

Dibazol ion-selective electrodes

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Abstract: Liquid-membrane and polyvinylchloride membrane dibazol ion-selective electrodes have been developed. They are based on ion-pair complexes of dibazol with dicyclohexylnaphthalene sulphonate, diisopentyl-naphthalene sulphonate, diisobutyl-naphthalene sulphonate and tetraphenylborate. The electrodes show near-Nernstian response for dibazol in the concentration range of $ca\ 10^{-5}$ – 10^{-2} M in the pH range 3–7. The electrodes can be used in the potentiometric determination of dibazol.

Keywords: *Dibazol ion-selective electrode; direct potentiometry; potentiometric titration.*

Introduction

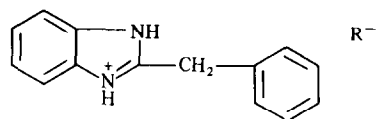
Dibazol (2-benzylbenzimidazole hydrochloride or bendazol) is a drug possessing vasodilating, antispasmodic and hypotensive properties. A number of analytical methods for the assay of dibazol are available including non-aqueous titration [1], spectrophotometry [2] and iodometry [3]. However, many organic impurities and other substances produce significant interferences in these procedures and a rapid specific method applicable to the assay of dibazol in the presence of co-formulated substances in pharmaceutical preparations is required. Gur'ev *et al.* have proposed two-phase potentiometric titration with sodium tetraphenylborate or sodium lauryl sulphate using liquid-membrane tetrabutylammonium lauryl sulphate or trioctylammonium lauryl sulphonate electrode [4–6]. These methods also suffer from lack of selectivity. Freiser *et al.* [7] have suggested dinonylnaphthalene sulphonate as the electroactive material for coated-wire ion-selective electrodes for the assay of certain drugs.

In the present paper dibazol ion-selective electrodes made with ion-pair complexes of dibazol with dicyclohexylnaphthalene sulphonate (DDCHNS), diisopentyl-naphthalene sulphonate (DDPNS), diisobutyl-naphthalene sulphonate (DDBNS) and tetraphenylborate (DTPB) are described and their performances are compared. The electrodes are suitable for the direct potentiometry and potentiometric titration of dibazol.

Materials and Methods

Apparatus

The recording system and the reaction cell were the same as previously reported [8], except where stated. All measurements were made in stirred solutions.



DDCHNS	$R^- = (C_6H_{11})_2C_{10}H_5SO_3^-$
DDPNS	$R^- = (C_5H_{11})_2C_{10}H_5SO_3^-$
DDBNS	$R^- = (C_4H_9)_2C_{10}H_5SO_3^-$
DTPB	$R^- = (C_6H_5)_4B^-$

Chemicals and solutions

All chemicals used were of analytical reagent or chemical pure grade. Dibazol was of >99.0% purity. Sodium dicyclohexylnaphthalene sulphonate, sodium diisopentyl-naphthalene sulphonate and sodium diisobutylnaphthalene sulphonate were synthesized as reported previously [8]. Deionized distilled water was used throughout. Dibazol solutions were prepared in the range 10^{-2} – 10^{-7} M. Standard 0.01 M sodium tetraphenylborate solution was prepared and standardized as described previously [9].

Preparation of ion-pair complexes

DDCHNS was precipitated by mixing 40 ml of 0.01 M solution of dibazol with 50 ml of 0.01 M solution of sodium dicyclohexylnaphthalene sulphonate. The mixture was allowed to stand overnight, and the precipitate was collected on a porosity-4 sintered-glass crucible, washed several times with distilled water and dried at 80°C. DDPNS, DDBNS and DTPB were prepared in a similar manner.

Electrode construction

The polyvinylchloride membrane electrodes were constructed using the technique as reported previously [8, 10]. The internal reference solution was 0.01 M dibazol in 0.01 M potassium chloride and a 1 mM solution of the ion-pair complex in dibutyl phthalate or other ester (as plasticizer) was used. The liquid-membrane ion-exchanger was prepared by making a solution of the ion-pair complex in nitrobenzene, and the liquid-membrane electrodes were assembled as reported previously [8, 10]. A double-junction saturated calomel electrode (SCE) with 0.01 M potassium chloride was used as the internal reference electrode.

Measuring cell

Dibazol ion-selective electrode–sample solution (pH 6–6.5, 0.1 M $NaNO_3$)–1 M $NaNO_3$ –SCE.

Results and Discussion

Linear response range and the effect of electroactive material

Calibration curves for the dibazol ion-selective electrodes in stirred dibazol solutions showed a linear response in the 10^{-2} – 10^{-5} M concentration range. The range of linear response, slope and detection limit for polyvinylchloride and liquid-membrane dibazol ion-selective electrodes with ion-pair complexes of dibazol with dialkylnaphthalene sulphonate and tetraphenylborate are summarized in Table 1. The slopes were calculated

Table 1
 Characteristics of dibazol ion-selective electrodes with various electroactive materials

Electroactive material	PVC membrane electrode Slope (mV/logC)	Linearity (M)	Detection limit (M)	Liquid-membrane electrode Slope (mV/logC)	Linearity (M)	Detection limit (M)
DDCHNS	57.0 ± 0.5	1.0×10^{-2} – 1.0×10^{-5}	5.0×10^{-6}	60.0 ± 0.7	1.0×10^{-2} – 1.3×10^{-5}	6.3×10^{-6}
DDPNS	56.0 ± 0.5	1.0×10^{-2} – 1.3×10^{-5}	6.3×10^{-6}	57.5 ± 0.7	1.0×10^{-2} – 1.6×10^{-5}	6.3×10^{-6}
DDBNS	55.0 ± 0.7	1.0×10^{-2} – 2.0×10^{-5}	7.9×10^{-6}	57.0 ± 1.0	1.0×10^{-2} – 2.5×10^{-5}	7.9×10^{-6}
DTPB	57.0 ± 0.7	1.0×10^{-2} – 1.3×10^{-5}	6.3×10^{-6}			

by using the least-squares method for the linear part of the calibration curves. The results show that the dibazol dialkyl naphthalene sulphonate electrodes with an electroactive material of high molecular weight show a slightly wider linear range and a greater response slope.

pH effect

The pH dependence of the potentials of the electrodes was investigated by measuring the emf of the cell in dibazol solutions in which the pH was adjusted by adding appropriate amounts of hydrochloric acid or sodium hydroxide solution using a 50 μ l microsyringe. pH values in the range 3–7 did not affect significantly the performance of the electrode for measuring dibazol concentrations. At pH values higher than 7, the dibazol base in the aqueous test solutions reduced the emf values and at pH values below 3, the interference of hydrogen ions occurred.

Influence of plasticizers on the performance of the polyvinyl chloride membrane electrode

The effect of plasticizers on the performance of the polyvinylchloride membrane electrode was studied. The results in Table 2 show that electrodes with dibutyl phthalate and diisooctyl phthalate as plasticizer-solvent show the best electrode performance. A study of the effect of dibazol dicyclohexyl naphthalene sulphonate concentration in dibutyl phthalate as polyvinylchloride membrane plasticizer-solvent showed that the electrode slope reached a maximum value at a membrane concentration of 1×10^{-3} M.

Selectivity

In the assay of dibazol by non-aqueous [1], iodometric [3] or two-phase potentiometric titration [4–6], certain substances that cause interference have to be removed before the analytical measurement. Interference by some of these substances and other commonly used compounds on the response of the dibazol dicyclohexyl naphthalene sulphonate electrode was studied by the “mixed-solution” method and the “separate-solution” method. The selectivity coefficients obtained with more than twenty substances are presented in Table 3. The dibazol ion-selective electrodes were found to respond to a number of amines, alkaloids and quaternary ammonium species, e.g. probanthine, tetrabutylammonium, chlorpheniramine, quinine, cinchonine, propranolol and diphenhydramine. Consequently these substances are likely to cause interference in the assay of dibazol, although they rarely are formulated in combination with dibazol. No significant interferences were caused by the other substances tested. The order of selectivity for inorganic cation is: $K^+ > Na^+$; $Ba^{2+} > Ca^{2+} > Mg^{2+}$. For symmetric quaternary

Table 2
Response characteristics of PVC membrane electrodes with different plasticizers-solvents

Plasticizer-solvent	Slope (mV/logC)	Linearity range (M)	Detection limit (M)
Dimethyl phthalate	54.5 ± 1.0	1.0×10^{-2} – 2.0×10^{-5}	1.0×10^{-5}
Diethyl phthalate	56.0 ± 1.0	1.0×10^{-2} – 1.3×10^{-5}	7.9×10^{-6}
Dibutyl phthalate	57.0 ± 0.5	1.0×10^{-2} – 1.0×10^{-5}	5.0×10^{-6}
Diisooctyl phthalate	57.0 ± 0.7	1.0×10^{-2} – 1.0×10^{-5}	5.0×10^{-6}
Didecyl phthalate	55.0 ± 0.7	1.0×10^{-2} – 1.6×10^{-5}	6.3×10^{-6}
Di(2-ethylhexyl)phosphonate	50.0 ± 1.0	1.0×10^{-2} – 1.3×10^{-5}	6.3×10^{-6}

Table 3
Selectivity coefficients for various dibazol ion-selective electrodes*

Interferent	Electrode DDCHNS	DDPNS	DDBNS	DTPB
Quinine	8.91×10^{-2}	0.22	0.28	9.55×10^{-2}
Propranolol	0.25	0.33	0.42	0.28
Chlorpheniramine	0.22	0.28	0.28	0.28
Glycopyrrolate	6.92×10^{-2}	8.91×10^{-2}	0.10	9.55×10^{-2}
Colchicine	3.00×10^{-3}	2.78×10^{-3}	2.78×10^{-3}	3.10×10^{-3}
Tris(hydroxymethyl)aminomethane	5.68×10^{-5}			7.80×10^{-5}
Glucose (1%)	does not interfere			
Theophylline	5.60×10^{-4}	3.87×10^{-4}	4.60×10^{-4}	4.10×10^{-4}
Caffeine	4.50×10^{-5}	4.50×10^{-5}	6.98×10^{-5}	8.41×10^{-5}
Moroxydine	1.26×10^{-2}	1.45×10^{-2}	1.55×10^{-2}	1.91×10^{-2}
Cinchonine	0.10	0.18	0.22	0.21
Tetrahydropalmatine	1.20×10^{-2}	3.98×10^{-2}	6.31×10^{-2}	3.98×10^{-2}
Probanthine	0.40	0.56	0.63	
Thiamine†	5.03×10^{-2}	4.99×10^{-2}	5.01×10^{-2}	2.47×10^{-2}
Sodium chloride	1.56×10^{-4}	1.68×10^{-4}	7.24×10^{-5}	1.57×10^{-4}
Ammonium chloride	1.86×10^{-4}	1.55×10^{-4}	9.06×10^{-5}	1.50×10^{-4}
Potassium chloride	6.25×10^{-4}	2.15×10^{-4}	4.55×10^{-4}	8.96×10^{-4}
Magnesium chloride	4.00×10^{-6}	1.45×10^{-5}	1.35×10^{-5}	1.80×10^{-5}
Barium chloride	4.15×10^{-5}	5.35×10^{-5}		5.45×10^{-5}
Calcium chloride	2.15×10^{-5}	2.77×10^{-5}	3.15×10^{-5}	4.86×10^{-5}
Tetramethylammonium iodide†	3.16×10^{-3}	4.83×10^{-3}	7.85×10^{-3}	5.03×10^{-3}
Tetraethylammonium iodide†	2.37×10^{-2}	2.58×10^{-2}	2.58×10^{-2}	1.83×10^{-2}
Tetrabutylammonium iodide†	5.74	4.83	8.17	8.17
Imidazole†	4.64×10^{-4}	4.64×10^{-4}	5.00×10^{-4}	3.55×10^{-4}

*Dibazol dicyclohexyl-naphthalene sulphonate PVC membrane electrode with dibutyl phthalate as plasticizer-solvent. Mixed-solution method.

†Separate-solution method ($C_i=C_j=10$ mM).

ammonium ions, an approximately linear relationship between $\log K_{ij}$ and the carbon atom number of the symmetric quaternary ammonium ions was observed. The study demonstrated that the selectivity coefficients are approximately similar for different electrodes tested with DDCHNS, DDPNS, DDBNS and DTPB as electroactive materials. This fact indicates that the electrode selectivity depends primarily on the nature of the interfering ions rather than the ion-pair complexes used as electroactive materials.

Response time

The response times of the polyvinylchloride membrane electrode were less than 20 s in 10^{-2} – 10^{-4} M solutions and 20–50 s in 10^{-5} – 10^{-6} M solutions. The liquid-membrane electrode response times ranged from 30 s for solutions $>10^{-4}$ M to 0.5–2 min for solutions $<10^{-4}$ M.

Reproducibility

The reproducibility of the measurements of potential in 1×10^{-3} M dibazol solution was checked on several occasions over a period of one week. Although a shift of about ± 0.5 mV (polyvinylchloride membrane electrode) and ± 1.0 mV (liquid-membrane electrode) in the absolute millivolt values was observed, the electrode response slopes remained constant.

Dibazol assay

The results obtained for the direct potentiometric assay of dibazol using the calibration curve are reported in Table 4. The average recovery obtained was 99.0% and the relative standard deviation was 1.4%. The results obtained for the potentiometric titration of dibazol with sodium tetraphenylborate showed an average recovery of 99.4% and a mean relative standard deviation of less than 1.0%. The results obtained were in good agreement with those obtained by using the non-aqueous titration method [1].

The polyvinylchloride membrane electrode is preferred in the potentiometric determinations of dibazol because it eliminates the use of harmful organic solvents such as nitrobenzene, and exhibits better reproducibility and faster response times.

Table 4
Assay of dibazol

Direct potentiometry			Potentiometric titration			Non-aqueous titration		
Taken mg	Found mg	Recovery %	Taken mg	Found mg	Recovery %	Taken mg	Found mg	Recovery %
5.1	4.9	96.1	7.9	7.8	98.7	147.3	149.1	101.2
11.0	10.9	99.1	10.7	10.8	100.9	151.1	151.6	100.3
5.7	5.6	98.2	12.8	12.7	99.2	150.7	149.1	98.9
8.6	8.7	101.2	15.9	16.0	100.6	154.3	152.8	99.0
14.6	14.4	98.6	17.6	17.5	99.4	148.9	149.1	100.1
15.5	15.3	98.7	18.7	18.4	98.4	151.4	150.4	99.3
21.1	20.9	99.1						

Assay of dibazol tablets

Dibazol tablets were analysed using the method proposed by Carmack and Freiser [11]. A sample of 25–30 tablets was finely powdered and a portion of the powder, equivalent to about 25 mg of dibazol, was transferred to a 50-ml volumetric flask and diluted to volume with water. Potentiometric measurements were made in replicate on the sample solution and on a standard solution containing approximately the same concentration of dibazol until reproducible (± 0.1 mV) values were obtained. The results of the potentiometric analyses of dibazol tablets with a nominal amount of 10 mg in each tablet and 20 mg in each tablet using the dibazol dicyclohexyl-naphthalene sulphonate polyvinylchloride membrane electrode were 9.8 and 19.7 mg/tablet, respectively and the standard deviations for 5 determinations were ± 0.2 and ± 0.4 mg, respectively. The respective results by non-aqueous titration [1] were 10.1 ± 0.2 and 19.9 ± 0.3 mg/tablet.

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