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Construction and Evaluation of Scopolamine Ion- Selective Electrode

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Abstract

The construction of plasticised PVC matrix-type scopolamine ion-selective membrane electrode and its use in the potentiometric determination of scopolamine in pharmaceutical preparations are described. It is based on the use of the ion-associate species, formed by scopolamine cation and 5-nitrobarbituric counter ion. The basic electrode performance characteristics are evaluated according to IUPAC recommendations. It exhibited a linear response for $1x10^{-2}$ –$1x10^{-5}$ M of scopolamine solutions with a cationic Nernstian slope over the pH range of 4-7. Common organic and inorganic cations showed negligible interference. Direct potentiometric determination of $1x10^{-2}$ – $1x10^{-5}$ M aqueous tubocurarine chloride using this membrane electrode system showed an average recovery of 99.05 with a mean standard deviation of 0.12. This electrode system was successfully applied to the potentiometric determination of scopolamine in some pharmaceutical preparations.

Keywords: Scopolamine membrane electrode, potentiometry, pharmaceutical analysis.

Introduction

Scopolamine butylbromide has antimuscarinic effects but, in contrast to atropine, it has a depressant effect on the CNS. Scopolamine is used in the prevention and control of motion sickness, in visceral spasms, and as a cycloplegic and mydriatic. Several methods for the determination of this drug have been published e.g., titrimetry [1-4], potentiometry [5-8], spectrophotometry[9-19], thin-layer chromatography[20-29], gas chromatography [30-36] and high performance liquid chromatography [37-46].

In this paper, attempt has been made to develop a simple potentiometric method using a PVC membrane electrode responsive for scopolamine butylbromide with sufficiently high accuracy, selectivity and speed.

Experimental

Apparatus:

Potentiometric measurements were carried out at 25 ± 1° C using PRACI TRONIC MV 870 digital pH/mV meter, with the PVC-scopolamine-5-nitrobarbiturate membrane electrode in conjunction with a double junction Ag/AgCl electrode Orion (90-02), containing 10% m/v potassium nitrate in the outer compartment. An Orion (91-02) glass-calomel combination electrode was used for pH adjustment. The IR absorption spectra of the ion-pair were recorded using PHILIPS PU 9706 infrared spectrophotometer.

Reagents:

All chemicals were of analytical- reagent grade and solutions were prepared with de-ionised water. Poly (Vinyl chloride) (PVC), tetrahydrofuran, dioctylphthalate and 5-nitrobarbituric acid were obtained from Sigma chemical Co. Scopolamine butylbromide and its

pharmaceutical preparations were obtained from Chemical Industries Development Co., (CID) Egypt.

Sensor Preparation:

The scopolamine-5-nitrobarbiturate was prepared by mixing 20 ml of 1 M aqueous scopolamine butyl bromide with 20 ml of 1 M ethanolic 5-nitrobarbituric acid solution [47]. After stirring for 15 min., the yellowish precipitate was filtered off on a porosity- 3 sintered- glass crucible, washed twice with doubly distilled water, followed by ethanol, dried at 100° C for one hour, then ground to fine powder. Elemental analysis and the infrared spectra of the products confirmed that 1:1 compounds had been formed. (Fig. 1)

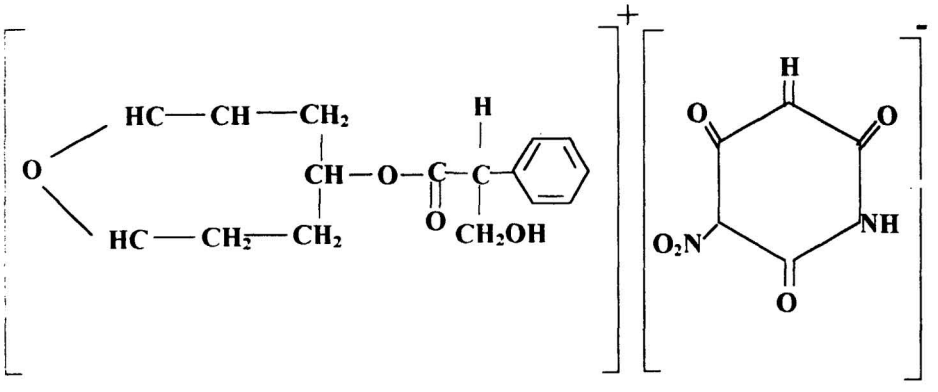

Fig. 1. **Scopolamine- 5-nitrobarbiturate complex**

Electrode Preparation:

The master membrane was fabricated by dissolving 190 mg of the powdered PVC, 350 mg of the plasticiser and 10 mg of the scopolamine 5-nitrobarbiturate ion pair complex in 5 ml of THF. The solution was poured into a petri-dish (3 cm diameter) and covered with a filter paper, the

solvent was allowed to evaporate slowly at room temperature. The light yellow transparent disk, approximately 0.2 mm thick, was cut from the membrane, mounted and glued to polyethylene tube (8 mm diameter) in an electrode configuration according to the procedure of Moody et al [48]. A mixture of equal volumes of $5x10^{-3}$ M scopolamine butyl bromide and $5x10^{-3}$ M potassium chloride was used as internal reference solution in which Ag/AgCl reference electrode is dipped. The electrode was pre-conditioned after preparation by soaking for at least 24 hours in $1x10^{-3}$ M aqueous solution of scopolamine butyl bromide and stored in the same solution.

Electrode Calibration:

Aliquots of 10 ml of $1x10^{-1}$ - $1x10^{-6}$ M scopolamine butyl bromide solution were transferred into 50 ml beakers and the PVC scopolamine-5-nitrobarbiturate membrane electrode in conjunction with an Orion double-junction Ag-AgCl reference electrode (Model 90-02) were immersed in the solution. The measured potential was plotted against the logarithm of the scopolamine butyl bromide concentration. The electrode was washed with deionized water and blotted with tissue paper between measurements.

Effect of pH:

The effect of pH on the potential of the electrode system was studied using two pH/mV meters. The combined glass calomel electrode was connected to one instrument and the PVC scopolamine membrane with the double junction Ag/AgCl reference electrode was connected to the second instrument. 30 ml aliquots of $1x10^{-3}$, $1x10^{-4}$ and $1x10^{-5}$ M scopolamine butyl bromide were transferred to a 100 ml beaker where the three electrodes were immersed, the potential reading corresponding to different pH values were recorded. The pH was gradually increased or

decreased by the addition of small aliquots of dilute solutions of sodium hydroxide or hydrochloric acid respectively and the mV- pH was plotted.

Interference Effects:

The response of the electrode was also examined in the presence of a number of organic and inorganic ions. The potentiometric selectivity coefficients $K^{Pot}_{Scop+.\ C}$ were used to evaluate the degree of interference [49, 50]. A 9.0 ml aliquot of distilled water was placed in a 50-ml beaker where the scopolamine PVC membrane electrode and the double junction Ag-AgCl electrode where immersed. The potential response upon addition of 1.0 ml aliquot of $1x10^{-2}$ M solution of the interferent was recorded and compared with that of $1x10^{-3}$ M pure scopolamine butyl bromide solution. The selectivity coefficients were calculated using the Eisenman-Nicolsky equation (I):

$$\log K^{Pot}_{Scop^{+}.\ C} = E_1\text{-}E_2/S \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \text{(I)}$$

Where E_1 and E_2 are the potential readings observed after one minute due to the same concentration of scopolamine butylbromide and the interferents respectively and S is the slope of the scopolamine calibration graph (mV/concentration decade). $Scop^{+}$ is the abbreviation of scopolamine.

Determination of scopolamine:

For direct potentiometeric determination of scopolamine in commercially available pharmaceutical preparations, three different formulations were investigated:

I. Buscopan amp. (10 mg/ml):

10 ml were diluted with deionized water to obtain the following concentrations: 0.1 mg/ml, 0.15 mg/ml, 0.20 mg/ml, 0.25 mg/ml, 0.30 mg/ml, 0.35 mg/ml and 0.40 mg/ml.

II. Buscopan tablet (10 mg/tab):

Tablet powder equivalent to 20 mg active ingredient was extracted with 30 ml deionized water in divided volumes using ultrasonic bath. After filteration, diluted to get a concentration of 0.1 mg/ml, 0.15 mg/ml, 0.20 mg/ml, 0.25 mg/ml, 0.30 mg/ml, 0.35 mg/ml and 0.40 mg/ml.

II. Buscopan Supp. (10 mg/Supp.):

10 grams of suppository base were taken to which 30 ml deionized water added, put in a water bath at 80° C for dispersion. The suspension was then placed in ultrasonic bath for 15 minutes, cooled, filtered and completed to 50 ml with deionized water. This solution was further diluted to give approximately scopolamine butyl bromide concentration of 0.1 mg/ml, 0.15 mg/ml, 0.20 mg/ml, 0.25 mg/ml, 0.30 mg/ml, 0.35 mg/ml and 0.40 mg/ml.

For all the previous final diluted solution the pH was adjusted to pH 4-7. The PVC- scopolamine-5- nitrobarbiturate membrane electrode and an Orion double-junction Ag-AgCl reference electrode were immersed in the solution. The electrode system was allowed to equilibrate with stirring and the e.m.f was recorded and compared with the calibration graph.

Official method:

The procedure for the official method was that of British pharmacopea, 1993 [51]. Spectrophotometeric measurements were made with a Shimadzu UV. 260 recording spectrophotometer with 10-mm matched fused-silica cuvettes.

Results and Discussion

Nature and response characteristics of the Electrode:

Scopolamine reacts with 5-nitrobarbituric acid to form a water insoluble scopolamine complex. The electrochemical performance characteristics of this electrode system were evaluated according to IUPAC recommendations using the following electrochemical cell:

Ag-AgCl/KCl ($5x10^{-3}$ M) + Scop. Bu. Br. ($5x10^{-3}$ M) ‖ scopolamine 5-nitrobarbiturate-PVC membrane‖ test solution/Ag-AgCl reference electrode.

The response of the electrode in the presence of foreign cations was measured using the following equation:

$$E = E_o + S \log [a_{Scop.}^{+} + K_{Scop.,C}^{Pot} (a_C)^{1/z}] \quad \text{..... (II)}$$

Where E_o represents the conditional standard potential of the electrode under the conditions used in the cell, S is the slope of scopolamine calibration graph, $K_{Scop.,C}^{Pot}$ is the selectivity coefficient, a_{Scop}^{+} and a_C are the activities or concentrations of scopolamine cation and the foreign ion respectively, having a charge z and present in the test solution.

The calibration graph (Fig. 2) exhibits a Nernstian response for $1x10^{-5}$ – $1x10^{-2}$ M scopolamine with a cationic slope of 59.5 ± 1.02 mV per decade change in concentration. Table 1 summarizes the critical response characteristics of this electrode from data collected over a period of 20 days.

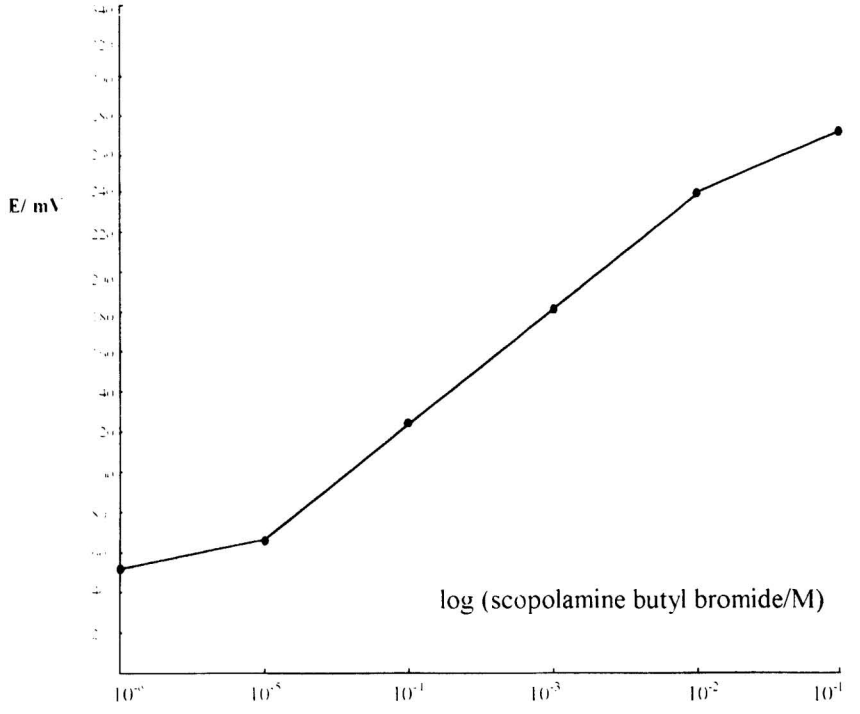

Fig. 2: Typical calibration graph for scopolamine- 5- nitrobarbiturate- PVC membrane electrode.

The dynamic response time of the electrode system was tested for $1x10^{-2}$ - $1x10^{-1}$ M scopolamine butyl bromide solutions. The measurement sequence was from low concentration to the higher, and back. The required time for the electrode to reach values within ± 0.5 mV from the final equilibrium potential after increasing the scopolamine butyl bromide concentration level to 10 fold is fairly short, it reaches 90% of its final steady potential after 15 sec.

Table 1: Response characteristics of scopolamine-5-nitrobarbitarate PVC membrane electrode.

Parameter	Value
• Slope, mV / log C	59.5 ± 1.02
• Correlation coefficient, r	0.999
• Linear range / M	1×10^{-2} - 1×10^{-5}
• Working pH range	4-7
• Response time for 10^{-3} M scopolamine/ s	20
• Intercept/ mV	88 ± 0.84
• Life time / day	20 days

The potential displayed by the scopolamine-5-nitrobarbiturate PVC membrane electrode for consecutive measurements of $1x10^{-2}$ – $1x10^{-5}$ M of standard scopolamine butylbromide solutions did not vary by more than ± 1 mV (n=5) in the same day. The calibration slope did not vary by more than ± 1.02 mV per decade change of concentration. The reproducibility and stability of the potential were evaluated over a period of 10 days by determining replication graphs (n=5). During this period, the electrode was stored in $1x10^{-3}$ M scopolamine butylbromide solution and washed thoroughly with de-ionized water between measurements. The detection limit, linear range, response time, and selectivity coefficient values were almost constant for this membrane electrode during this period.

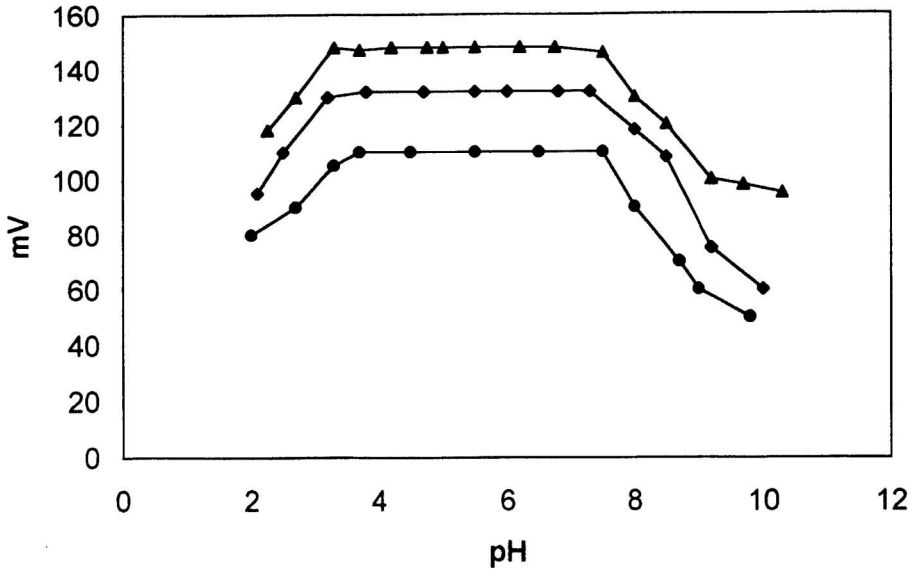

Fig. 3: Effect of pH on the potential response of scopolamine- 5-nitrobarbiturate PVC membrane electrode.

The pH dependence of the scopolamine butyl bromide is shown in (Fig. 3) at three different scopolamine concentration levels. It can be seen that electrode response is independent of pH over 4-7 pH range and that the region of pH independence is mildly concentration dependent. The interference effect of different organic and inorganic cations, on the electrode response was evaluated. The interference of these compounds was assessed by measuring the selectivity coefficient $K^{Pot}_{Scop.^+, C}$ using the separate solutions method [50, 52, 53] with 10^{-3} M concentration of both the standard scopolamine and the interferents. The results obtained, table 2 shows reasonable selectivity for scopolamine in the presence of many interferents. In most cases, no significant influence on the electrode performance.

Table 2: Selectivity coefficients of scopolamine-5-nitrobarbiturate PVC membrane electrode.

Interferent, C	$K^{pot}_{Scop, C}$
• Glycine	0.331×10^{-3}
• Cysteine	0.307×10^{-3}
• Urea	0.331×10^{-3}
• Ammonium chloride	0.225×10^{-3}
• Succinamide	0.273×10^{-3}
• Diethylamine	0.273×10^{-3}
• Dibutylamine	0.284×10^{-3}
• Aminopropanol	0.243×10^{-3}
• Ethanolamine	0.208×10^{-3}

Direct potentiometric determination of scopolamine butyl bromide using the scopolamine 5-nitrobarbiturate-PVC membrane electrode was performed and calculated from the calibration curve. The statistical data of the analytical results obtained by the proposed method and the official method[72] for the tested drug in pure form has been illustrated in table (3). The results obtained by both methods are approximately in good agreement, however, the electrode method offers several advantages in term of simplicity, selectivity, less time consuming and precision. Further, the results obtained were encouraging to apply the proposed method for the determination of scopolamine butylbromide in some pharmaceutical preparations. The results listed in table (4), show agreement with those given with the official methods. Thus it is recommended for the precise direct potentiometric assay of scopolamine butyl bromide in pure form and in pharmaceutical preparations.

Table 3: Comparative analytical results of the proposed and official method for the scopolamine in pure form.

Statistical Parameters	Direct potentiometric method	Official Method
• Mean recovery (P = 0.05)	99.95	99.93
• N	6	6
• Variance	0.01	0.01
• S. D.	0.12	0.10
• S. E.	0.05	0.04
• t- test	0.11 (2.26)	
• F- test	0.68 (5.05)	

N = Number of experiments S.D. = Standard deviation
S.E. = Standard error F = Variance test t = t test of unpaired data

Table 4: Comparative analytical results of the proposed and official method for the scopolamine in some pharmaceutical preparations.

Sample and Source	Scopolamine butylbromide (nominal amount)	Statistical Parameters	Direct potentiometric method	Official Method
Buscopan amp. Boehringer Ing. CID. Egypt	20 mg / ml	• Man recovery (P = 0.05)	99.36	100.29
		• N	7	7
		• Variance	2.91	3.43
		• S. D.	1.71	1.85
		• S. E.	0.65	0.70
		• t-test	0.98 (2.18)	
		• F-test	1.18 (4.28)	
Buscopan tab. Boehringer Ing. CID. Egypt	15 mg / tablet	• Mean recovery (P = 0.05)	99.11	98.80
		• N	7	7
		• Variance	4.66	2.57
		• S. D.	2.16	1.60
		• S. E.	0.81	0.61
		• t-test	0.31 (2.18)	
		• F-test	1.81 (4.28)	
Buscopan Supp. Boehringer Ing. CID. Egypt	10 mg / supp.	• Mean recovery (P = 0.05)	98.13	98.47
		• N	7	7
		• Variance	4.12	3.57
		• S. D.	2.03	1.89
		• S. E.	0.77	0.72
		• t-test	0.05 (2.18)	
		• F-test	1.15 (4.28)	

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