	100.76±0.012	3.13	0.06	0.51
	0.197	0.196	99.49±0.008	4.04	-	-	0.196	99.49±0.002	1.02	-	-
IV	3.939	3.899	98.98±0.081	2.06	0.31	0.46	4.038	102.51 ±0.114	2.82	0.16	2.31
	0.394	0.387	99.22±0.009	2.32	0.11	2.23	0.391	99.23±0.007	1.66	0.18	2.42
	0.197	0.196	99.49±0.007	3.35	-	-	0.198	100.51±0.004	1.93	-	-
Official Method [32]	3.930	3.880	98.73±0.045	1.402.2							
	1.871	1.840	98.50±0.001	5							
	0.393	0.400	101.78±0.003	3.07							

SD: Standard deviation
RSD: Relative standard deviation
F & t-test: Statistical tests for comparing different sets of data
No. of replicates (n=5)

Table 3 which indicated that these sensors have high sensitivity and can be used for determination of low concentration of Ox.HCl drug. LOQ is the lowest amount of compound that can be measured in sample matrix at an acceptable level of accuracy and precision. It was found that LOQ is 3.33×10^{-5} mol L^{-1} as shown in Table 3 which indicates the high sensitivity of these electrodes.

Accuracy is important requirement of analytical methods. It is the closeness between the true or accepted reference value and the obtained value. As seen from Table 4, the high values of % recovery ensure the high accuracy of this method. Precision is the measurement of how close results to each other. It usually expressed as standard or relative standard deviations of the replicated analysis. Inter and intra-day precisions were assessed using three concentrations from the Ox.HCl drug and five replicates for each concentration. The relative standard deviation values were found to be small indicating the good repeatability and reproducibility of the proposed method Table 5. Linearity measures how well calibration plot of electrochemical potential versus concentrations approximates a straight line. The standard calibration curve was obtained by using five concentration of Ox.HCl standard. The linear relationship was obtained between negative logarithm [Ox.HCl] and potential (mV) as shown in Table 3. The linear range for both MCPE was 1.0×10^{-5}–1.0×10^{-2} mol L^{-1}. Specificity was done by observing any interference from the common excipients of the pharmaceutical formulation. It was found that these components did not interfere with the result of proposed method as given in Table 2.

The proposed method was compared with previously reported potentiometric methods used for the determination of oxybutynin.[7,36] The comparison of the results of the two presented sensors to those in literature as given in Table 6 shows that the sensors proposed in this study have a wide range of selectivity with respect to a large number of inorganic cations and sugars, when compared to the other methods. The sensors exhibit longer life span (more than 90 days), and have wide stable pH range under both batch and FIA conditions. The sensors can thus be used for routine analysis and verification in quality assurance during manufacture of oxybutynin and related pharmaceuticals, as well as for checking dissolution. As can be seen, the proposed lead-selective electrode improved many of those reported in relevant characteristics of response such as concentration range, detection limit, selectivity coefficients for potential interfering ions (especially for Hg(II) which was considered as a main interferent in the previously reported Pb(II) ISEs) and response time, however they have nearly the same Nernstian

Table 5 — Evalution of accuracy and precision (intra and inter-day) of MCPE (Electrodes I-IV)

Drug Form	Electrode Type	[OxHCl]	Intra-day			Inter-day		
		Taken (mg mL^{-1})	Found (mg mL^{-1})	Recovery (%)±SD	RSD(%)	Found (mg mL^{-1})	Recovery (%)±SD	RSD(%)
Pure Form	I	3.939	3.918	99.46±0.043	1.09	3.880	98.51±0.073	1.88
		0.394	0.392	99.49 ±0.004	1.02	0.401	101.86±0.009	2.12
		0.197	0.196	99.49± 0.003	1.33	0.192	97.92±0.008	4.05
	II	3.939	4.038	102.50±0.165	4.07	3.952	100.33 ±0.051	1.29
		0.394	0.396	100.87±0.007	1.72	0.388	99.57 ±0.011	2.82
		0.197	0.199	101.02±0.003	1.73	0.192	97.92 ±0.008	4.02
	III	3.939	3.864	98.01± 0.160	4.15	3.958	100.50 ±0.039	0.99
		0.394	0.399	101.51±0.012	2.96	0.404	102.48 ±0.011	2.80
		0.197	0.200	101.67±0.007	3.28	0.201	102.20±0.009	4.31
	IV	3.939	3.921	99.54 ± 0.092	2.34	3.930	99.78 ±0.127	3.25
		0.394	0.391	99.28 ± 0.005	1.14	0.388	99.57±0.009	2.27
		0.197	0.196	99.49±0.003	1.30	0.196	99.49 ±0.003	1.30
Uriban	I	3.939	3.863	98.07±0.087	2.24	3.897	98.92 ±0.049	1.26
		0.394	0.393	99.74±0.007	1.73	0.397	100.90 ±0.007	1.85
		0.197	0.197	100.00±0.006	3.05	0.199	101.05± 0.004	2.08
	II	3.939	3.940	100.03±0.051	1.29	3.922	99.56 ±0.019	0.50
		0.394	0.389	98.75±0.006	1.61	0.390	99.03 ±0.006	1.61
		0.197	0.195	98.28±0.003	1.40	0.192	97.54 ±0.007	4.08
	III	3.939	3.919	99.50±0.039	0.99	3.988	101.24 ±0.008	1.97
		0.394	0.390	99.06±0.010	2.62	0.396	101.61 ±0.005	1.24
		0.197	0.196	99.49±0.008	4.04	0.198	100.50±0.006	2.84
	IV	3.939	3.899	98.98±0.081	2.06	3.884	98.61 ± 0.069	1.79
		0.394	0.387	99.22±0.009	2.32	0.390	99.16± 0.004	1.07
		0.197	0.196	99.49±0.007	3.35	0.195	98.98±0.008	4.05

No. of replicates (n = 5)

Table 6 — Comparison between performance characteristics of OxHCl sensors and previously reported sensors

Ref.	Modifier	Slope (mVdecade^{-1})	Linear range (mol L^{-1})	pH range	Life time (day)
[7]	Ox-PTA				
	Batch	58.02	1×10^{-5}–1×10^{-2}	2.0-8.0	30
	FIA	59.20	5×10^{-5}–1×10^{-2}	1.0–6.0	>90
	Ox-PMA		1×10^{-6}–1×10^{-2}	2.0–7.0	30
	Batch		5×10^{-5}–1×10^{-2}	1.0–6.0	>90
	FIA				
[36]	Ox-PTA	<59.9	1×10^{-6}–1.0×10^{-2}	5.0–8.0	30
Present study	Ox-TPB	58.50±0.71	1×10^{-5}–1.0×10^{-2}	2.0–6.0	36
	Ox-RN	58.71±1.20 54.80±1.30			26
	Ox-PMA	59.20±0.70			30
	Ox-PTA				30

slopes and working pH ranges. In addition, all of the listed electrodes are PVC membrane based which suffers from increased system impedance and the electrode response time, but this work is carbon paste electrode based which is simple, cheap and renewable. So, it is apparent that these electrodes are superior to previously reported electrodes in most cases as it can be used in a wider concentration range with an enhanced sensitivity and selectivity for Ox.HCl drug from a wide variety of metal ions sugar and excipients (which is more proper for industrial pharmaceutial samples) with a very fast response time and a fairly long lifetime.

Conclusions

MCPEs have high sensitivity, high selectivity, fast response time and high stability over reasonable pH and temperature ranges. This method is valid and the validation parameter, have a good agreement with the official method. These electrodes were precise and sensitive for determination of Ox.HCl in pure and

pharmaceutical samples by using calibration and standard addition method. The preparation processes of MCPEs are very simple, cheap, quick and reproducible. Good limit of detection obtained for Ox.HCl determination in this work is adequate for determining various real samples from the pharmaceuticals. This authenticates MCPEs would be considered as promising sensors for Ox.HCl determination.

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