



Short communication

Ion-selective electrode for the determination of prazosin in tablets

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Received 15 January 2003; received in revised form 29 May 2003; accepted 31 May 2003

Abstract

A poly (vinylchloride) (PVC) membrane electrode selective for prazosinium cation based on prazosinium-phosphotungstate (PZ)₃PT ion-associate is prepared. The electrode exhibits a linear response with an approximate Nernstian slope over the range of 2.7×10^{-6} – 10^{-2} M. Calibration graph slope of the electrode is 58 mV PZ⁻¹ concentration decade when preconditioned by soaking in distilled water for 1 h–20 days. The working pH of the electrode ranged from 1.5 to 6.4 and exhibits very good selectivity for the PZ with respect to a large number of inorganic cations and organic substances of biological importance. The standard additions method and potentiometric titration are used to determine the PZ in pure solution and in pharmaceutical preparations with satisfactory results.

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Keywords: Prazosin (PZ) ion-selective electrode; Poly (vinylchloride) membrane; Potentiometric titration; Drug analysis

1. Introduction

Prazosin;1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanyl-carbonyl) piperazine, is a potent vasodilatory agent which has gained widespread acceptance in the management of hypertension [1] and also has been found to be value in the treatment of heart failure [2]. The drug and its formulations are official in the European Pharma-

copoeia [3] and United States Pharmacopoeia [4]. Many methods, other than potentiometry, such as HPLC, GLC, TLC or Spectrophotometry have been reported for the determination of PZ [5–25]. However, most of these methods involve several manipulation steps before the final result of the analysis is obtained. The low cost and ease of operation of potentiometric instrumentation make the potentiometric determination of PZ⁺ a highly desirable alternative. In the present work, a plastic membrane electrode is prepared based on incorporation of an ion pair complex of phosphotungstate (PT) anion with prazosinium cation in a poly (vinylchloride) (PVC) matrix plasticized with dioctylphthalate (DOP). The electrode has been em-

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ployed successfully as a potentiometric sensor for the determination of PZ in pure solutions and in pharmaceutical formulation (Minipress Tablets).

2. Experimental

2.1. Reagents and materials

All reagents used in this investigation were AR grade and solutions were prepared in bidistilled water. Prazosin was provided by Misr Company for Pharmaceuticals and Chemical Industries, sodium phosphotungstate (III) (NaPT) by Aldrich, dioctyl phthalate (DOP) and the PVC for ISEs by Fluka and the pharmaceutical formulation (Minipress Tablets) was from Pfizer.

The precipitate of the (PZ)₃ PT ion-associate was prepared from aqueous medium by adding portion wise 50 ml 10⁻² M phosphotungstic acid solution to 150 ml 10⁻² M PZ. The precipitate was filtered, washed thoroughly with distilled water and dried at room temperature. The predicted composition of the ion-associate complex has a molar ratio of 3:1 for PZ–PT and was ascertained by elemental analysis (C₅₇H₆₉N₁₅O₅₂PW₁₂: calculated C, 16.96; H, 1.71; N, 5.20. Found: C, 17.02; H, 1.68; N, 5.16%). The calculated and observed elemental analysis data for the ion-associate complex are in good agreement with its structure.

2.2. Membrane composition

The membrane composition (W/W) was 5% (12.6 mg) (PZ)₃ PT, 47.5% (120 mg) DOP and 47.5% (120 mg) PVC. The components were dissolved in about 10 ml of tetrahydrofuran (THF) and the resulting solution was poured into a petri dish of 7.5 cm diameter and left to dry in air.

2.3. Electrode construction and electrochemical system

The electrode was prepared as previously described [26,27]. A transparent membrane of about 0.3 mm thickness was obtained, from which a disc

of about 12 mm diameter was cut out and glued to the polished end of PVC tube by means of a PVC–THF solution. The electrode was then filled with a solution that contains NaCl and PZ of 10⁻¹ and 10⁻³ M concentration, respectively.

The electrochemical system was as follow: Ag, AgCl/internal filling solution (0.1 M NaCl and 10⁻³ M PZ)/membrane/test solution//KCl-saturated salt bridge/saturated calomel electrode.

The potential was measured 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.

2.4. Selectivity

The selectivity coefficients $\log K_{PZ}^{pot} + J^{Z+}$ were evaluated by the separate solution method [28,29] in which the following equation was applied:

$$\log K_{PZ}^{pot} + J^{Z+} = (E_2 - E_1)/s + \log[PZ^+] - \log[J^{z+}]^{1/z} \quad (1)$$

where E_1 is the electrode potential in 10⁻³ M PZ solution and E_2 is the potential of the electrode in a 10⁻³ M solution of the interferent J^{z+} .

2.5. Effect of temperature

To study the effect of temperature change on the electrode potential, 50 ml of 10⁻⁴, 10⁻³, or 10⁻² M solution of PZ was transferred to the measuring cell, connected to a circulator thermostat. The emf of the cell was recorded at different temperature ranging from 25 to 75 °C.

2.6. Potentiometric determination of PZ

The standard additions method [30], in which a known increment is made through the addition of a standard solution to the sample, was applied. This was achieved by adding known volumes of 0.02 M PZ–50 ml of PZ sample of various concentrations.

For the analysis of PZ formulations, the extrapolation method was applied.

3. Results and discussion

3.1. Response characteristics

The response characteristics of the PZ electrodes under investigation are studied by constructing electrodes containing 4, 5, 6 and 8% (PZ)₃ PT ion-associate. It was found that a membrane containing 5% ion-associate has the best response characteristics which was used in all subsequent studies.

3.2. Life span of the electrode

Calibration plots (pPZ vs. *E*, mV) were obtained after electrode soaking in distilled water for different intervals extending from 1/2 h to several weeks. The electrode exhibits calibration graph slope of 58 mV after soaking for 1/2 h up to 24 h then the slope decreases gradually reaching 55 mV per decade after 12 days. The rectilinear concentration range remains constant, namely 2.7×10^{-6} – 10^{-2} M and also constant throughout the time of soaking.

3.3. Response time, detection limit and reproducibility

The response time of the electrode was less than 25 s in the range 10^{-5} – 10^{-3} mol dm⁻³. The detection limits observed for (PZ)₃ PT electrode, which was determined according to the IUPAC recommendations [31], was found to be in the range 2×10^{-6} – 1×10^{-5} mol dm⁻³. The reproducibility of the potential readings was better than ± 0.9 mV over the entire range of concentrations but in the first 2–4 days after electrode preparation the absolute potential varied by approximately 5–10 mV, necessitating a one-point restandardization before each run. The potential drift in 10^{-3} M solutions was less than ± 0.3 mV h⁻¹.

3.4. Effect of pH

The effect of pH of the test solution (10^{-4} , 10^{-3} and 10^{-2} M PZ) on the electrode potential was investigated by following the variation of potential

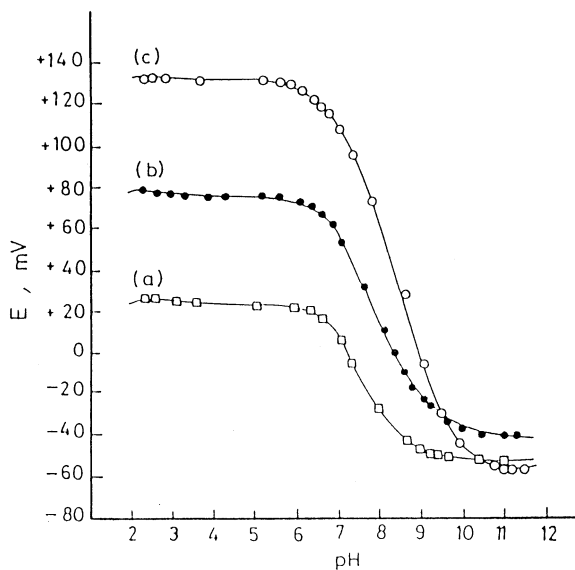


Fig. 1. Effect of pH of the test solution on the electrode potential reading. (a) 10^{-4} , (b) 10^{-3} and (c) 10^{-2} M PZ solutions.

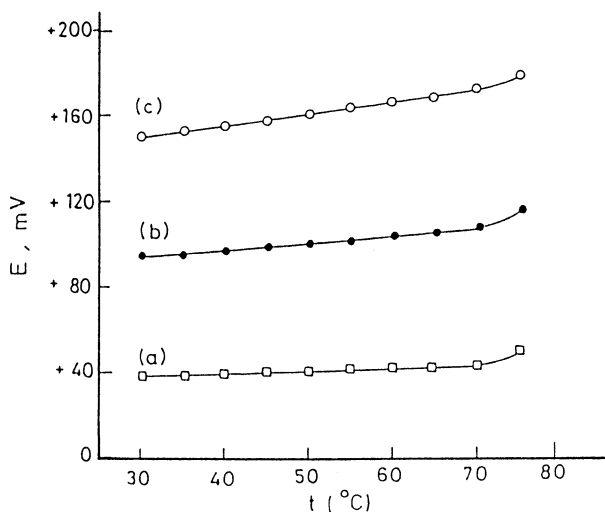


Fig. 2. Effect of temperature on the potential reading. (a) 10^{-4} , (b) 10^{-3} and (c) 10^{-2} M PZ solutions.

with change in pH by the addition of very small volumes of HCl and/or NaOH (0.1–1 M of each; Fig. 1). From the graph obtained it is clear that the working pH of the electrode is from 1.5 up to 6.4, after which the potential reading decrease sharply. The decrease may be attributed to transformation

Table 1
Selectivity coefficients of the PZ electrode

Interferent	$\log K_{PZ,J^{z+}}^{pot}$	Interferent	$\log K_{PZ,J^{z+}}^{pot}$
Na ⁺	-2.69	Sucrose	-2.86
K ⁺	-2.92	Glycine	-3.25
Ba ²⁺	-3.00	Alanine	-3.24
Mg ²⁺	-4.85	Phenylalanine	-3.15
Ca ²⁺	-4.65	Me ₂ NH ₂ ⁺	-3.12
D(+)-Glucose	-2.82	Et ₂ NH ₂ ⁺	-2.67
Lactose	-2.69	Et ₃ NH ⁺	-3.15
Maltose	-2.72	Me ₄ N ⁺	-2.76

of prazosinium cation into free prazosin base and penetration of hydroxyl ions. It is noteworthy that the slope of this descending part of the curve is nearly Nernstian (60 mV/pH unit) over pH range of 7.0–9.3 in the relatively concentrated solution 10⁻² M (Fig. 1C) pointing to a hydroxyl ion exchange at the membrane surface-test solution interfacial junction. The ion exchanger in the PVC network contacting the alkaline test solution is most probably prazosin base molecules adsorbed at the membrane surface from the solution. This is in accordance with the previous work of Shoukry et al. [32].

3.5. Effect of temperature of the test solution

The potential reading *E*, mV was followed as a function of temperature in the range 25–75 °C (Fig. 2). From the plot obtained, it is evident that the electrode can not be used in solution of temperature above 70 °C as indicated by the deviation of the curves at these temperatures (Fig. 2). The electrode is more sensitive to changes in temperatures in more concentrated solutions.

Table 2
Potentiometric determination of PZ in pure solution and in Minepress tablets

Sample ^a	Standard addition method			Extrapolation method	
	mg taken/50 ml	Recovery (%)	S.D. (%)	Recovery (%)	S.D. (%)
Pure PZ	35–100	99.5	0.76	99.9	0.87
Minipress ^b	50–150	100.2	0.82	100.1	0.98

^a In case of tablets, sampling was made by grinding 100 tablets into a very fine powder.

^b Pfizer.

Thus in 10⁻² M PZ solution the potential readings increase in a rate of 0.45 mV °C⁻¹ for 10⁻³ and 10⁻⁴ M solutions, respectively.

Accordingly, it is recommended to thermostat the solution on carrying potentiometric measurements with the present electrode, especially in concentrated PZ solution. The isothermal temperature coefficient dE^o/dT of the electrode has been determined from the temperature potential plots by aid of the equation:

$$dE^{\circ}/dT = dE/dT - (2.3R/F)\log[PZ^{+}] \quad (2)$$

Where dE/dT is determined as the slope of the E-temperature straight line plot. The obtained mean value of dE^o/dT for PZ-electrode as obtained from Fig. 2, amounts to 0.00085 V °C⁻¹, revealing a very high thermal stability of the electrodes within the permitted temperature range.

3.6. Selectivity of the electrode

The influence of some inorganic cations, sugars, amino acids and large organic cations on the PZ-electrode was investigated. The selectivity coefficients (Table 1) were determined by the separate solution method [28,29] using equation (1). None of the investigated species was found to interfere, as shown by the very small values of log K_{PZ}⁺, J^{Z+}. This reflects a very high selectivity of the investigated PZ electrode. The inorganic cations do not interfere owing to the differences in ionic size, and consequently their mobilities and permeability, as compared with those of PZ⁺. The high selectivity of sugars, amino acids and amines is mainly attributed to the differences in polarity and lipophilic nature of their molecules relative to those of PZ.

3.7. Analytical applications

The electrode proved to be useful in the potentiometric determination of PZ in pure solutions and in Minipress tablets applying the extrapolation and standard addition methods. Collective results are given in Table 2. The values of standard deviation and recovery given in Table 2 prove that the electrode is very successful for the determination of PZ either in pure solutions or in the pharmaceutical preparations.

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