Int. J. Electrochem. Sci., 7 **(2012)** 650 - 662

International Journal of
ELECTROCHEMICAL
SCIENCE
www.electrochemsci.org

Potentiometric Determination of Chlorpromazine HCl Using Carbon Paste Electrode in Pure and Pharmaceutical Preparations

Eman Y.Z. Frag, M.A. Zayed, M.M. Omar, Sally E.A. Elashery, Gehad G. Mohamed[*]

Chemistry Department, Faculty of Science, Cairo University, Gamaa Str., 12613, Giza, Egypt
[*]E-mail: ggenidy68@hotmail.com

Received: 15 October 2011 / *Accepted:* 29 November 2011 / *Published:* 1 January 2012

Carbon paste electrode has been developed for the potentiometric determination of chlorpromazine HCl drug. This work has focused on the fabrication of carbon paste ion selective electrode for determination of the drug under investigation using potentiometric titration with sodium tetraphenylborate. The performance of such sensor in the potentiometric determination of chlorpromazine HCl is compared with those of PVC membrane, coated wire and coated graphite electrodes. This carbon paste electrode was applied to the determination of chlorpromazine HCl in pharmaceutical preparations. The repeatability and accuracy of measurements performed in the analysis of these pharmaceutical matrices using new carbon paste sensor were evaluated. The influence of the electrode composition, conditioning time of the electrode and pH of the test solution, on the electrode performance were investigated. The drug electrode showed Nernstian response in the concentration range from 1×10^{-7} to 1×10^{-2} mol L^{-1} with slope of 58.06 ± 0.34 mV $decade^{-1}$, and was found to be very precise and usable within the pH range 2–6. This sensor exhibited a low detection limit (1×10^{-7} mol L^{-1}), a long lifetime (>2 months) and good stability. The percentage recovery obtained is 97.72 % with a relative standard deviation ≤ 0.28%.

Keywords: Chlorpromazine HCl; carbon paste electrode; potentiometric determination; tablets; official method.

1. INTRODUCTION

Chloropromazine HCl has the IUPAC name of 3-(2-chloro-10*H*-phenothiazin-10-yl)-*N*,*N*-dimethyl-propan-1-amine (Figure (1)) [1]. Its molecular formula is $C_{17}H_{19}ClN_2S$.HCl and its molecular weight is 355.33 g mol^{-1}. Chlorpromazine HCl (CPZ.HCl) is a phenothiazine drug with an aliphatic side chain, used in the management of psychotic conditions [2]. It controls excitement, agitation and other psychomotor disturbances in schizophrenic patients and reduces the manic phase of manic-

depressive conditions. It is used to control hyperkinetic states and aggression and is sometimes given in other psychiatric conditions for the control of anxiety and tension. CPZ.HCl is also used in palliative care to act as an antiemetic.

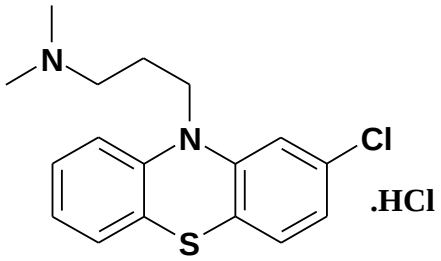

Figure 1. Structural formula of chlorpromazine HCl.

The methods available for the determination of chlorpromazine HCl included hollow fiber liquid phase micro-extraction (HF-LPME) in conjunction with reversed-phase HPLC/UV [3], flow injection [4,5], PVC ion selective electrode [6,7], spectrophotometric [8], gas chromatographic [9], spectrofluorimetric [10], capillary zone electrophoresis with ultraviolet visible detection [11] methods.

Applications of potentiometric sensors in the field of pharmaceutical and biomedical analysis have been reported [12] where it provides simple, fast, and selective technique for determination of various drugs [13-15]. This work is undertaken in order to test the sensitivity, accuracy and selectivity of new potentiometric method and to develop a new method able to analyze pharmaceuticals formulations, avoiding or minimizing the number of steps needed to assess the concentration of the CPZ.HCl. Also experimental parameters of the analytical procedure were optimized. The results were compared with those given by the official method.

2. EXPERIMENTAL

2.1. Reagents

All chemicals and reagents used were of analytical reagent grade. Bidistilled water was used throughout all experiments. Chlorpromazine hydrochloride (CPZ.HCl) provided by Misr Company for Pharmaceutical Industry and its Pharmaceutical preparation Neurazine was produced by Misr Company for Pharmaceutical Industry, Cairo, Egypt (Each tablet contains 100 mg of chlorpromazine hydrochloride). *o*-Nitrophenyloctylether (*o*-NPOE) was supplied from Fluka while dioctylphthalate (DOP), dibutylphthalate (DBP) and dioctylsebacate (DOS) were supplied from BDH and tricresylphosphate (TCP), polyvinylchloride (PVC relative high molecular weight) and graphite powder (synthetic 1–2 μm) were supplied from Aldrich.

Sodium tetraphenylborate (NaTPB) was applied as a titrant for the drug under investigation and ammonium reineckate (RN) $[NH_4(Cr(NH_3)_2(SCN)_4).H_2O]$ were purchased from Fluka. Phosphomolybdic acid (PMA); $H_3[PMo_{12}O_{40}]$, was purchased from BDH.

Glucose, lactose, fructose, maltose, starch, sucrose, glycine, $CoCl_2$, $NiCl_2$, $CaCl_2$, NH_4Cl, $ZnCl_2$, NaCl, $CdCl_2$ and $AlCl_3$ were used as interfering materials and they were purchased from El-Nasr Company, Egypt.

2.2. Solutions

10^{-2} mol L^{-1} Stock solution of CPZ.HCl drug was prepared by dissolving 0.1776 g of CPZ.HCl in 100 mL bidistilled water. Dilute solutions were prepared by accurate dilution from the stock one to get the desired concentrations.

NaTPB solution (10^{-2} mol L^{-1}) was prepared by dissolving an accurate weighed amount of the substance in warm water, adjusted to pH 9 by adding sodium hydroxide and completed to the desired volume with water. The resulting solution was standardized potentiometrically against standard (10^{-2} mol L^{-1}) thallium (I) acetate solution [16].

2.3. Apparatus

Laboratory potential measurements were performed using JENWAY 3505 pH meter, which was more convenient to be used. Silver-silver chloride double - junction reference electrode (Metrohm 6.0222.100) was used.

Digital multimeter connected to a portable PC and Brand digital burette was used for the measurement of the drug under investigation.

2.4. Procedure

2.4.1. . Electrode preparation

2.4.1.1. Preparation of carbon paste electrode (CPE)

The sensing electrode was prepared by intimate mixing accurately 500 mg of highly pure graphite powder and plasticizer (0.2 ml of DOP, TCP, DBP, DOS or *o*-NPOE). This matrix was thoroughly mixed in the mortar and the resulted paste was used to fill the electrode body. 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.

2.4.1.2. Preparation of coated wire and coated graphite electrodes

For the preparation of sliver CWE, the metal wire (1.5 mm diameter) was sealed into the end of

PVC tube.

The wire was polished, carefully cleaned in strong ammonia solution, rinsed, carefully dipped in 50% nitric acid for 1 min, rinsed with distilled water but don't dry. The wire was cathodized [17, 18] against a sliver anode at 5 mA /cm^2 in 0.1 M HCl for 30 s, the bubble was allowed to disperse from the wire and the electrode was washed and left to dry. The electrode was immersed in the cocktail consisting of (240 mg *o*-NPOE + 240 mg PVC + 6 ml THF) 20 times and after each the solvent evaporated using air gun.

Consequently, a commercially available Pencil fine Japanese type was used as a graphite-based material for the ion-sensitive electrode. The rod was immersed in chloroform for 10 min, formed to the required size and then ignited in a colorless flame for 1 min. After cooling, the rod was mounted into a Teflon tube.

The open end of the tube was then connected to a slight vacuum and the other end containing carbon rod was immersed into the cocktail 20 times after each the solvent evaporated using air gun.

The electrode was kept dry at room temperature for 24 hr and preconditioned by soaking in suspended surfactant ion pair solution for 24 hr.

2.4.1.3. Preparation of PVC membrane electrode with an internal reference solution:

For PVC electrode, the cocktail (consisting of 240 mg *o*-NPOE, 240 mg PVC and 6 mL THF) was stirred for 5 min and poured into Petri dish "5 cm" diameter. After 24 hr of slow evaporation of solvent, a master membrane with 0.11 mm thickness was obtained which was mounted on the softened end of the PVC tubing with the help of adhesive solution prepared by dissolving PVC in THF. The PVC closed tube with the membrane was filled with 0.25 mL of 1 mol L^{-1} KCl and completed to 25 mL with 0.01 mol L^{-1} CPZ.HCl drug solution using Ag /AgCl as internal reference electrode. The fabricated electrodes were soaked in ion pair solution for 24 hr.

2.4.2. Determination of chlorpromazine HCl

Before measurements, the electrode surface was mechanically renewed. Then the carbon paste and the calomel reference electrodes were immersed in 3 mL of 10^{-2} mol L^{-1} CPZ.HCl, the solution was stirred by a magnetic stirrer and titrated with a standard solution of 10^{-2} mol L^{-1} NaTPB solution. The end points were determined from the S-shaped curves.

In the calibration method, the indicator electrode plasticized with TCP was immersed in conjunction with the double junction Silver-silver chloride reference electrode in solutions of CPZ.HCl in the range of 10^{-2}–10^{-7}mol L^{-1}.

They were allowed to equilibrate whilst stirring and recording the e.m.f. readings within ±1mV. The CPE sensor was washed between measurements with water. The mV–concentration profiles were plotted. The calibration graph was used for subsequent determination of unknown concentrations of CPZ.HCl.

2.4.3. Determination of CPZ.HCl in tablets

10 Tablets of each pharmaceutical product (Neurazine 100 mg) were weighed, and then dissolved in 100 mL of bidistilled water by sonication for 10 min. The solution mixture was shacked in a mechanical shaker and the mixture was filtered then transferred accurately to 100 mL measuring flask, completed to the mark with bidistilled water shacked and finally determined by the proposed sensor.

3. RESULTS AND DISCUSSION

3.1. Construction of the calibration graphs

The CPE sensor was calibrated by immersing the electrode plasticized with TCP in conjunction with the double junction Ag/AgCl reference electrode in solutions of CPZ.HCl in the range of 10^{-2}–10^{-7} mol L^{-1}. They were allowed to equilibrate whilst stirring and recording the e.m.f. readings. The E (mV) – p [CPZ.HCl] profile was plotted as shown in Figure (2). The CPE showed a linear response over the concentration range from 10^{-7} to 10^{-2} mol L^{-1} with Nernstian slope of 58.06 ± 0.34 mV $decade^{-1}$.

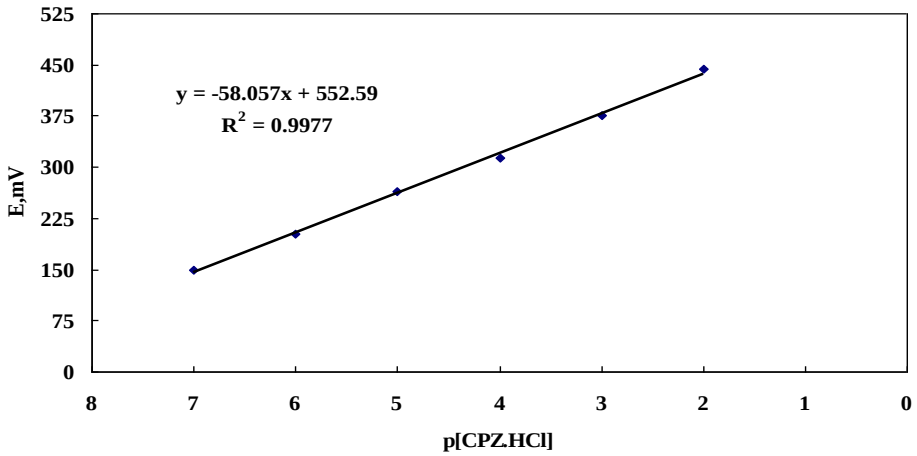

Figure 2. Calibration curve for CPZ.HCl using CPE.

3.2. Effect of soaking time

Freshly prepared CPE electrode must be soaked to activate the surface of the membrane to form an infinitesimally thin gel layer at which ion exchange occurs. This preconditioning process requires different times depending on diffusion and equilibration at the electrode-test solution interface; a fast establishment of equilibrium is certainly a condition for a fast potential response [19]. Thus, the performance characteristics of the CPZ.HCl ion-selective electrode were investigated as a function of soaking time. For this purpose the CPE electrode was soaked in CPZ.HCl-TPB ion-pair

and the titration curves were plotted from which the total potential changes are recorded after 0, 15, 30, 60, 120 min. and 12 and 24 h. The optimum soaking time was found to be 0 min, where the highest total potential change and potential break at the end point are obtained. They decreased with increasing soaking time, at 25 °C. Soaking for longer than 24 h is not recommended to avoid leaching of, although very little, the electro-active species into the bathing solution. The CPE electrode should be stored in a refrigerator while not in use. The end point, potential change and total potential changes are shown in Table (1).

Table 1. Effect of soaking time on the CPE performance in the potentiometric titration of 3 mL of 10^{-2} mol L^{-1} CPZ.HCl with 10^{-2} mol L^{-1} NaTPB.

Time of soaking	Total potential change , mV	Potential break at the end point, mV	ΔE/ΔV mV/mL
Without	271	195	508
15 min	251	172	455
30 min	230	152	402
60 min.	238	147	386
120 min.	243	141	374
12 h	261	121	328
24 h	283	100	278

3.3. Effect of pH

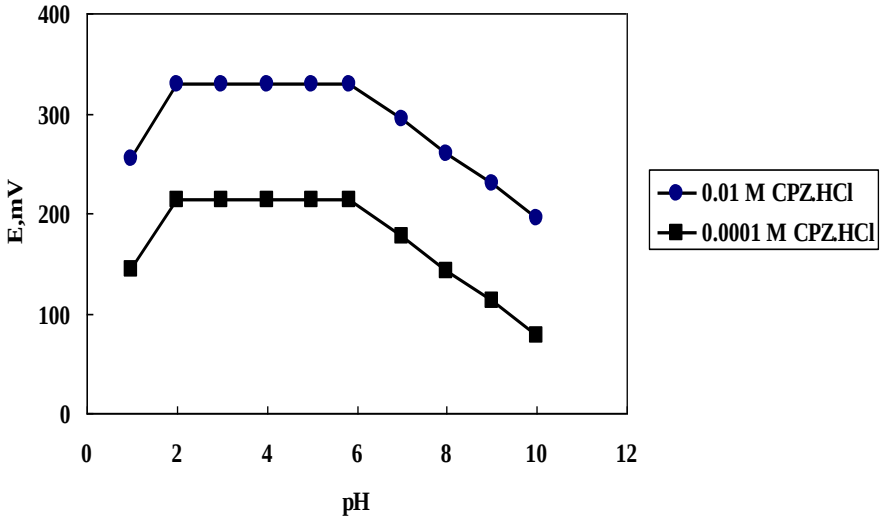

Figure 3. Effect of pH at different CPZ.HCl concentrations using CPE.

The effect of pH on the performance of the potentiometric titration of the drug with NaTPB was evaluated in concentrations of 1.0×10^{-2} and 1.0×10^{-4} mol L^{-1} of CPZ.HCl at different pH values (1-10) by addition of small volumes of HCl and/or NaOH solution (0.1−1 mol L^{-1} of each) to the

solution medium using CPE. The potential change at each pH value was reported. It is obvious that, within the pH range from 2.0 to 6.0 the electrode potential is practically independent on pH and in this range the CPE can be safely used for CPZ.HCl determination (Figure 3). The decrease in mV readings at pH < 2 may be due to interference of hydronium ion. At higher pH values (pH > 6.0), 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.

3.4. Effect of temperature

To study the effect of temperature, the electrode potential of 10^{-2}–10^{-7} mol L^{-1} CPZ.HCL solutions were measured at different temperature intervals of 10, 20, 30, 40, 50 and 60 °C and the calibration graphs were constructed. For the determination of the isothermal coefficient (dE^0/dt) of the CPE electrode, the standard electrode potentials (E^0) against the normal hydrogen electrode at the different temperatures were obtained from calibration graphs as the intercepts at p[CPZ.HCl] = 0 (after subtracting the values of the standard electrode potential of the calomel electrode at these temperatures) and were plotted versus (t−25), where t was the temperature of the test solution in °C (Figure (4)). A straight-line plot is obtained according to Antropov's equation-1 [20, 21].

$$E° = E°_{(25)} + (dE°/dt)\,(t\text{-}25) \quad (1)$$

Where $E^0_{(25)}$ is the standard electrode potential at 25 °C, the slope of the straight-line obtained represents the isothermal coefficient of the electrode (0.285 V/°C). The value of the obtained isothermal coefficient of the electrode indicates that the electrode has a fairly high thermal stability within the investigated temperature range. The investigated electrode was found to be usable up to 60 °C without noticeable deviation from the Nernstian behaviour.

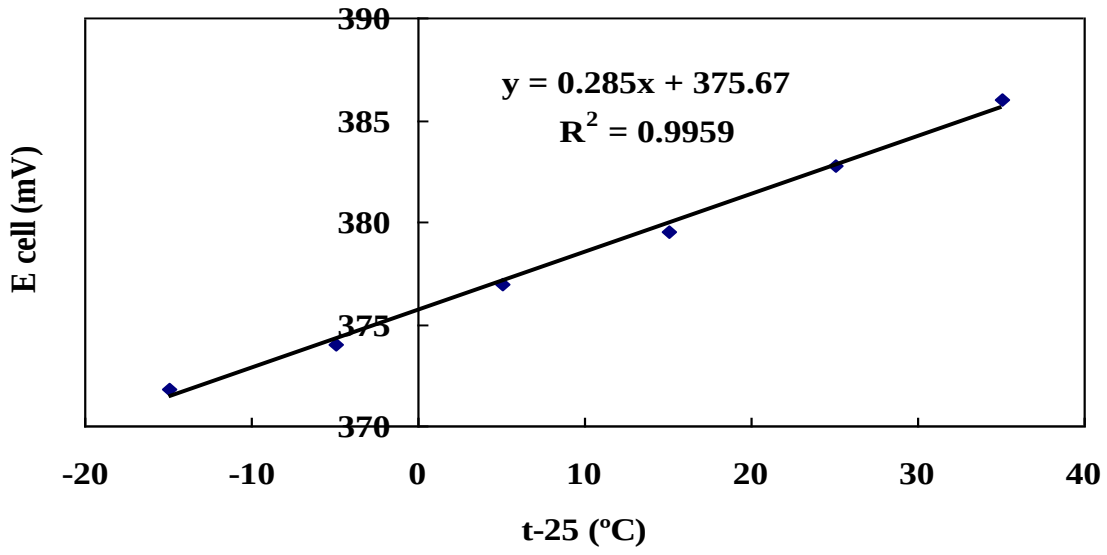

Figure 4. Variation of the cell e.m.f. with the temperature for the CPE electrode.

3.5. Selectivity of the electrode

The influence of some inorganic cations, sugars and glycine on the electrode was investigated. The selectivity coefficients were determined by the modified separate solution method using the rearranged Nicolsky equation (2) [22-24]:

$$\text{Log } K_{D,B}^{pot} = ((E_1-E_2)/S) + (1 + (z_1/z_2)) \log a \qquad (2)$$

where, E_1 is the potential measured in 1×10^{-3} mol L^{-1} CPZ.HCl (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 CPZ.HCl (D) and interfering species (B), respectively and S is slope of the electrode calibration plot.

Table 2. Potentiometric selectivity coefficient of CPE plasticized with TCP.

Interfering ions (B)	$K_{D,B}^{pot}$
	CPE
Glucose	2.80×10^{-6}
Lactose	4.51×10^{-6}
Fructose	3.55×10^{-5}
Maltose	9.59×10^{-6}
Starch	3.03×10^{-5}
Sucrose	4.89×10^{-6}
Glycine	1.31×10^{-4}
Co^{2+}	2.39×10^{-4}
Ni^{2+}	1.48×10^{-3}
Ca^{2+}	4.31×10^{-2}
NH_4^+	1.81×10^{-4}
Zn^{2+}	1.67×10^{-3}
Na^+	3.84×10^{-5}
Cd^{2+}	8.52×10^{-5}
Al^{3+}	7.88×10^{-5}

The results obtained are summarized in Table (2). The mechanism of selectivity is mainly based on the stereo-specificity and electrostatic environment, and is dependent on how much matching is present between the location of the lipophilic sites in the two competing species in the bathing solution side and those present in the receptor of the ion exchanger. A reasonable selectivity toward CPZ.HCl in the presence of many nitrogenous compounds such as amines, glycine, and some inorganic cations was observed. The results showed no serious interference by a number of pharmaceutical excipients 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 CPZ.HCl.

3.6. Effect of plasticizer

It is well known that the sensitivity and selectivity obtained for a given ion-selective electrode is greatly influenced by the polarity of the electrode matrix, which is defined by the dielectric constant of the electrode plasticizer [25, 26]. The influence of the plasticizer on the CPE electrode performance was studied using five plasticizers having different dielectric constants, namely, o-NPOE, DOS, DOP, DBP and TCP. Electrode plasticized with *o*-NPOE shows the highest total potential change (408 mV) and the highest potential break at the end point ($\Delta E/\Delta V$ = 740 mV/mL) [20, 27].

No electrode preconditioning is needed before applying in the potentiometric titration and excellent titration curves can be achieved from the second titration process, while electrodes fabricated using other plasticizers need either to operate the titration process at least 5-7 times or to soak the electrode in the aqueous solution of the ion pair for 15 min before using these electrodes in the titration process.

3.7. Effect of concentration of CPZ.HCl

The effect of concentration of CPZ.HCl on the performance of the potentiometric titration of CPZ.HCl is investigated by addition of different volumes (1, 3, 5 and 10 mL) of 10^{-2} mol L^{-1} CPZ.HCl drug to the titration medium which prove that the reaction between the drug and NaTPB occurs with ratio of 1:1 (i.e.$[CPZ]^+$:$[TPB]^-$).

3.8. Effect of titrant

Table 3. Potentiometric titration of 3 mL of 10^{-2} mol L^{-1} CPZ.HCl with different titrants using CPE: a) 1×10^{-2}mol L^{-1} NaTPB, b) 3.3×10^{-3} mol L^{-1} PTA, c) 3.3×10^{-3} mol L^{-1} PMA, d) 1×10^{-2} mol L^{-1} RN.

Titrants	Total potential change, mV	Potential break at the end point, mV	$\Delta E/\Delta V$ mV/mL
NaTPB	363	250	665
PTA	230	133	373
PMA	154	59	198
RN	117	20	102

The effect of titrant on the performance of the potentiometric titration of CPZ.HCl is investigated as NaTPB is replaced by ammonium reineckate (RN), phosphotungstic acid (PTA) and phosphomolybdic acid (PMA). CPZ.HCl reacts with PMA and PTA in the molar ratio of 3:1 while with NaTPB and RN the ratios are 1:1. The highest total potential change is obtained using NaTPB as a titrant with good reproducibility compared with other titrants (Table 3).

3.9. Life time

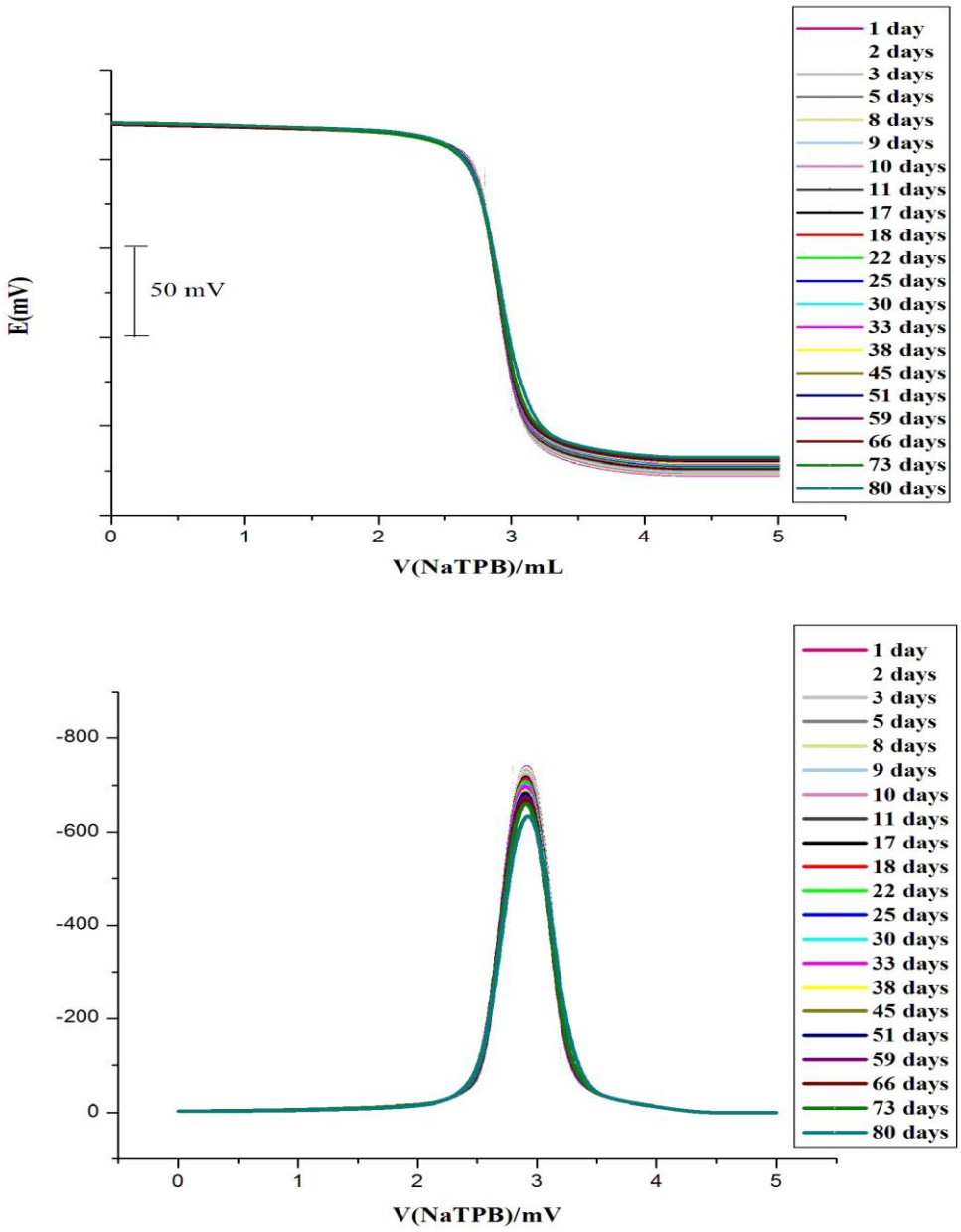

Figure 5. Life time of the carbon paste electrode performance in the potentiometric titration of 3 mL of 10^{-2} mol L^{-1} CPZ.HCl with 10^{-2} mol L^{-1} NaTPB using *o*-NPOE.

Life time, the period in which the electrode functions properly, was measured by plotting the titration curve (Figures 5) periodically of CPZ.HCl with NaTPB standard solution on different days and calculating the total potential change, potential break at the end point and end point investigated the lifetime of the electrodes (Tables 4). It is clear from the figures that there is a change in the potential break at the end point by 26% after 80 days, 31% after 80 days, 37% after 72 days, 25% after 73 days and 48% after 73 days for *o*-NPOE, TCP, DBP, DOP, DOS, respectively. A new surface for measurement can be achieved daily by simply squeezing out a small amount of the paste and polishing the electrode surface on a smooth filter paper till a shiny surface is obtained.

Table 4. Life time of the carbon paste electrode in the potentiometric titration of 3 mL of 10^{-2} mol L^{-1} CPZ.HCl with 10^{-2} mol L^{-1} NaTPB using *o*- NPOE.

Time (day)	End point (mL)	Recovery %	Total potential change, mV	Potential break at the end point, mV	ΔE/ΔV (mV/mL)
1	2.94	98.00	396	275	788
2	2.94	98.00	394	275	783
3	2.93	97.67	392	273	778
5	2.92	97.33	390	273	773
8	2.92	97.33	392	270	768
9	2.94	98.00	390	268	763
10	2.94	98.00	388	267	758
11	2.95	98.33	389	265	753
17	2.96	98.67	387	265	748
18	2.96	98.67	385	264	743
22	2.96	98.67	383	262	738
25	2.96	98.67	385	260	733
30	2.95	98.33	383	257	728
33	2.95	98.33	381	256	723
38	2.96	98.67	379	249	718
45	2.94	98.00	381	248	713
51	2.93	97.67	379	244	708
59	2.94	98.00	377	239	703
66	2.95	98.33	375	237	698
73	2.96	98.67	377	232	693
80	2.96	98.67	375	204	688

3.10. Electrode performance

Table 5. The performance characteristics of different fabricated electrodes in the potentiometric titration of 3 mL 10^{-2} mol L^{-1} CPZ.HCl with 10^{-2} mol L^{-1} NaTPB.

Electrode*	Total potential change (mV)	ΔE/ΔV mV/mL
CPE	408	740
PVC	259	432
CWE	142	156
CGE	220	357

The analytical performance of CPE is compared with the traditional PVC, CWE and CGE electrodes and the data obtained are summarized in Table (5). From the results obtained, one can conclude that the CPE shows better performance with respect to total potential change and potential break at the end point in comparison with other electrodes.

3.11. Analytical application

The CPE electrode will be used for the determination of chlorpromazine HCl in aqueous solutions and in pharmaceutical preparations by using the potentiometric titration.

The application of the proposed method for the potentiometric determination of CPZ.HCl in pharmaceutical preparation gives good results as shown in Table (6). The results are compared with the official method [28] and have shown that the CPE has good efficiency as regard of sensitivity, index of retrieving and repetition.

Table 6. Potentiometric determination of CPZ.HCl drug in Neurazine tablets using CPE plasticized with TCP, o-NPOE and DBP.

Plasticizer	Sample	Proposed [Drug] mg mL^{-1}		Official [Drug] mg mL^{-1}		% Recovery		SD^{*} (RSD^{*}, %)	SD^{**} (RSD^{**}, %)
		Taken	Found	Taken	Found	Proposed	Official		
TCP	Neurazine (100 mg/tablet)	30.00	29.76	20.00	19.96	99.20	99.98	0.008 (0.28)	0.008 (0.41)
o-NPOE		30.00	29.80			99.33		0.017 (0.59)	
DBP		30.00	29.10			97.00		0.021 (0.72)	

* Average of four determinations.
** Average of four determinations.

4. CONCLUSION

The potentiometric procedure proposed here eliminates the prior separation steps that are usually necessary in the determination of CPZ.HCl in pharmaceutical preparations. Additionally, the proposed method proved to be successful, providing a rapid, simple and low cost potentiometric method for the determination of CPZ.HCl in pure solutions and in pharmaceutical preparations.

References

1. http://en.wikipedia.org/wiki/main_page.
2. T.J.R. Lambert, D.J. Castle, *Schizophrenia MJA* 178 (2003) 57.
3. R.S. Hamid, Y. Yadollah, H.H.B.A. Reza, *J. Pharma. Biomed. Anal.*, 45, 769 (2007).
4. S.M. Sultan, *Analyst* 116 (1991) 177.
5. S.M. Sultan, *Talanta* 40 (1993) 681.
6. M.G.F. Sales, J.F.C. Tomas, S.R. Lavandeira, *J. Pharm. Biomed. Anal.*, 41 (2006) 1280.
7. J.A. Ortuno, J. Hernandez, S.C. Pedreno, *Sens. Actuators B*, 119 (2006) 282.
8. C. Yamazaki, N. Suzaki, M. Nakao, S. Kamino, T. Yamaguchi, Y. Fujita, *Bunseki. Kagaku.*, 55 (2006) 733.
9. C. Sanchez-de-la-Torre, M.A. Martinez, E. Almarza, *Forensic. Sci. Int.*, 155 (2005) 193 (2005).

10. F.A. Mohamed, H.A. Mohamed, S.A. Hussein, S.A. Ahmed, *J. Pharm. Biomed. Anal.*, 39 (2005) 139.
11. F.J. Lara, A.M.G. Campana, F.A. Barrero, J.M.B. Sendra, *Electrophoresis*, 26 (2005) 2418.
12. V.V. Cosofret, R.P. Buck, Pharma. App. of Membrane Sensors (CRC Press, Florida, **(1992).**
13. V.K.Gupta, M.K. Pal, A.K. Singh, *Electrochim. Acta*, 55 (2010) 1061.
14. V.K.Gupta, M.K. Pal, A.K. Singh, *Electrochim. Acta*, 54 (2009) 6700.
15. M.S. Rizk F.M. Abdel-Haleem, *Electrochim. Acta*, 55 (2010) 5592.
16. M. Sak-Bosnar, D. Madunic-Cacic, R. Puac, B.S. Grabaric, *Anal. Chim. Acta*, 581 (2007) 355.
17. I.Svancara, K. Vytras, *Chem. Listy*., 88 (1994) 138.
18. P. Peter, L. Bailey, "Analysis with ion Selective Electrode" Sec. Edition Hayden & Son. Ltd., 20 (1980).
19. E. Linder, K. Toth, E. Pungor, Dynamic Characteristics of Ion-Selective Electrodes, Chemical Rubber Company (CRC) Press. Boca Raton. FL., 1988.
20. S.M. Ghoreishi, M. Behpour, M. Nabi, *Sen. Actuators B*, 113 (2006) 963.
21. L.I. Antropov, "Theoretical Electrochemistry", Mir Publisher Moscow, 1997.
22. A.M. Othman, N. M. H. Rizk, M. S. El-Shahawi, Anal. Chim. Acta., 515 (2004) 303.
23. T.S. Ma, S. S.M. Hassan, "Organic Analysis Using Ion Selective Electrodes", 1982.
24. S.S. M. Hassan, W.H. Mahmoud, A. M. Othman, *Talanta*, 44 (1997) 1087.
25. E. Bakker, P. Buhlmann, E. Pretsch, *Chem. Rev.*. 97 (1997) 3083.
26. W.E. Morf, The Principles of Ion-Selective Electrodes and Membrane Transport, Elsevier, New York, 1981.
27. M. N. Abbas, E. Zahran, *J. Electroanal. Chem.*, 576 (2005) 205.
28. H. A. Okeri P. O. Alonge E. Etareri, *Int. J. Health Res.*, 1 (2008) 21.