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Research Article

POTENTIOMETRIC DETERMINATION OF RANITIDINE HYDROCHLORIDE UTILIZING MODIFIED CARBON PASTE ELECTRODES

GEHAD G. MOHAMED[a*], M. M. KHALIL[b], E. Y. Z. FRAG[a] AND GAMAL M. ABED EL AZIZ[b]

[a]Chemistry Department, Faculty of Science, Cairo University, 12613, Giza, Egypt, [b]Chemistry Department, Faculty of Science, Beni-Suef University, Beni- Suef, Egypt. Email: Ggenidy@hotmail.com

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ABSTRACT

Sensitive potentiometric method is reported in this work for the determination of ranitidine hydrochloride (RNH) in pure form and pharmaceutical preparation using modified carbon paste (MCPE) and insitu carbon paste (ICPE) electrodes. The MCPE and ICPE electrodes are based on ranitidine-tetraphenyl borate ion pair (RNH-TPB) and sodium tetraphenyl borate ion pairing reagent (Na TPB), respectively, by using tricresyl phosphate (TCP) as plasticizer. The MCPE and ICPE electrodes exhibit suitable response to RNH in the concentration range from 1 $x10^{-6}$ to 1 $x10^{-2}$ mol L^{-1}. The slope of the electrodes were 56.8±1.4 and 57.9±1.65 mV $decade^{-1}$ over the pH range 3-8 and 3-9 for MCPE and ICPE electrodes, respectively. Selectivity coefficients of RNH relative to a number of potential interfering substances were investigated. The MCPE and ICPE electrodes showed fast response time of 4 and 3.5 sec, respectively, and were used over a period of two months with good reproducibility. The sensors were applied successfully to determine RNH in pure and pharmaceutical preparations.

Keyword: Ranitidine hydrochloride, MCPE, ICPE, Potentiometry, Ion selective electrodes.

INTRODUCTION

Ranitidine hydrochloride (RNH) (Figure 1) is a histamine H_2-receptor antagonist that inhibits stomach acid production. It is commonly used in treatment of peptic ulcer disease (PUD) and gastroesophageal reflux disease (GERD). Ranitidine is also used alongside with fexofenadine and other antihistamines for the treatment of skin conditions such as hives. Chemically, it is N-[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N′-methyl-2-nitro-1,1-ethene-damine HCl.

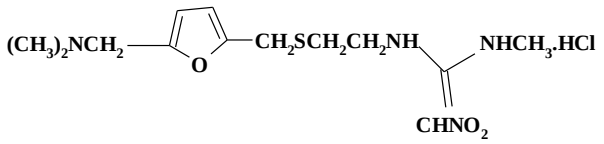

Fig. 1: Structural formula of RNH drug.

Various analytical techniques have been employed for the quantitative analysis of RNH. Most of these analytical methods were based on high performance liquid chromatography (HPLC) which was applied for determination of RNH and its metabolites in biological fluids [1-6], capillary electrophoresis using UV or capillary electrophoresis-electrochemiluminescent detection [7, 8], and spectrophotometric methods [9-14]. Different electrochemical analytical methods were applied for determination of RNH which included voltammetric behaviour [15, 16], coulometric titration [17] and potentiometry using ion-selective electrodes based on liquid-membrane, polyvinyl chloride (PVC)-matrix ion-selective electrodes (ISE) and unmodified carbon paste electrodes that respond to the cationic forms of RNH [18-21].

Most of these methods, however, utilize expensive instrumentation, suffer from lack of selectivity, involve careful control of the reaction conditions or derivatization reactions, and require time-consuming pretreatment steps, which affect their usefulness for routine analysis. On the other hand, applications of potentiometric sensors in the field of pharmaceutical and biomedical analysis have been advocated [22]. The approach provides simple, fast, and selective technique for determination of various drugs [22-31].

However, as far as the available literature is concerned, very little is known about the use of this technique for RNH quantification [20, 21, 32, 33]. The present work describes preparation, characterization and application of modified carbon paste (MCPE) and insitu carbon paste (ICPE) electrodes for continuous determination of RNH in pure and pharmaceutical preparations. Performance characteristics of both sensors (MCPE and ICPE) reveal low detection limit, high sensitivity, good selectivity, fast response, long life span and application for accurate determination of RNH in pharmaceutical preparations.

MATERIALS AND METHODS

All chemicals were of analytical preparation of RNH and reagent grade unless otherwise specified. Doubly distilled water was used for the preparation of stock solutions of RNH, pure ranitidine hydrochloride (RNH) which was provided by GlaxosmithKline Egypt.

Sodium tetraphenylborate (NaTPB), ammonium reineckate (RN), phosphotungstic acid (PTA) and acetone were purchased from Fluka (Switzerland). Phosphomolybdic acid (PMA) was purchased from Aldrich (USA). NaTPB, PTA, PMA and RN were used for precipitation of different ion pairs.

o-Nitrophenyloctylether (*o*-NPOE) was supplied from Fluka (Switzerland), while dioctylphthalate (DOP), dibutylphthalate (DBP) and dioctylsebacate (DOS) were supplied from Merck (Germany) and tricresylphosphate (TCP) and graphite powder (synthetic 1–2 µm) were supplied from Aldrich (USA). Glucose, lactose, starch, sucrose, maltose, fructose, glycine, cadmium chloride, cobalt chloride, ferric chloride, ammonium chloride and sodium fluoride were used as interfering materials from El-Nasr Company.

The RNH pharmaceutical preparations were Aciloc (Ranitidine hydrochloride, 75 mg tablets, SIGMA Pharm. Ind., Egypt), Rantidol [Ranitidine HCl, 150 mg film coated tablets, El Nasr Pham. Chem. Co., Egypt) and Histac (Ranitidine, 150 mg tablets, RANBAXY, Egypt).

Apparatus

Laboratory potential measurements were performed using HANNA pH-mV meter model 211. Silver-silver chloride double - junction reference electrode (Metrohm 6.0222.100) in conjugation with different drug ion selective electrode was used. Digital multimeter connected to a portable PC and Brand digital burette was used for the measurement of the drug under investigation. Prior to analysis, all glassware used were washed carefully with distilled water and dried in the oven before use.

Preparation of ion pairs

An ion-pair was made from ranitidine hydrochloride (RNH) and one of the following substances: sodium tetraphenylborate (NaTPB), phosphotungstic acid (PTA), phosphomolybdic acid (PMA) or

ammonium reineckate (RN) according to previously reported method [21, 34].

Electrode preparation

Modified and insitu carbon paste electrodes were prepared as previously described [35]. The sensor was used directly for potentiometric measurements without preconditioning. A fresh surface of the paste was obtained by squeezing more out. The surplus paste was wiped out and the freshly exposed surface was polished on a paper until the surface showed shiny appearance.

Effect of pH

The effect of pH on the potential values of the MCPE and ISPE electrodes was studied over the pH range of 1–12 at 1-pH interval. This is done by immersing the electrodes in 10^{-2} and 10^{-4} mol L^{-1} RNH solutions. The pH was gradually increased or decreased by adding aliquots of diluted sodium hydroxide or hydrochloric acid solutions, respectively. The potential obtained at each pH was recorded.

Selectivity coefficient determination

The response of the two studied electrodes was also examined in the presence of a number of other related substances.

The potentiometric selectivity coefficients were evaluated according to IUPAC guidelines using the separate solution method [36] in which the potential of cell compromising the MCPE and ICPE electrodes and a reference electrode is measured with two separate solutions, D and B where D (RNH ions) and B (interfering ion) at the same activity $a_D = a_B$. Selectivity coefficients were calculated by the separate solutions method, where potentials were measured for 10^{-3} mol L^{-1} RNH solution and then for 10^{-3} mol L^{-1} interfering solution, separately. Then potentiometric selectivity coefficients were calculated using the following equation [36]:

$$\text{Log } K^{pot}_{D,B} = ((E_1 - E_2)/S) + (1 + (Z_1/Z_2) \log a$$

Where S is the slope of the calibration plot, E_1 is the potential measured in 1×10^{-3} mol L^{-1} RNH (D), E_2 the potential measured in 1×10^{-3} mol L^{-1} of the interfering compound (B), z_1 and z_2 are the charges of the RNH (D) and interfering species (B), respectively.

In addition to the SSM, the selectivity of the investigated electrodes was determined by the matched potential method (MPM) [37]. In this method, the potentiometric selectivity coefficient is defined as the activity ratio of primary and interfering ions that give the same potential change under identical conditions.

At first, a known concentration ($C`_D$) of the drug ion solution is added into a reference solution that contains a fixed concentration (C_D) of drug ions, and the corresponding potential (ΔE) is recorded. Next, solution of an interfering ion is added to the reference solution until the same potential change (ΔE) is recorded. The change in potential produced at the constant background of the drug ion must be the same in both. The selectivity coefficient can be calculated using the equation:

$$K^{pot}_{D,B} = (C`_D - C_D)/C_B$$

Where, C_B is the concentration of the interfering ion.

Application to pharmaceutical form

Ranitidine hydrochloride was determined in different pharmaceutical preparations namely Aciloc, Rantidol and Histac. Samples of ranitidine hydrochloride (tablets) ranging from 1.0×10^{-6} to 1.0×10^{-2} mol L^{-1} were determined by the standard addition and the calibration curve methods. Three tablets were powdered and homogenized as described previously [21]. About 175.5 mg of RNH was accurately weighed and dissolved in 50 mL of bi-distilled water. This procedure produced 10^{-2} mol L^{-1} solution of ranitidine hydrochloride and then series of solutions from 1.0×10^{-6} to 1.0×10^{-2} mol L^{-1} were prepared. Different volumes of these solutions were analyzed by the above method using the present electrodes (MCPE and ICPE). Each analysis was repeated 5 times.

RESULTS AND DISCUSSION

The development and application of ion-selective electrodes (ISEs) continue to be of interest for pharmaceutical analysis because they offer the advantages of simple design and operation, fast response, reasonable selectivity, low detection limit, high accuracy, wide concentration range applicability to coloured and turbid solutions, and possible interfacing with automated and computerized systems [38].

Elementary analysis

The ion-pairs RN-TPB, RN-RN, RN-PTA and RN-PMA which have a white, pink, yellowish white and dark yellowish white colours, respectively, result from reaction between RNH and NaTPB, RN, PTA and PMA ion-pairing agents, respectively, which can be used as modifiers in RNH sensors. Table 1 shows that the calculated and the observed analysis data for the ion-associate complexes are in good agreement with their proposed structures.

Table 1: Composition of the ion pairs.

Type of ion pair	Calculated values			Found values			Stoichiometric ratio
	%C	%H	%N	%C	%H	%N	
RN-TPB	70.00	6.78	8.82	70.07	6.84	8.79	1:1
RN-RN	31.30	5.37	23.62	31.17	4.86	22.91	1:1
RN-PTA	12.24	1.80	4.39	11.84	1.60	4.12	3:1
RN-PMA	16.90	2.49	6.07	15.94	2.18	5.80	3:1

Table 2: Effect of ion-pair (RN-TPB) and ion-pairing agent (NaTPB) content on the electrodes performances.

Electrode type	IP content (mg)	Concentration range (mol L^{-1})	Slope (mV $decade^{-1}$)	R*
	2.50	10^{-6}- 10^{-2}	18.20±0.42	0.969
MCPE	5.00	10^{-6}- 10^{-2}	23.30±1.80	0.968
	7.50	10^{-6}- 10^{-2}	26.80±1.18	0.991
	10.00	**10^{-6}- 10^{-2}**	**56.80±1.40**	**0.9882**
	12.50	10^{-6}- 10^{-2}	25.60±0.90	0.991
	15.00	10^{-6}- 10^{-2}	22.30±1.12	0.9946
ICPE	2.50	10^{-6}- 10^{-2}	34.10±1.44	0.998
	5.00	10^{-6}- 10^{-2}	38.60±1.94	0.9984
	7.50	10^{-6}- 10^{-2}	42.11±0.94	0.992
	10.00	**10^{-6}- 10^{-2}**	**57.90±1.65**	**0.993**
	12.50	10^{-6}- 10^{-2}	50.10±0.66	0.992
	15.00	10^{-6}- 10^{-2}	46.45±1.11	0.986

*R: Correlation coefficient

Construction of Electrodes

Composition of the electrodes

Six electrodes containing 2.5, 5, 7.5, 10, 12.5 and 15 mg of RN-TPB ion pair (in case of MCPE) or NaTPB ion pairing agent (in case of ICPE) were prepared. Electrodes with 10 mg RN-TPB or NaTPB show the best Nernstian behaviour (slope = 56.80±1.40 and 57.90±1.65 mV decade^{-1} for MCPE and ICPE electrodes respectively) as shown in Table 2. None of the compositions gives the true theoretical slope because of the expected lack of thermodynamic ion-exchange equilibrium at the solution–solid interface.

Effect of ion pair and ion pairing agent types

Different ion pairs (IPs) including RN-TPB, RN-RN, RN-PTA and RN-PMA (10 mg) were incorporated as ion exchangers in preparation of MCPE electrodes. While, different ion pairing agents such as NaTPB, PMA, PTA and RN were incorporated as ion exchangers in preparation of ICPE electrodes. It is found that the best electrodes are which contain RN-TPB ion pair and TPB$^-$ ion pairing agent for MCPE and ICPE electrodes, respectively. The data obtained are summarized in Table 3.

Calibration of the electrodes

The fabricated electrodes (MCPE and ICPE) plasticized with TCP in conjunction with the double junction Ag/AgCl reference electrode were calibrated by immersing them in solution of RNH in the concentration range of 1.0 x10^{-6} – 1.0 x10^{-2} mol L^{-1}. They were allowed to equilibrate while stirring and recording the e.m.f reading, the MCPE and ICPE sensors showed a linear response over the concentration range from 1.0 x10^{-6} to 1.0x10^{-2} mol L^{-1} with Nernstian slope of 56.80±1.40 and 57.90±1.65 mV decade^{-1}, respectively [36] (Figure 2). On comparing with the previously published potentiometric method of determination of RNH drug, the unmodified CPE shows a lower Nernstain slope of 55.7±1 mV decade^{-1} than the electrodes under study [21].

Table 3: Effect of incorporating different ion pairs and ion-pairing agents on the performances of MCPE and ICPE electrodes, respectively.

Electrode type	Content type (10 mg)	Concentration range (mol L^{-1})	Slope (mV decade^{-1})	R
	RN-TPB	**10^{-6}- 10^{-2}**	**56.80±1.40**	**0.992**
MCPE	RN-RN	10^{-6}- 10^{-2}	35.00±1.30	0.978
	RN-PTA	10^{-6}- 10^{-2}	45.00±1.60	0.995
	RN-PMA	10^{-6}- 10^{-2}	35.50±2.40	0.996
ICPE	**TPB$^-$**	**10^{-6}—10^{-2}**	**57.90±1.60**	**0.993**
	RN	10^{-6}—10^{-2}	37.40±1.50	0.979
	PTA	10^{-6}—10^{-2}	50.10±0.80	0.991
	PMA	10^{-6}—10^{-2}	41.80±1.30	0.998

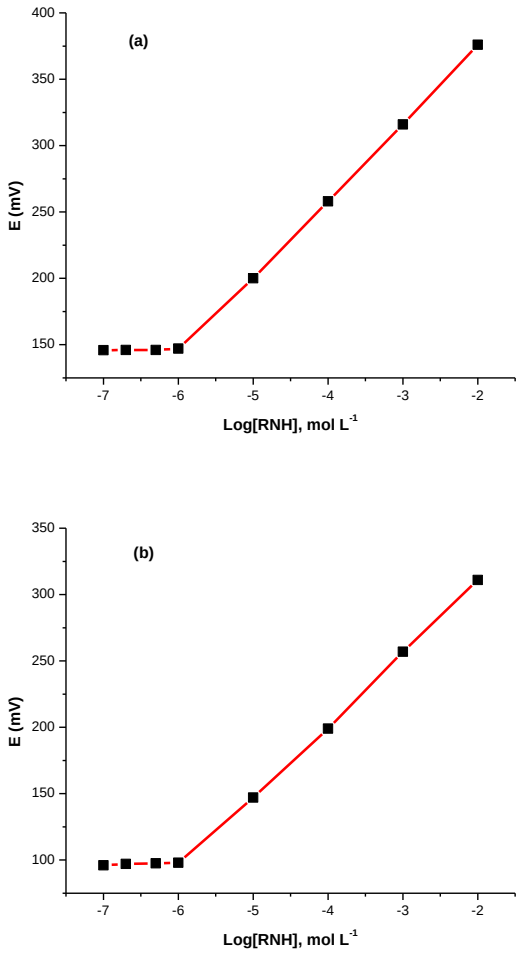

Fig. 2: Calibration curves of RNH using (a) ICPE and (b) MCPE potentiometric electrodes.

Life time

The performance of the fabricated MCPE and ICPE sensors has been tested by calibration method in the concentration range of 10^{-6} - 10^{-2} mol L^{-1} of RNH on different days from one day to 70 days and the measurement of the Nernstian slopes are recorded. The data obtained for MCPE and ICPE electrodes are shown in Figure 3. For MCPE, it is clear that a change in Nernstian slope was observed after 62 days. While For ICPE, there is a change in Nernstian slope after 65 days. It is clear that the incorporation of RN-TPB ion pair (in case of MCPE) or NaTPB (in case of ICPE) increases the life time of the electrodes when compared with the previously published data using unmodified CPE (47 days) [21].

Response time

The response time of a fabricated sensor is the average time required for the electrode to reach a steady potential response within ± 1 mV of the final equilibrium value after successive immersion in a series of RNH solutions, each having a 10 fold–difference in concentration [37]. The response time of the MCPE and ICPE sensors was defined from the slope of the calibration curve of RNH solution when the RNH concentration was rapidly increased from 10^{-6} to 10^{-3} mol L^{-1} (Figure 4). It is found that the response time of the MCPE and ICPE is 4s and 3.5 s, respectively, and the equilibrium potentials essentially remained constant for over 18 min, comparing with the previous potentiometric method of determination of RNH drug where the response time was 4s [21].

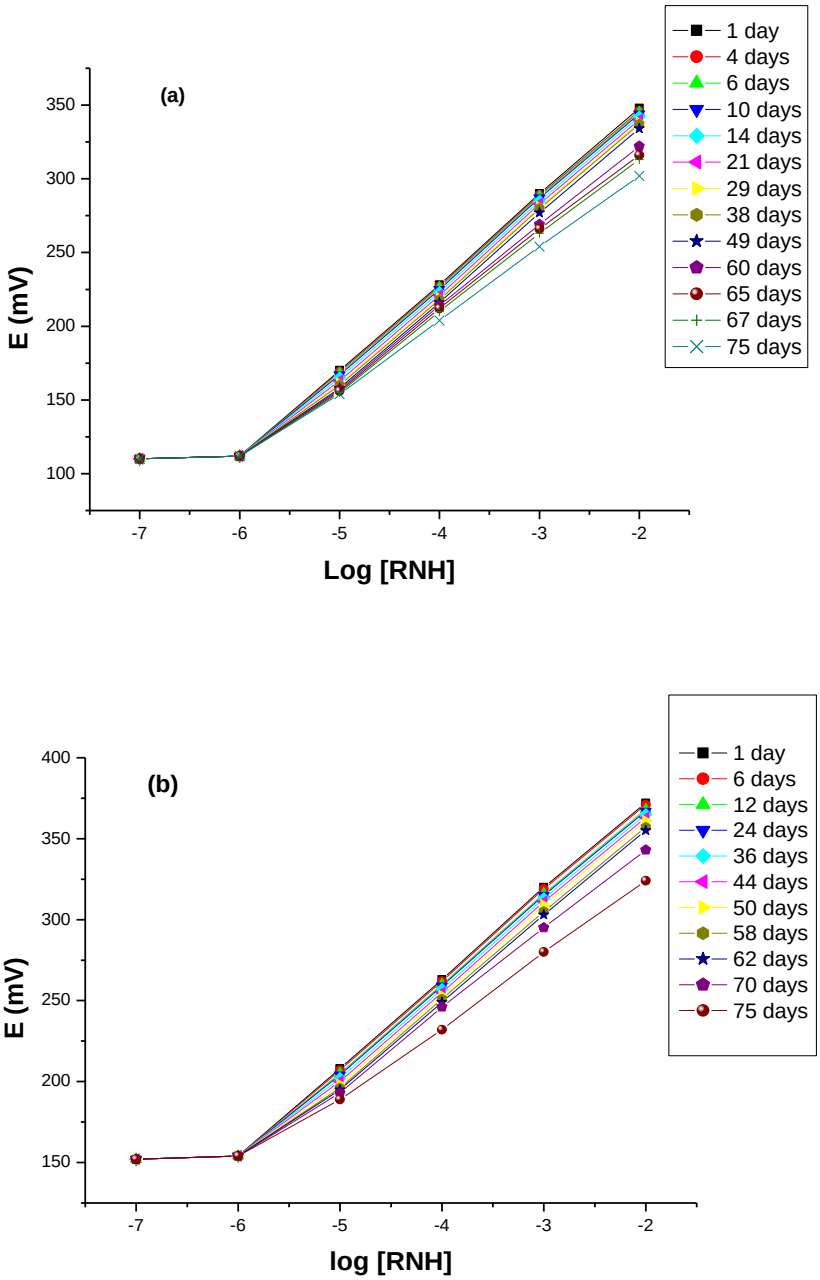

Fig. 3: Life time of (a) ICPE and (b) MCPE potentiometric electrodes.

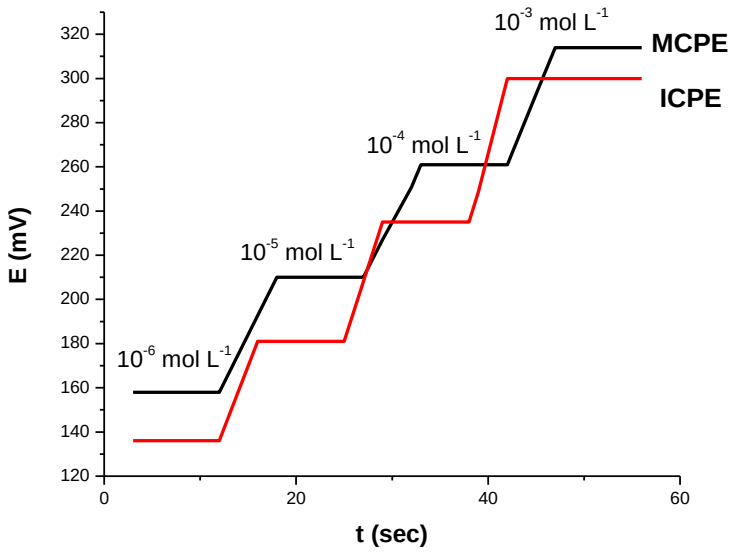

Fig. 4: Dynamic response time of MCPE and ICPE potentiometric electrodes.

Effect of pH

The effect of pH on the MCPE and ICPE electrodes was evaluated using RNH different concentrations from 10^{-2} to 10^{-4} mol L^{-1} within the pH range of 1-12. It is carried out by addition of small volume of HCl and/or NaOH solution (0.1-1 mol L^{-1} of each). It is obvious that within the pH range from 3 to 8 and 3 to 9 for MCPE and ICPE, respectively, the electrode potential is practically independent of pH. In this range the electrodes; MCPE and ICPE, can be safely used for RNH determination (Figure 5). Comparing with the previously reported data the pH range was 3 to 5 which indicates the improvement of the electrodes response in the presence of ion exchangers [21]. The increase in mV reading at pH less than 3 can be due to interference of hydronium ion [39-42]. At higher pH value (pH >9), free base precipitates in the test solution and consequently, the concentration of unprotonated species gradually increased. As a result, lower e.m.f readings were recorded [39-42]. The decrease in the potential readings at pH >9, on the other hand, can be probably attributed to penetration of hydroxyl ions into the gel layer of the electrodes.

Effect of temperature

To study the effect of temperature on the response of the electrodes utilized, the potential of 1.0×10^{-6} - 1.0×10^{-2} mol L^{-1} RNH solutions were determined in different temperatures (10, 20, 30, 40, 50 and 60 °C) and calibration graphs were constructed, and the standard electrode potentials ($E°_{elec.}$) (obtained from the calibration graphs) corresponding to each temperature was calculated. For the determination of the isothermal coefficient (dE°/dT) of the electrode, the standard electrode potential ($E°_{elec.}$) at different temperatures was plotted vs. (t – 25), where t is the temperature of the test solution. A straight-line plot was obtained according to the following equation [43]:

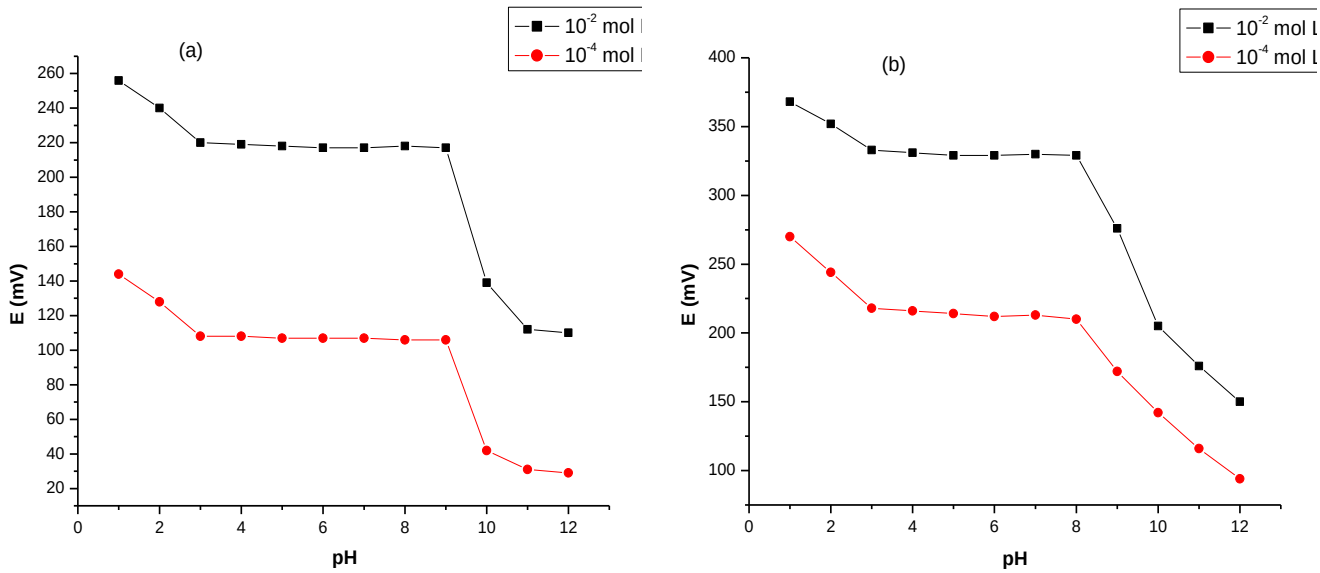

Fig. 5: Effect of pH on (a) ICPE and (b) MCPE potentiometric electrodes.

$$E° = E°_{(25)} + (dE° / dT)(t - 25)$$

The values of the obtained isothermal coefficient of the MCPE and ICPE sensors were found to be 0.00035 and 0.0004 V/^{o}C, respectively. This indicates that the electrodes have a high thermal stability within the investigated temperature range. The investigated electrodes were found to be stable up to 60 ^{o}C without noticeable deviation from the Nernstian behaviuor [21].

Selectivity

The influence of various basic substances on the response of MCPE and ICPE sensors was investigated by measuring the potentiometric interference from many sugars, inorganic cations and glycine. The selectivity coefficients were determined by the separate solution [36] and matched potential [37] methods. The results obtained are summarized in Table 4.

A reasonable selectivity towards RNH in the presence of many nitrogenous compounds such as carbohydrates, glycine and some inorganic catains was observed. The results showed no serious interference by a number of pharmaceutical excipients, diluents and active ingredients commonly used in the drug formulations (e.g. glucose, lactose, maltose, fructose, starch and sucrose) at concentration as high as a 10 -100 fold molar excess over RNH. The inorganic cations did not interfere due to the differences in their mobilities and permeabilities as compared with RNH cation. With respect to glycine, the high selectivity is mainly attributed to the difference in polarity and lipophilic character of their molecules relative to RNH.

Analytical application

The performance characteristics of MCPE and ICPE sensors are given in Table 5. The proposed potentiometric method is applied for determination of RNH in pure form and in pharmaceutical preparations using MCPE and ICPE plasticized with TCP. The results are summarized in Table 5.

The results are compared with the official method [44] and show that the proposed MCPE and ICPE electrodes have good efficiency as regard of sensitivity, index retrieving and repetition. The percentage recovery data obtained using the proposed MCPE and ICPE sensors are comparable with these obtained using the official method. As the conventional method for determination of RNH was difficult and time consuming as well as using of expensive solvents, this method (potentiometric determination) is easy, fast and inexpensive. One of the important applications of these drug-selective electrodes would have the study and investigation of RNH.

In the proposed potentiometric method, RNH is determined in aciloc, rantidol and histac tablets using potentiometric calibration and standard addition (SAM) methods (Tables 6, 7).

The concentration of RNH was determinate by SAM which depends on the application of the following equation [45] to each each volume of the standard concentrated solution added to the unknown concentration.

$$C_x = C_s[V_s)/(V_x - V_s)]x10^{n(\Delta E/s)} - (V_x)/(V_s - V_x)]$$

Where C_x and V_x are the concentration and the volume of unknown, respectively. C_s and V_s are the concentration and the volume of the standard, respectively. S the slope of the calibration graph and E is the change in millivolt due to the addition of the standard. The data obtained reflect the success of the MCPE and ICPE sensors in the determination of RNH in pure form and pharmaceutical preparations. Also, it reflects the possibility of using these sensors for RNH routine analysis.

Table 4: Potentiometric selectivity coefficient of MCPE and ICPE electrodes.

	$K^{pot}_{D,B}$			
	MCPE		**ICPE**	
	SSM	**MPM**	**SSM**	**MPM**
Glucose	----	$1.46x10^{-6}$	----	$2.21x10^{-6}$
Lactose	----	$1.53x10^{-6}$	----	$1.54x10^{-6}$
Fructose	----	$8.07x10^{-6}$	----	$2.27x10^{-5}$
Maltose	----	$3.39x10^{-6}$	----	$8.45x10^{-6}$
Starch	----	$6.65x10^{-6}$	----	$1.27x10^{-5}$
Sucrose	----	$4.43x10^{-6}$	----	$8.62x10^{-6}$
Glycine	----	$2.06x10^{-5}$	----	$2.33x10^{-5}$
Co^{2+}	$6.14x10^{-4}$	----	$4.61x10^{-4}$	----
Mn^{2+}	$5.85x10^{-4}$	----	$5.71x10^{-4}$	----
Fe^{3+}	$3.28x10^{-6}$	----	$6.78x10^{-6}$	----
Na^{+}	$1.39x10^{-5}$	----	$3.93x10^{-5}$	----
Cd^{2+}	$3.73x10^{-4}$	----	$4.00x10^{-4}$	----
$NH4^{+}$	$2.54x10^{-6}$	----	$2.66x10^{-6}$	----

Table 5: Critical response characteristics of MCPE and ICPE electrodes.

Parameters	**MCPE**	**ICPE**
Slope (mV decade^{-1})	56.8±1.4	57.9±1.6
Correlation coefficient (r)	0.979	0.974
Concentration range (mol L^{-1})	1 x10^{-6} to 1 x 10^{-2}	1 x10^{-6} to 1 x 10^{-2}
Detection limit (mol L^{-1})	1 x10^{-6}	1 x10^{-6}
Response time (s)	4	3.5
Work pH range	3-8	3-9
Life time /day	62	65
Percent recovery (%)	98.55-99.72	98.10-100.85
Accuracy (%)	98.85	98.92
Relative Standard deviation (%)	1.65	1.48

Table 6: Potentiometric determination of RNH in pure form and pharmaceutical preparation using MCPE and ICPE electrodes plasticized with TCP.

Sample	[RNH] Taken (mg mL^{-1})	Proposed Method						Official Method			
		MCPE			ICPE						
		[RNH] Found (mg mL^{-1})	Recovery (%)±SD	RSD* (%)	[RNH] Found (mg mL^{-1})	Recovery (%)±SD	RSD* (%)	[RNH] Taken (µg mL^{-1})	[RNH] Found (µg mL^{-1})	Recovery (%)±SD	RSD* (%)
Pure form	20.00	19.71	98.55±0.16	1.67	19.73	98.65±0.16	1.58	10.00	9.93	99.30±0.17	1.75
	40.00	39.65	99.13±0.17		39.75	99.38±0.15					
Aciloc	20.00	19.59	97.95±0.18	1.89	19.67	98.35±0.17	1.63	10.00	9.95	99.50±0.18	1.89
	40.00	39.66	99.15±0.17		39.73	99.33±0.16					
Rantidol	20.00	19.66	98.30±0.23	2.16	19.62	98.10±0.20	1.69	10.00	9.84	98.40±0.25	2.53
	40.00	39.55	98.88±0.22		39.66	99.15±0.19					
Histac	20.00	19.51	97.55±0.21	1.79	19.65	98.25±0.19	1.53	10.00	9.75	97.50±0.21	2.19
	40.00	39.46	98.65±0.19		39.50	98.75±0.17					

* Average of four determinations.

Table 7: Determination of RNH in pharmaceutical samples by direct potentiometric calibration and standard addition methods using MCPE and ICPE electrodes.

Druge	Electrode type	[RNH] taken mg mL^{-1}	[RNH] found mg mL^{-1}		Recovery %		(RSD %)[a]	
			Calibration	SAM	calibration	SAM	calibration	SAM
Aciloc	MCPE	7.03	6.90	7.00	98.19	99.62	1.78	1.72
		10.54	10.40	10.51	98.67	99.72	1.81	1.74
	ICPE	7.03	6.96	7.04	99.05	100.04	1.31	1.26
		10.54	10.55	10.63	100.1	100.85	1.28	1.23
Rantidol	MCPE	7.03	6.92	6.98	98.29	99.29	182	1.69
		10.54	10.38	10.57	98.48	100.28	1.73	1.76
	ICPE	7.03	7.01	7.05	99.72	100.28	1.37	1.33
		10.54	10.52	10.60	99.81	100.57	1.26	1.21
Histac	MCPE	7.03	6.86	6.96	97.58	99.00	1.89	1.84
		10.54	10.35	10.50	98.20	99.62	1.86	1.79
	ICPE	7.03	7.06	7.07	100.43	100.57	1.41	1.36
		10.54	10.45	10.58	99.15	100.38	1.35	1.34

[a] Mean of four determinations

Table 8: Inter and Intra-days precision using different RNH-ISEs.

Drug	Electrode type	[RNH] Taken, (mg mL^{-1})	Intra-day				Inter-day			
			[RNH] Found, (mg mL^{-1})	Recovery %	SD	RSD %	[RNH] Found, (mg mL^{-1})	Recovery %	SD	RSD %
Pure form	MCPE	5.50	5.49	99.75	0.026	0.43	5.52	100.4	0.016	0.53
		9.80	9.76	99.62	0.033	0.76	9.82	100.2	0.037	0.44
		15.70	15.75	100.3	0.041	0.49	15.64	99.64	0.058	0.35
	ICPE	5.50	5.47	99.48	0.017	0.49	5.49	99.89	0.024	0.43
		9.80	9.82	100.19	0.030	0.51	9.77	99.66	0.051	0.36
		15.70	15.78	100.5	0.057	0.66	15.77	100.4	0.062	0.59
Aciloc	MCPE	4.90	4.89	99.71	0.031	0.52	4.88	99.65	0.024	0.41
		9.00	8.99	99.88	0.028	0.56	8.91	98.95	0.062	0.97
		14.50	14.53	100.2	0.023	0.47	14.46	99.72	0.076	0.65
	ICPE	4.90	4.88	99.57	0.037	0.93	4.91	100.2	0.032	0.89
		9.00	8.95	99.41	0.060	0.76	8.97	99.68	0.045	0.47
		14.50	14.55	100.4	0.063	0.59	14.49	99.92	0.027	0.56
Rantidol	MCPE	4.90	4.85	98.96	0.023	0.58	4.84	98.85	0.028	0.53
		9.00	8.96	99.56	0.032	0.46	8.94	99.38	0.045	0.68
		14.50	14.56	100.4	0.038	0.31	14.46	99.73	0.036	0.54
	ICPE	4.90	4.87	99.34	0.018	0.64	4.83	98.59	0.069	0.85
		9.00	8.90	98.93	0.025	0.44	9.05	100.5	0.045	0.67
		14.50	14.45	99.68	0.047	0.53	14.41	99.41	0.039	0.53
Histac	MCPE	4.90	4.87	99.31	0.029	0.56	4.85	99.04	0.035	0.71
		9.00	8.89	98.79	0.043	0.49	8.86	98.48	0.061	0.95
		14.50	14.55	100.3	0.032	0.39	14.48	99.89	0.047	0.48
	ICPE	4.90	4.88	99.56	0.036	0.86	8.84	98.72	0.052	1.09
		9.00	8.94	99.29	0.040	0.69	8.88	98.67	0.038	0.81
		14.50	14.56	100.4	0.033	0.35	14.43	99.53	0.045	0.56

Validation of the proposed method

Accuracy

The accuracy of the proposed method is investigated by determination of the RNH in different pharmaceutical samples and RNH reference standard. The results are summarized in Tables (6 and 7) and show that the proposed method is an accurate one, as indicated by percentage recovery values, for the determination of RNH in its pharmaceutical preparations without interferences from the co-formulated adjuvant.

Precision

Data summarized in Table (8) gives the inter- and intra-day precision of the proposed sensors for the potentiometric determination of RNH in pure and pharmaceutical preparations. The RSD% values for the repeated determinations of RNH in pure, Aciloc, Rantidol and Histac tablets using MCPE and ICPE electrodes are less than 2% indicating good precision of the proposed method.

Linearity

Under the optimal experimental conditions, linear relationships exist between the electrode potential/mV and the log [RNH]. The regression data, correlation coefficients (r) and other statistical parameter are listed in Table 5.

Detection limit

The detection limit of the investigated RNH drug was calculated according to IUPAC recommendation [46, 47]. The detection limit is defined as the concentration at which the measured potential differs that predicted by the linear regression by more than 18 mV. The values previously reported in Table 5, indicate that the proposed MCPE and ICPE sensors are sensitive to detection of very small concentrations of RNH.

CONCLUSION

The potentiometric procedure proposed here eliminates the prior separation steps that are usually necessary in the determination of RNH in pharmaceutical preparations. Additionally, the proposed method has some important advantages: the electrode proved to be successful, providing a rapid, simple and low cost potentiometric method for the determination of RNH in pure solutions and in pharmaceutical preparations (aciloc, ranitidine and histac). It ensures a good accuracy for the RNH assay due to the possibility to control the ion activity continuously and also a fast assay of RNH tablets.

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