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Potentiometric and thermal studies of a coated-wire benazepril-selective electrode

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Abstract

A coated-wire benazepril-selective electrode based on incorporation of the benazepril–tetraphenylborate ion pair in a poly(vinylchloride) coating membrane was constructed. The influences of membrane composition, temperature, pH of the test solution, and foreign ions on the electrode performance were investigated. The electrode showed a Nernstian response over a benazepril concentration range of 1.26×10^{-5} to 0.58×10^{-2} M, at 25 °C, and was found to be very selective, precise, and usable within the pH range 2.5–9.2. The standard electrode potentials, $E°$, were determined at 20, 25, 30, 35, 40 and 45 °C, and used to calculate the isothermal temperature coefficient ($dE°/dT$) of the electrode. Temperatures higher than 45 °C seriously affect the electrode performance. The electrode was successfully used for potentiometric determination of benazepril hydrochloride both in pure solutions and in pharmaceutical preparations.

Keywords: Benazepril ion selective electrode; Poly(vinyl chloride) membrane; Potentiometric titration; Drug analysis

1. Introduction

Benazepril hydrochloride (BZ.HCl), {(3*S*)-3-[(2*S*)-1-ethoxycarbonyl-3-phenylpropylamino]-2,3,4,5-tetrahydro-2-oxo-1*H*-1-benzaze-pin-1-yl} acetic acid hydrochloride, is a potent angiotensin-converting enzyme inhibitor that is used in the treatment of mild and moderate essential and reno-vascular hypertension [1]. The literature reveals only few papers concerning the determination of BZ.HCl in plasma and urine capillary gas chromatography [2,3], an electron capture gas chromatographic technique [4], a high-performance liquid chromatography for its determination in pharmaceuticals [5] and a spectrophotometric method for its determination in its single and multi-component dosage forms [6,7], liquid chromatographic methods [8,9] and liquid chromatography (LC), high-performance thin layer chromatography (HPTLC) [10]. However, most of these methods involve several manipulation steps before the final result of the analysis is obtained. Although potentiometric methods of analysis using ion-selective electrodes are simple, cheap, applicable to samples, no selec-

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tive electrode is, so far, available for the determination of benazepril.

The present work, thus, describes a new selective membrane electrode of the coated-wire type, for determination of benazepril (in the concentration range, 6.85–42.50 μg/ml) in pure solutions and in pharmaceutical preparations. This electrode is based on incorporation of an ion-pair complex of tetraphenylborate anion $(TPB)^-$ with benazepril cation (BZH^+) in poly(vinyl chloride) matrix.

It is noteworthy that all previously reported investigations using poly(vinylchloride) (PVC) membrane-selective electrodes for determination of species of pharmaceutical and/or medical importance have been carried out at only one temperature, mostly 25 °C. No attention was paid to the higher temperature range, 25–45 °C, although many potentiometric measurements concerning biological media and fluids are made at such temperatures [11]. In this paper, the effect of the temperature of the test solution on the performance characteristics of the proposed coated-wire electrode (CWE) is reported.

2. Experimental

2.1. Reagents and materials

All chemicals used were of analytical or pharmacopoeial grade (can be used for manufacturing pharmaceutical preparations). Bidistilled water was used throughout all experiments. The pharmaceutical preparations containing benazepril (Cibacin (10 mg/tablet) and Cibadrex (25 mg/tablet)) tablets were obtained from local drug stores. The BZH–TPB ion pair was prepared by a method similar to that described previously [12]. The base component of the produced ion pair has been determined by the nonaqueous titration method [13]. The agreement between calculated and found values was very good confirming the postulated stoichiometry, the 1:1 (BZH:TPB) molar ratio stoichiometry was also confirmed by elemental analysis. The electrode and the calibration graphs were constructed as described in the previous work [12].

2.2. Potentiometric studies and electrochemical system

Potentiometric measurements were carried out with an Orion (Cambridge, MA, USA) model 701 A digital pH/mV-meter. A Techne circulator thermostat, model C-100, was used to control the temperature of the test solution. The electrochemical system was as follow: Cu/membrane/test solution//KCl salt bridge//KCl (sat.)/Hg_2Cl_2–Hg.

2.3. Selectivity of the electrode

The selectivity coefficients, $K^{pot}_{BZH,J^{z+}}$ were evaluated by the separate solution method described by Badawy et al. [14].

2.4. Potentiometric determination of benazepril

The standard addition method was applied in which small increments of standard benazepril hydrochloride solution (10^{-2} M) were added to 50 ml aliquot samples of various concentrations (3.0×10^{-4} to 1.5×10^{-3} M). The change in the potential reading (at constant temperature of 25 °C) was recorded for each increment and used to calculate the concentration of BZ.HCl sample solution.

For analysis of benazepril formulations, 9.50–36.75 or 10.75–40.18 mg Cibacin (20 tablets) or Cibadrex (16 tablets), respectively, was dissolved in 1000 ml distilled water and the standard addition technique was applied as already described.

3. Results and discussion

3.1. Composition of the coating membrane

Four coating membrane compositions were investigated as presented in Table 1. CWE made using coated solution A exhibited a calibration plot of very good Nernstian slope (59.0 mV/concentration decade, at 25 °C; Table 1) over a relatively wide range of BZH^+ concentration (1.26×10^{-5} to 0.58×10^{-2} M) with a response time < 12 s. Consequently, the electrode made using coating solution A was selected for carrying out all the following studies.

Table 1
Composition of the coating membranes and slopes of the corresponding calibration graphs, at 25°C, using electrode A

Membrane	Coating solution[a] (mg)			Membrane composition (%) (m/m)			Slope (mV/decade)	S[b] (%)
	PVC	DOP	ion pair	PVC	DOP	ion pair	1.5 h presoak	
A	120.0	100.0	30.0	48	40	12	59.0	1.1
B	112.5	100.0	37.5	45	40	15	53.5	1.2
C	115.0	112.5	22.5	46	45	9	52.0	1.4
D	120.0	112.5	17.5	48	45	7	48.0	1.3

[a] Dissolved in the least amount of tetrahydrofuran possible (3–4 ml). DOP, Dioctylphthalate.
[b] Relative standard deviation values of slopes (five determinations).

3.2. Effect of soaking

The performance characteristics of the BZFT CWE were studied as a function of soaking time. For this purpose, the electrode was soaked in 10^{-3} M solution of BZ.HCl and the calibration graphs (pBZH versus E_{elec} (mV)) were plotted after 5 min and 0.5, 1.0, 1.5, 2, 3, 4, 8, 24, and 48 h. The optimum soaking time was found to be 1.5–2.0 h, when the slopes of the calibration curves were 57.0–59.0 mV/pBZH decade, at 25 °C. Soaking for longer than 24 h is not recommended to avoid leaching of, although very little, the electroactive species into the bathing solution. The electrode 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.

3.3. Effect of the temperature of the test solution

Calibration graphs constructed, as previously described, at test solution temperatures 20, 25, 30, 35, 40, 45, and 50 °C are represented in Fig. 1a–g, respectively. The slope, usable concentration range, and response time of the electrode corresponding to each temperature are reported in Table 2. From the table, it is clear that the electrode gave a good Nernstian response in the temperature range 20–45 °C. At 50 °C, the electrode potential did not show a linear relationship with concentration (Fig. 1g). This behaviour may be due to the following reason: At such high temperatures, the phase boundary equilibrium at the gel layer–test solution interface is disturbed by the thermal agitation of the solution. Furthermore, as the temperature exceeds 45 °C, the consequent change in the physical features of the coating plastic membrane would considerably affect the electrode performance. From Fig. 1, the standard electrode potentials ($E°$) were determined, as the intercepts of the calibration graphs at pBZH = 0, and used to obtain the isothermal temperature coefficient ($dE°/dT$) of the electrode by aid of the following equation [15]:

$$E° = E_{25} + (dE°/dT)(t - 25)$$

A plot of $E°$ versus $(t - 25)$ gave a straight line, the slope of which was taken as the isothermal temperature coefficient. It amounts to -0.0009 V/°C, revealing a fairly good thermal stability of the electrode.

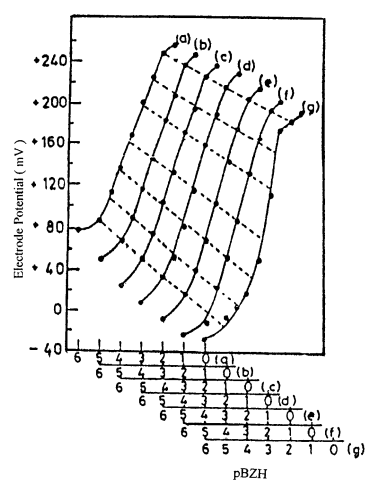

Fig. 1. Calibration graphs at (a) 20, (b) 25, (c) 30, (d) 35, (e) 40, (f) 45, and (g) 50 °C using a benzapril-coated wire electrode (membrane A) soaked for 1.5 h.

Table 2
Performance characteristics of benazepril CWE at different temperatures as determined in aqueous solutions using electrode A

Temperature (°C)	Slope (expt) (mV/decade)	Usable range (M)	Response times (s)	Intercept at pBZH = 0 (E°_{elec})
20	53.0	1.16×10^{-5} to 2.73×10^{-2}	≤12	365.0
25	59.0	1.26×10^{-5} to 20.58×10^{-2}	≤12	361.5
30	61.5	1.53×10^{-5} to 20.74×10^{-2}	≤12	354.6
35	65.0	1.56×10^{-5} to 20.72×10^{-2}	≤12	349.0
40	69.0	1.82×10^{-5} to 20.58×10^{-2}	12	345.0
45	73.0	1.49×10^{-5} to 20.43×10^{-2}	12	341.5

Preconditioned by soaking for 1.5 h; approximate film thickness is 1.0 mm.

3.4. Effect of pH

The effect of pH of the BZ.HCl test solution on the electrode potential is graphically represented in Fig. 2. 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). Fig. 2 indicates that the pH has a negligible effect within the pH range 2.5–9.2. In this range, the electrode can be safely used for benazepril determination.

During the operative life of the electrode (3 months), no significant change in the potential–pH behaviour is observed. The decrease in potential readings at pH < 2.5 and pH > 9.2 until pH ≈ 10.3 may be attributed to penetration of Cl^- and OH^- ions, respectively. At pH 10.3, a turbidity due to precipitation of benazepril base was first detected and associated with concurrent increase in the electrode potential up to pH 11.0. This increase is most probably due to a corresponding decrease in the penetration of the OH^- ions as a result of their reaction with the protonated benazepril species. Beyond pH 11.0, the sharp decrease in potential may be attributed to two reasons. The first is the disappearance of the BZH^+ species from the medium as a result of precipitation. The second reason is the penetration of the OH^- ions into the gel layer of the membrane and replacing, partially, the TPB^- anions of the ion pair. Thus the electrode works as a sensor for the OH^- ions at highly alkaline media, exhibiting a decrease in potential as the pH value increases.

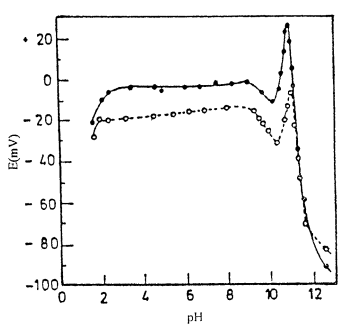

Fig. 2. Effect of pH of the test solution on the potential reading: (●) 4.6×10^{-3} M BZ.HCl, (○) 2.4×10^{-3} M BZ.HCl solution at 25 °C, using electrode A.

3.5. Selectivity of the electrode

The selectivity coefficients $K^{pot}_{BZH,J^{z+}}$ presented in Table 3 clearly showed that the proposed CWE is very selective toward BZH^+ with respect to many common inorganic and organic cations, sugars, and amino acids that are frequently

Table 3
Selectivity coefficients of the BZpT CWE calculated by the separate solution method (10^{-3} both BZH^+ and the interferent) at 25 °C, using electrode A

Interferent	$K^{pot}_{BZH,J^{z+}}$	Interferent	$K^{pot}_{BZH,J^{z+}}$
Na^+	1.38×10^{-3}	Lactose	2.43×10^{-3}
K^+	1.43×10^{-3}	Sucrose	1.53×10^{-3}
NH_4	1.35×10^{-3}	Glycine	1.22×10^{-3}
Mg^{2+}	3.57×10^{-4}	Alanine	9.41×10^{-4}
Ca^{2+}	1.32×10^{-4}	Phenylalanine	1.12×10^{-3}
Fe^{2+}	1.55×10^{-4}	$(Me)_2\ NH^+$	1.45×10^{-3}
Fe^{3+}	1.31×10^{-4}	$(Et)_2\ NH_2^+$	2.23×10^{-3}
Glucose	2.53×10^{-3}	$(Et)_3\ NH^+$	1.23×10^{-3}
Maltose	1.78×10^{-3}	$(Et)_4\ N^+$	2.93×10^{-3}

Table 4
Potentiometric determination of benazepril in aqueous solution and in pharmaceutical preparations with a BZH electrode by the standard addition method, at 25 °C, using electrode A

Sample	Amount taken (μg)	Recovery (%)	Relative standard deviation (%)
Pure BZH^+ solution	6.85–42.50	100.25	0.76
Cibacin tablets[a]	9.50–36.75	99.86	1.28
Cibadrex tablets[b]	10.75–40.18	99.15	0.79

[a] Ciba, Egypt.
[b] Ciba, Switzerland.

present in biological fluids and pharmaceutical preparations.

3.6. Analytical applications

The present CWE has been successfully used for the determination of benazepril in aqueous solution and in the pharmaceutical preparations Cibacin and Cibadrex (tablets) using the standard addition method already described.

The recovery, and standard deviation values presented in Table 4 were calculated from ten determinations in the case of pure BZ.HCl solution and from six determinations in the case of pharmaceutical preparations. Generally, the present method is applicable over a wider concentration range (6.85–42 50 μg/ml) than the spectrophotometric methods of Fawzy et al. [6] and Panderi [7]. where benazepril was determined in the ranges 8–24 and 14.80–33.80 μg/ml, respectively. It is also better than the liquid chromatographic methods of Panderi and Parissi-Poulou [8], Radhakrishna et al. [9] and the LC and HPTLC methods of El-Gindy et al. [10], where benazepril was determined in the ranges 5–20, 50–800 and 10–60 μg/ml, respectively. The present method is not applicable to cream products since the presence of greasy material poisons the membrane surface

In pharmaceutical analysis, it is important to test the selectivity toward the excepiences and the fillers added to the pharmaceutical preparations.

Fortunately, such materials mostly do not interfere. This is clear from the results obtained for the pharmaceutical preparations (Table 4) that these excepiences do not interfere.

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