

ANALYSIS

POLYMERIC MEMBRANE ELECTRODES FOR SELECTIVE DETERMINATION OF METHIADEN

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Abstract: Polyvinyl chloride matrix membrane ion-selective electrodes for the determination of methiaden hydrochloride based on the ion-pair of methiaden cation with tetraphenylborate anion were prepared using bis(2-ethylhexyl)sebacate, (electrode A), 2-nitrophenyl octyl ether (electrode B), 2-nitrophenyl dodecyl ether (electrode C) and 1-isopropyl-4-nitrobenzene (electrode D) as the membrane solvents. The electrodes exhibit near-Nernstian response in different concentration ranges, depending on the used membrane solvents. The basic analytical parameters of these electrodes were evaluated. The potentiometric titration method was used to determine methiaden hydrochloride with good precision and accuracy.

Keywords: Methiaden ion-selective electrode, potentiometric titration, methiaden hydrochloride determination.

Ion-selective electrode constitutes a simple, rapid and inexpensive means of measuring the activity of an ionic analyte over a wide concentration range, typically of 3–6 orders of magnitude without extensive sample preparation. One of the many existing principles for the construction of ion-selective membrane is the addition of a lipophilic ion-pair complex into a highly plasticized polymer membrane. Potentiometric application of ion-selective electrodes has been used in the control of pharmaceutical products and it has been considered as a successful alternative to the conventional analytical methods (1,2). Ion-selective electrodes with a polyvinyl chloride membrane have been developed for potentiometric determination of following antihistamine drugs: chlorpheniramine (3,4), cyproheptadine (5), diphenhydramine (6), ranitidine (7,8), tripelemamine (9,10), promethazine (11), ketotifen (12) and cetirizine (13). Methiaden hydrochloride (N,N-dimethyl-3-[methyldibenzo[b,e]thiepin-11(6H)-ylidene-1-propanamine) shows the antihistaminic activity and it can be considered a first generation H₁ antagonist (14).

This paper describes the construction and performance characteristics of ion-selective electrodes for the determination of methiaden hydrochloride. They are based on the use of methiaden-tetraphenylborate as a novel electroactive compound with bis(2-ethylhexyl)sebacate, 2-nitrophenyl octyl ether, 2-nitrophenyl dodecyl ether and 1-isopropyl-4-nitrobenzene as the membrane sol-

vents. Electrode with methiaden-tetraphenylborate and 2-nitrophenyl ether was used for the determination of methiaden hydrochloride.

EXPERIMENTAL

Materials and reagents

Methiaden hydrochloride (M) was supplied by Lečiva (Prague), sodium tetraphenylborate (Na-TPB), bis(ethylhexyl)sebacate (BEHS), 2-nitrophenyl octyl ether (NPOE), 2-nitrophenyl dodecyl ether (NPDE) and 1-isopropyl-4-nitrobenzene (IPNB) and tetrahydrofuran were obtained from Fuka (Switzerland). Powdered polyvinyl chloride (PVC) of high molecular mass was purchased from Aldrich (USA).

All other chemicals were analytical – reagent grade, and double distilled water was used throughout to prepare the solutions.

Apparatus

Potentiometric measurements were made at $21 \pm 2^\circ\text{C}$ with PHM-22 digital pH/mV with a scale expander type pH=630 Radiometer (Denmark) equipped with a saturated calomel electrode K-401 (SCE) and Ag/Ag₂S membrane electrode of the same company.

The pH measurements were performed with a pH-meter type Nr 515 (Mera-Tronic, Poland) with a combination electrode (Eurosensor, Poland).

A magnetic stirrer was used, but the readings of the potential value were taken when the stirrer was switched off. The UV determination were

performed on a spectrophotometer UV-VIS Lambda 15, Perkin-Elmer (Germany).

Preparation of the electroactive compound

The ion-pair was prepared by mixing stoichiometric amounts of 1×10^{-2} mol l^{-1} aqueous Na-TPB solution with an equimolar aqueous solution of M. The white precipitate of M-TPB was isolated by filtration with a G4 sintered glass crucible, extensively washed with double distilled water and dried at room temperature and ground into fine powders. The m.p. of methiaden-TPB ion-pair was 172–174°C.

Preparation of PVC membrane electrodes

The membrane electrodes were prepared by dissolving 170 mg of PVC in 6 ml of tetrahydrofuran and 360 mg of bis-(2-ethylhexyl)sebacate (electrode A), 2-nitrophenyl octyl ether (electrode B), 2-nitrophenyl dodecyl ether (electrode C) or 1-isopropyl-4-nitrobenzene (electrode D) as membrane solvents and 20.0 mg of M-TPB ion-pair was added to this mixture. The homogeneous cocktails were poured into a 3.1 cm i.d glass ring and were covered with a sheet of filter paper and a cover of a glass plate and then a membrane was formed as the solvent was evaporating at room temperature for about 12 h.

Construction of the electrode

To prepare an electrode, a membrane disc of 0.8 cm diameter was cut from the obtained film and glued onto the front end of PVC electrode body containing an inner Ag/AgCl junction. 1×10^{-3} mol l^{-1} methiaden hydrochloride in a 1×10^{-3} mol l^{-1} NaCl solution was used as the inner electrolyte.

The electrodes were constructed according to Craggs et al. (15). The electrode potential was measured against the SCE as the reference electrode. The electrodes were preconditioned for about 12 h by soaking in 1×10^{-3} mol l^{-1} M solution and stored in the same solution before use.

Characteristics electrodes

The performance of the electrodes (A,B,C,D) was investigated by measuring the e.m.f. values of 1×10^{-2} – 1×10^{-6} mol l^{-1} of M in 1×10^{-3} mol l^{-1} NaCl solution. The potential was recorded when the readings were stable. A calibration graph was made by plotting the observed potential as a function of the logarithm of M concentration.

Potentiometric titration of methiaden hydrochloride

The sample was prepared by dissolving about 3.0 – 11.0 mg of M in 45 ml of water, and 5 ml of

1×10^{-2} mol l^{-1} NaCl solution. The solution was titrated with a 1×10^{-2} mol l^{-1} NaTPB standard solution (16) using electrode B and SCE as the reference electrode. The end-point corresponds to the maximum slope on the titration curve (1 ml of 1×10^{-2} mol l^{-1} NaTPB solution is equivalent to 3.46 mg of methiaden hydrochloride).

RESULTS AND DISCUSSION

Nature and response of the methiaden electrodes

Methiaden reacts with NaTPB to form a stable ion-pair which is water insoluble but readily soluble in organic solvent such as tetrahydrofuran, nitrobenzene and carbon tetrachloride. The composition of the ion-pair was verified by data obtained from elementary analysis. A 1:1 molar ion-pair ratio M to TPB was found. The obtained ion-pair was tested as the ion-exchanger in the PVC membrane electrodes with the following solvent mediators: BEHS (electrode A), NPOE (electrode B), NPDE (electrode C) and IPNB (electrode D). The working characteristics of for the A, B, C and D electrodes were examined on the basis of the calibration curves obtained by measuring of the e.m.f. values of the set of methiaden hydrochloride solutions in an interval of 1×10^{-2} – 1×10^{-6} mol l^{-1} .

With the ionic strength adjusted to 1×10^{-3} mol l^{-1} NaCl all the electrodes were found to respond to M ion in wide concentration ranges with nearly Nernstian slopes. The concentration ranges depended on the used membrane solvents. The general operating characteristics of M electrodes are summarized in Table 1. The slopes of B, C and D electrodes were somewhat higher compared with A electrode, which contains the BEHS non-polar membrane solvent, but other analytical parameters (linear concentration range, limit of detection) were comparable with the investigated electrodes. The response times (90% final signal) of the four analysed electrodes were about 60 s. In the range of 1×10^{-2} – 1×10^{-4} mol l^{-1} , the electrodes provided a stable potential within 25 – 35 s. At lower concentration the response time increased to 50–60 s which is typical for PVC membrane electrodes. The performance characteristics of electrode A remained constant for 3 weeks and B, C, D electrodes for about 4–6 weeks afterwards the membranes should be renewed.

Effect of pH on the response of electrodes

The effect of pH on the potential readings of methiaden electrodes A, B, C and D was checked by recording the e.m.f. of a cell containing 1×10^{-3} mol l^{-1} M solution of various pH values. The pH of the solution was changed by the addition of small

volumes of concentrated solution of hydrochloric acid and/or sodium hydroxide. The plots of the dependence of electrode potential on pH of M solution are presented in Figure 1. The pH range, where the potential remains constant is 4.5 – 6.5 for the investigated electrodes. In this range the potential does not vary more than ± 3 mV. At higher pH values, however, there is a substantial decrease in the potential because of the gradual increase in the concentration of unprotonated M and precipitation of M – base or may be due to the decomposition of ion-pair at the membrane surface. At lower pH values, below pH 4.5, probably the tested electrodes become progressively sensitive to hydrogen ion.

Selectivity of the electrodes

The response of A, B, C and D electrodes for M were examined in the presence of some drugs and drugs of antihistamine group. The potentiometric selectivity coefficients K_{ij}^{pot} were determined by the separate solution method and calculated from the equation log:

$$K_{ij}^{pot} = \frac{E_j - E_i}{S}$$

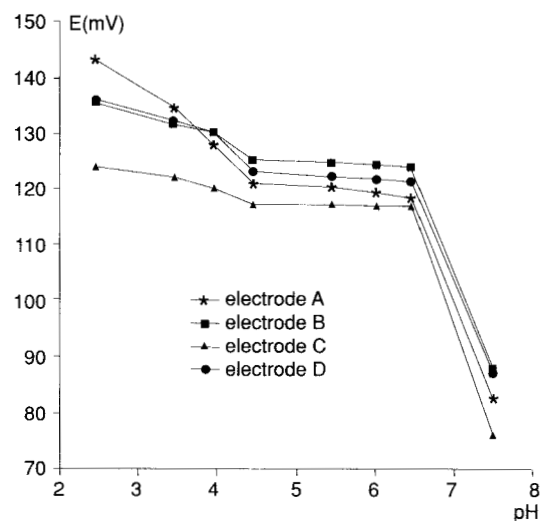


Figure 1. Effect pH values on electrode response for 1×10^{-3} mol l^{-1} methiaden hydrochloride solution.

where E represented the e.m.f. readings measured for the primary ion (i) and the interfering ion (j), respectively, and S is the slope observed for primary ion (17). The values for K_{ij}^{pot} were calculated from the e.m.f. values measured for 1×10^{-3} mol l^{-1} of the primary and interfering ions in 1×10^{-3} mol l^{-1}

Table 1. Response characteristics of PVC methiaden electrodes A, B, C and D

Parameters	Electrodes			
	A	B	C	D
Slope/mV decade ⁻¹	53.0 \pm 1.6*	61.4 \pm 0.6*	61.7 \pm 1.0*	61.6 \pm 1.2*
Lower limit of linear range/mol l^{-1}	10^{-4}	9.0×10^{-5}	9.5×10^{-5}	10^{-4}
Lower limit of detection/ mol l^{-1}	2.5×10^{-5}	0.5×10^{-5}	2.0×10^{-5}	2.5×10^{-5}
Working acidity (pH)	4.5–6.5	4.5–6.5	4.5–6.5	4.5–6.5
Response time for 10^{-3} mol l^{-1} /s	35	20	30	30
Usable concentration range mol l^{-1}	10^{-2} – 10^{-4}	10^{-2} – 9.0×10^{-5}	10^{-2} – 9.0×10^{-5}	10^{-2} – 10^{-4}

* SD standard deviation

Table 2. Potentiometric selectivity of methiaden PVC membrane electrodes A, B, C and D

Interfering species (j)	Log K_{ij}^{pot}			
	Electrodes			
	A	B	C	D
Chlorpyramine	-0.19	-0.03	-0.09	-0.06
Diphenhydramine	-0.85	-1.05	-1.02	-0.87
Phenazoline	-0.74	-0.96	-0.93	-0.99
Ephedrine	-1.25	1.46	-1.55	-1.44
Atropine	-1.23	-1.48	-1.48	-1.09
Aminophylline	-3.16	-3.46	-3.45	-3.27
Benzoate	-1.60	-1.70	-1.59	-1.58

Table 3. Results of methiaden hydrochloride determination with statistical evaluation

No.	Amount of methiaden			RSD %	Spectrophotometry UV*	
	Taken (μg)	Found			$\bar{x}/\% \pm \text{SD}$	RSD %
		$\bar{x}/\mu\text{g}$	$\bar{x}/\% \pm \text{SD}$			
1	3.46	3.46	100.12 \pm 0.08	2.34	100.6 \pm 0.91	0.89
2	6.92	6.88	99.34 \pm 0.03	0.37		
3	8.65	8.52	98.52 \pm 0.37	0.43		
4	10.38	10.37	99.96 \pm 0.03	0.302		

Average of five determinations.

* Spectrophotometric method at 200.4 nm in methyl alcohol

NaCl solution. The results presented in Table 2 show, high selectivity for aminophylline, ephedrine, atropine and benzoate. The comparable selectivity coefficients were observed for electrodes B, C and D, but that of electrode A was a slightly worse.

Analytical application

Electrode B could be successfully applied in the potentiometric determination of methiaden hydrochloride in aqueous solution. Sodium TPB of $1 \times 10^{-2} \text{ mol l}^{-1}$ standard solution (17) turned out to be the most suitable titration agent. Typical titration curves with potential breaks of about 80–120 mV at the points corresponding to 1:1 methiaden tetraphenylborate reaction were obtained. The Gran's method (18) was used to determine the equivalence points. Table 3 shows the results obtained from the determination of M in aqueous solution by means of the proposed procedure and the UV spectrophotometric method as the reference method. The spectrophotometric determination were made using the standard curve method measuring the absorbance at 200.4 nm in methyl alcohol.

The potentiometric and spectrophotometric determinations of methiaden hydrochloride provided the mean result and mean standard deviation of 99.48 ± 0.13 and 106 ± 0.9 with a relative standard deviation of 0.86% and 0.89%, respectively.

The proposed membrane system offers a simple, rapid and accurate technique for the determination of methiaden hydrochloride.

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