



Potentiometric Determination of Amineptine Hydrochloride in Pure Form and Urine Using Coated Wire Ion-Selective Electrode

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ABSTRACT

Amineptine hydrochloride (AMP) coated wire graphite electrode based on amineptine-phosphotungstate (AMP-PT) as electroactive material in the presence of dibutyl phthalate DBP as the plasticizing solvent mediator has been described. The sensor exhibited a linear response with a good Nernstian slope over a relatively wide range of concentration. The sensor displays Nernstian response of 58.7 mV/decade over the concentration range of 1.0×10^{-5} to 1.0×10^{-2} M. The potentiometric measurements can be done in the pH range of 2.0 to 4.0. The measurement interferences in the presence of inorganic cations and organic substances were studied using matched potential method for selectivity coefficient determination. Application of this potentiometric sensor for the amineptine determination in pure form and urine was satisfactory results.

Keywords: Amineptine hydrochloride (AMT); Coated graphite electrode; Potentiometry.

INTRODUCTION

Amineptine hydrochloride (AMT), (Fig 1), 7-[(10,11-Dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)amino]heptanoic acid hydrochloride is a tricyclic compound used as an antidepressant for treatment of mental depression and manic depressive disorders¹.

Several methods have been published for determination of amineptine hydrochloride drug in bulk or in different pharmaceutical formulations as well as in biological fluids.

These methods include Electrochemical methods^{2,3}, HPLC method employing different mobile phases and columns^{4,5} and Spectrophotometric method⁶.

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 and applicable to samples, no selective electrode is, so far, available for the determination of amineptine HCl.

The advantage of using coated wire over conventional liquid membrane ISE is that they can be used in small volume of sample, simple design (absence of internal solution), mechanical flexibility, and the possibility of miniaturization and microfabrication.

The present investigation deals with the fabrication and characterization of coated graphite ion selective electrode for the determination of AMP.

The electrochemical sensitivity of the electrode is based on the incorporation of amineptine-phosphotung state (AMP-PT) as a sensing element.

The electrode was used successfully for the determination of amineptine HCl in the pure form and in urine.

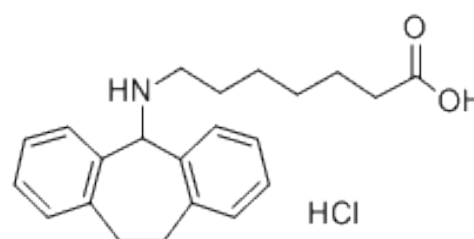


Figure 1: The chemical structure of amineptine hydrochloride

MATERIALS AND METHODS

All chemicals used were of analytical grade, double distilled water was used throughout all experiments. Pure grade amineptine hydrochloride was provided by Servicer Co. (Egypt). Phosphotungstic acid (PT), poly (vinyl chloride) of high molecular weight (PVC), tetrahydrofuran (THF) and dibutyl phthalate (DBP) were purchased from Merck (Germany). The metal salts were provided by BDH company (UK) as nitrates or chlorides. Stock solutions of the metal salts were prepared in bidistilled water and standardized when-ever necessary. The ion-pair, amineptine-phosphotungstate (AMP-PT) was prepared as previously described⁷. The chemical composition of the ion-pair as identified by elemental analysis was found to be 3:1. Stock amineptine hydrochloride solution (1×10^{-2} M) was prepared daily by dissolving an appropriate amount of the drug in double distilled water. More dilute solutions were prepared by appropriate dilution. All amineptine hydrochloride solutions were kept in dark brown bottles.

Apparatus

Potentiometric measurements were carried out with an Orion (Cambridge, MA, USA) Model 701 A digital pH/mV-meter. The internal reference electrode was a coated wire Ag/AgCl electrode. The electrochemical system for the membrane electrode is represented as follows:

Graphite rod/membrane/test solution/KCl salt bridge/Ag/AgCl

Preparation of the coated graphite electrode

Commercial graphite rod (1mm diameter) was inserted into a plastic tube. The protruding part of the graphite out of the tube was around 0.5 cm; the contact of graphite with the plastic tube was closed with a drop of sylgard insulating material. The electrode was polished with a fine emery paper and sonicated in bidistilled water. The graphite was dipped for few seconds in a solution of THF containing PVC, ion pair and DBP several times (5 times). After each dip, the electrode was left to dry at room temperature for 10 min.

Construction of calibration curves

Suitable increments of standard drug solution were added to 50.0 ml doubly distilled water so as to cover the concentration range from 1.0×10^{-6} - 1.0×10^{-2} M. In this solution the sensor and reference electrode were immersed and the *emf* values were recorded after each addition. The values were plotted against the negative logarithm of drug concentration. The electrode was washed with double distilled water and dried between measurements.

Selectivity coefficient determination

The selectivity coefficient values $K_{AMP, B^{2+}}^{pot.}$ for the proposed electrode were evaluated by the modified form of the Matched Potential Method (MPM)⁸.

Analytical applications

Potentiometric determination of amineptine hydrochloride

The standard addition method⁹ was applied, in which small increments of a standard VEN solution 1×10^{-2} M

were added to 50 ml aliquot samples of various drug concentrations.

The change in potential reading at a constant temperature of 25°C was recorded for each increment and used to calculate the concentration of the drug sample solution using the following equation:

$$C_x = C_s \left(\frac{V_s}{V_s + V_x} \right) \left(10^{n(\Delta E/S)} - \frac{V_x}{V_s} \right)^{-1}$$

eq. (1)

where C_x and V_x are the concentration and volume of the unknown, respectively, C_s and V_s are the concentration and volume of the standard, respectively, S is the slope of the calibration graph, and ΔE is the change in potential due to the addition of the standards.

Determination of amineptine hydrochloride in biological fluids

Different amounts of amineptine hydrochloride, and 5 mL of urine of a healthy person were transferred to 50 mL measuring flask and completed to the mark using bidistilled water. The contents of the measuring flask were transferred to a 100 mL beaker, and subjected to potentiometric determination of amineptine hydrochloride by standard addition method.

RESULTS and DISCUSSION

Composition of the membrane

Since the sensitivity and selectivity degree of an ion-pair based electrode is greatly related to the membrane ingredients, the membrane composition influence on the potential responses of the CWE was studied. Six membrane compositions (Table 1) were investigated, the best performance characteristics was obtained by using composition containing 12% AMP -PT, 44.0% of each PVC and DBP with resulting slopes of 58.7 mV/decade. The highest value of the correlation coefficient (r^2) within the usable concentration range was 1.0×10^{-5} - 1.0×10^{-2} M and response time < 10s. Other membranes exhibit slopes less than 44.9 or about 64.0-67.0 mV/decade, but linearity ranges of the calibration curves are shorter and correlation coefficients are worse (0.88–0.92). A typical calibration plot for electrode is shown in Fig. 2.

Table 1: Optimization of membrane compositions of the coating membranes and slopes of the corresponding calibration graphs at 25 °C

Composition % (w/w) Ion Pair DBP PVC			Slope (mV/decade)	Correlation Coefficient
2.0	49.0	49.0	50.0	0.88
4.0	48.0	48.0	44.9	0.91
7.0	46.5	46.5	67.0	0.92
10.0	45.0	45.0	64.0	0.88
12.0 ^a	44.0	44.0	58.7	0.99

^a Optimum composition



Table 2: Selectivity coefficients $K_{AMP, B^{Z+}}^{pot.}$ for the proposed electrode at 25.0 °C

Interfering (B)	$K_{AMP, B^{Z+}}^{pot.}$	Interfering (B)	$K_{AMP, B^{Z+}}^{pot.}$
K ⁺	2.9×10 ⁻⁴	Lactose	9.8×10 ⁻²
Na ⁺	8.5×10 ⁻⁴	Fructose	3.8×10 ⁻²
Zn ²⁺	1.6×10 ⁻³	Glucose	2.5×10 ⁻²
Co ²⁺	2.5×10 ⁻³	Maltose	5.8×10 ⁻²
Al ³⁺	6.50×10 ⁻²	Glycine	3.3×10 ⁻⁴

Table 3: Determination of amineptine hydrochloride in pure solutions and in urine applying the standard addition method.

Sample	R Pure solution		
	Amount taken (mg)	Recovery %	RSD*
	10.50	100.90	0.8
	21.03	99.67	1.20
	42.05	98.19	1.34
Mean		99.56	1.11
Mean ± SD		99.56 ± 1.11	
Sample	Human urine		
	Amount taken (mg)	Recovery %	RSD*
	10.50	99.03	1.22
	21.03	99.56	1.43
	42.05	98.09	1.67
Mean		98.89	1.44
Mean ± SD		99.56 ± 1.44	

*RSD (three determination)

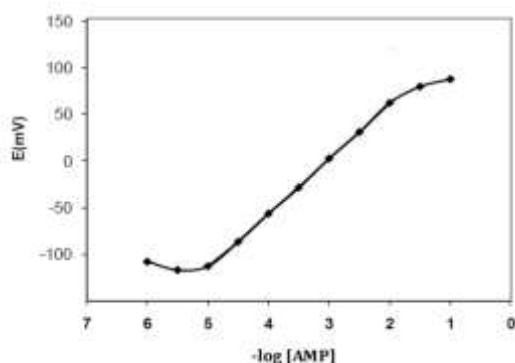


Figure 2: Calibration curve of coated wire graphite of AMP-PT electrode

Effect of soaking

The effect of soaking time on the performance of the electrode was investigated as a function of soaking time. For this purpose the electrode was soaked in a 1.0×10⁻³ M drug solution and the calibration graphs (pAMP vs. E_{elec}, mV) were plotted after 0.5 and 1.0, 1.5, 2, 2.5, 5, 10, 24, and 48 h. The optimum soaking time was found to be 1.0–5.0 h, at which the slopes of the calibration curves were 57.0–59.0 mV per p AMP decade, at 25°C. The electrode was soaked continuously in 10⁻³ M drug

solution for longer than 48 h. The slope of the electrode started to decrease, gradually reaching 47.5mV/decade. The decrease in the efficiency of the electrode can be attributed to the formation of a thin aqueous layer between the membrane and the graphite rod¹⁰⁻¹⁴.

The reproducibility of ten repeated measurements on the same solution was ± 1 mV. The electrodes should be stored in a refrigerator when not in use.

Effect of Temperature of the test solution

To study the thermal stability of the electrode, calibration graphs (cell potential, E_{cell} vs pAMP) were constructed at different test solution temperatures covering the range 25-55°C. The standard electrode potentials (E°) were determined, as the intercepts of the calibration graphs at pVEN = 0, and used to obtain the isothermal temperature coefficient (dE°/dT) of the electrode by Antropov's equation¹⁵.

$$E^{\circ} = E^{\circ}_{25.0} + (dE^{\circ}/dT) (t - 25.0) \tag{eq. (2)}$$

A plot of E° vs (t – 25.0) gave a straight line, the slope of which was taken as the isothermal temperature coefficient. It amounts to 0.00083 V per °C, revealing a fairly good thermal stability of the electrode within the

investigated temperature range and show no deviation from the theoretical Nernstian behavior.

Dynamic response time

Dynamic response time is the required time for the electrode to achieve values within ± 1 mV of the final equilibrium potential after successive immersions in the sample solutions. Its calculation involved the variation and the recording of the amineptine HCl concentration in a series of standard solutions. This electrode exhibits a fast dynamic response in the whole concentration range. The average time in the whole concentration range for wire coated electrode was about 10s.

Effect of pH

The effect of the pH of the test solution 1.0×10^{-3} M AMP on the electrode potential was investigated by following the variation in potential with changes in pH occurring at an addition of very small volumes of hydrochloric acid and sodium hydroxide (0.1 ± 1.0 M of each) (Fig. 3). As is obvious, within the pH range 2.0–4.0 the electrode potential is practically independent of pH, and in this range, the electrode can be safely used for AMP determination.

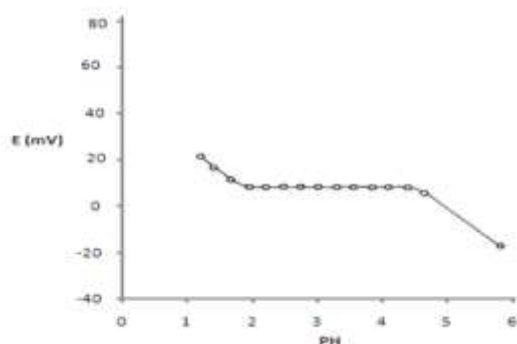


Figure 3: Effect of the pH of the test solution 1.0×10^{-3} M AMP on the response of coated graphite electrode.

Selectivity of the electrode

The selectivity of the electrode depends on the selectivity of the ion-exchange process at the membrane–test solution interface and the mobilities of the respective ions within the membrane¹⁶. The influence of some excipients, inorganic cations, amino acids and sugars on the response of APM electrode was investigated applying the modified form of the Matched Potential Method (MPM)⁸. The selectivity coefficients were then given by the resulting primary to interfering ion activity ratio. The resulting values are listed in Table 2. As is evident, the results of the selectivity coefficients are smaller than (1.0) which means that the proposed electrode is highly selective toward AMP. The inorganic cations did not interfere owing to the differences in ionic size and consequently in their mobilities and permeabilities as compared with AMP ion. In the case of glucose and histidine, the high selectivity may be attributed to the

difference in polarity and to the lipophilic nature of their molecules relative to AMP cation.

Analytical Applications

The present coated wire graphite electrode has been successfully used for the determination of amineptine hydrochloride in aqueous solution and in urine by using the standard addition method described above. The recovery and standard deviation values given in (Table 3) were calculated from three determinations. These results revealed that the amineptine hydrochloride can be accurately determined using the proposed electrode.

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