خصائص الاستجابة الكهروكيميائية والتطبيق التحليلى لمجسات انتقائية ذات أغشية بوليميرية للنورتريبتيلين

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تتضمن الدراسة ابتكار وأداء مجسات انتقائية ذات أغشية بوليميرية لعقار النورتريبتيلين باستخدام حمض الفسفومولبيديك كمبادل أيونى وإذابته فى أنواع مختلفة من المذيبات ، مثل ثنائى أوكتيل فثالات، ثنائى بيوتيل سبيسات، ثلاثى كرزيل الفوسفات ونيتروفينيل أوكتيل إثير. وقد تميزت المجسات المذابة فى كل من ثنائى أوكتيل فثالات (I) ، وثنائى بيوتيل سبيسات (III) فى الأداء الأحسن من حيث الحساسية، المدى الخطى و كذلك الحد الأدنى للتقدير، حيث أعطى المجس (I) حساسية عالية تصل إلى $4x10^{-6}$ مولارى ، أما المجس (III)فقد وصل الحد الأدنى للتقدير إلى 6.0×10^{-6} مولارى ، وكل منهما أعطى ميلا يكاد يصل إلى القيمة النظرية لنرنيستيان. لكن الميل كان دون القيمة النظرية لنرنيستيان فى حالة المجس (IV) حيث تم إذابة المادة الفعالة فى ثلاثى كرزيل الفوسفات . وعلى العكس، فإن الميل كان أعلى من القيمة النظرية لنرنيستيان عند استخدام نيتروفينيل أوكتيل إثير كمذيب فى المجس (V).

كما اشتملت الدراسة - أيضا - على تأثير بعض المضافات المحبة للدهون على سلوك المجس (I). وقد أظهرت النتائج انتقائية ملحوظة للنورتريبتيلين فى وجود بعض المركبات العضوية وغير العضوية التى تمت دراستها للمجسات (I)، (III) و (IV) مقارنة بالمجس (V). وقد تميزت هذه الطريقة بإمكانية تقدير مركب النورتريبتيلين فى المستحضر الدوائى (موتيفال) مباشرة على الرغم من وجود مركب الفلوفينازين فى نفس المستحضر الدوائى حيث سجلت المجسات انتقائية عالية للنورتريبتيلين. وكانت نسبة الاسترجاع بين 101.4 و 97.48 % بانحراف معيارى نسبى يتراوح بين 0.43 و 0.99 % لكل من المجس (I) والمجس (III) على التوالى.

وتفيد هذه الدراسة فى تقدير تركيز المستحضرات الدوائية بدرجة تركيز تصل إلى جزء من المليون بطريقة مباشرة بدون أية معالجات سابقة .

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(III) using the calibration plot method gave mean recoveries of 101.43± 0.44 % (RSD = 0.43) and 97.48± 0.57% (RSD = 0.59) , respectively. At the same time, mean recoveries of 98.93± 0.98% (RSD = 0.99) and 99.36± 0.58 % (RSD = 0.59) are obtained by sensors (I) and (III), respectively using the standard addition method.

Conclusion

The data presented in this work revealed that the chemical nature of PVC membrane plasticizers and lipophilic additives play a crucial role in the response slope, linear domain and selectivity coefficients of the sensor. From the potentiometric response point of view, it seems that DOP and DBS as low polarity solvent mediators among the investigated plasticizers provide more suitable response. Incorporation of the highly lipophilic NT-PM ion-pair associate as a sensing material provide a high sensitivity, reasonable selectivity and wide linear response range. The developed sensors display fast response and are sufficiently stable to give satisfactory results within two months with no noticeable degradation. The accuracy, precision and selectivity of the sensors for nortriptyline over fluphenazine offer a fast, simple, accurate and cost-effective methodology for the determination of nortriptyline in dosage forms.

Table (2)
Potentiometric Selectivity Coefficients
$log k^{pot}_{NT,j}$ of NT Membrane Sensors

Interferents	DOP (I)	DOP KTpClPB (II)	DBS (III)	TCP (IV)	NPOE (V)
Amitriptyline	- 0.277	- 0.084	- 0.652	- 0.314	- 0.113
Imipramine	- 0.171	- 0.138	- 0.563	- 0.468	- 0.168
Trimipramine	- 0.364	- 0.405	- 0.794	- 0.574	- 0.372
Fluphenzine	- 2.381	- 2.322	- 2.761	- 2.381	- 2.209
Ephedrine	-2.046	-1.850	-2.189	- 2.077	- 1.551
Nor-ephedrine	-2.154	-1.904	- 2.396	- 2.157	- 1.589
Glycine	- 2.135	- 1.615	- 2.129	- 2.270	- 1.654
Alanine	- 2.238	- 1.811	- 2. 018	- 2.397	- 1.744
K^+	- 2.016	- 1.886	- 2.371	- 2.035	- 1.670
NH_4^+	- 2.440	- 2.143	- 2.290	- 2.460	- 1.726
Ca^{2+}	- 2.889	- 2.640	- 2.993	- 3.193	- 2.569
Ba^{2+}	-3.130	- 2.535	- 2.943	- 3.219	- 2.362

3.4. Analytical Application

The acceptable performance characteristics and higher selectivity of nortriptyline sensor with DOP (I) and DBS (III) plasticized membranes for nortriptyline drug over fluphenazine suggests the use of the proposed sensor for determining nortriptyline in its pharmaceutical preparations without any pretreatment. Direct potentiometric determination of nortriptyline by DOP (I) and DBS

$$log k_{NT,j}^{pot} = \frac{E_j - E_{NT}}{S} + \left(1 - \frac{1}{z_j}\right) \log 1x10^{-3} M\, NT \qquad (2)$$

Where E_j and E_{NT} are the electrode potentials for interfering ions and NT, respectively, z_j is the charge of interfering ions and S is the slope of calibration plot.

The influence of the plasticizer on the selectivity of the sensors was also evaluated from the data depicted in Table 2. In general, for sensors plasticized with less polar plasticizers DOP (I), DBS (III) and TCP (IV) better selectivity with respect to the investigated interferents is obtained as compared with one of high polar plasticizer (NPOE). This is in agreement with a previous work [25]. No significant interference from the inorganic cations, amino acids, ephedrine and norephedrine due to their lower lipophilicities, small ionic sizes, and consequently their low mobilities and permeabilities, particularly for the inorganic cations, compared with that of NT.

It is reasonable to expect that amitriptyline, imipramine and trimipramine showed relatively high selectivity coefficient values owing to the similarity of their structures with nortriptyline; tricyclic structures. This is consistent with the origin of interfering phenomena, where larger lipophilic species induced serious interference on ion-pairing agents based sensors [26]. However in this case, the interference is not serious because these substances are seldom formulated in combination with nortriptyline.

Fundamentally, the selectivity of an ion-exchange liquid membrane electrode is mainly governed by the partition coefficient of ions between the electrode membrane and an aqueous solution as indicative of the hydrophobicity of the ions [27]. This explains the higher selectivity afforded by all sensors to nortriptyline over fluphenazine which formulated in combination with nortriptyline in the dosage forms as a result of higher lipophilicity of nortriptyline comparing to fluphenazine.

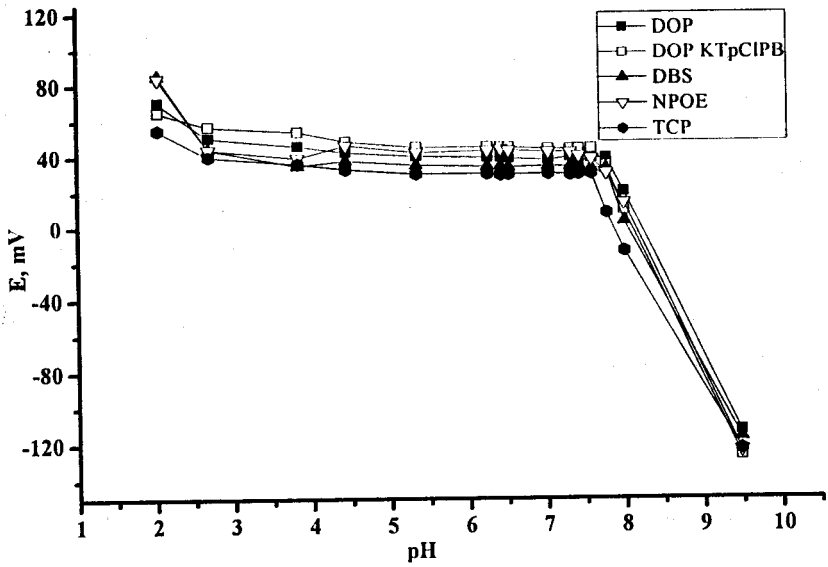

Fig. 4. Effect of pH on the Response of NT Sensors for 1.0 x 10^{-3} M Nortriptyline Hydrochloride Solution

3.3. Selectivity

The potentiometric selectivity coefficients k_{ij}^{pot} is obviously one of the most essential parameter of an electrochemical sensor as it measures the relative affinity of target ion (i) and interfering ion (j) toward the ion selective electrode. The extent of interference provided by different inorganic and organic ions toward NT-PM based membrane sensors is performed using the separate solutions method [24]. This method was preferred and successfully applied as it usually corresponds more closely to the situation of the sample. The concentrations of nortriptyline hydrochloride and the interferents are kept at a level of 1 x 10^{-3} M solutions of the same pH 7.0 and the potentiometric selectivity coefficients are evaluated according to equation 2.

3.2. Effect of pH

The pH dependence of the proposed membrane sensors was tested over a pH range of 2.0-10.0 in 1.0×10^{-3} M NT hydrochloride solutions using 0.1 M HCl or 0.1 M NaOH. A plot of E *versus* pH (Fig. 3) indicates that all proposed sensors properly operated in the same pH range (5.5-7.8). The potential remains constant over this pH range. Beyond this pH range, a sharp change in the potential was detected. The observed potential drift at higher pH values may be due to the formation of nortriptyline free base in the solution and also to the contribution of OH^-. At lower pH values, the potentials slightly and gradualy increase due to the membrane sensors response for H^+ ions.

Evaluation of the main operating features for all sensors under constant pH is carried out in several buffer solutions prepared within the corresponding operational pH ranges. It was found that of the buffers investigated, 0.05 M Tris-HCl buffer at pH 7.0 ± 0.05 proved to be the optimal.

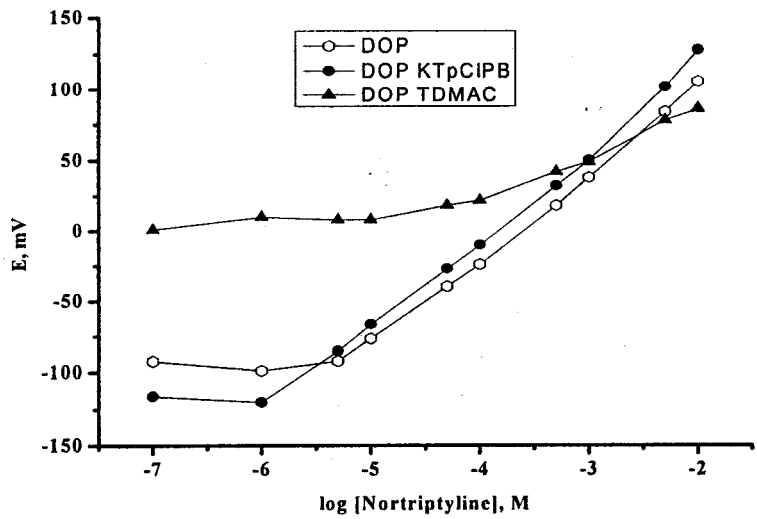

Fig. 3. Effect of the Membrane Ionic Additives on the Response of NT Sensors at pH 7.0

Examination of the lifetime of the sensors by repeated monitoring of the slope of the calibration plot of nortriptyline periodically shows that potential stability and fluctuation of the calibration slope does not exceeding ± 0.5 and ± 0.7 mV/decade over a period of 8 weeks for sensors plasticized with DOP (I), (II) and DBS (III), respectively.

On the other hand, sensors plasticized with TCP (IV) and NPOE (V) the fluctuations are ± 0.8 and ±1.4 mV/decade within 6 and 4 weeks life span, respectively. After that the calibration slope and the linear range of response gradually decrease probably due to the leaching out of one or more components of membrane matrix into the aqueous sample. Most membrane sensors exhibit day-to-day reproducibility of better than ± 0.7 mV for the same standard solution.

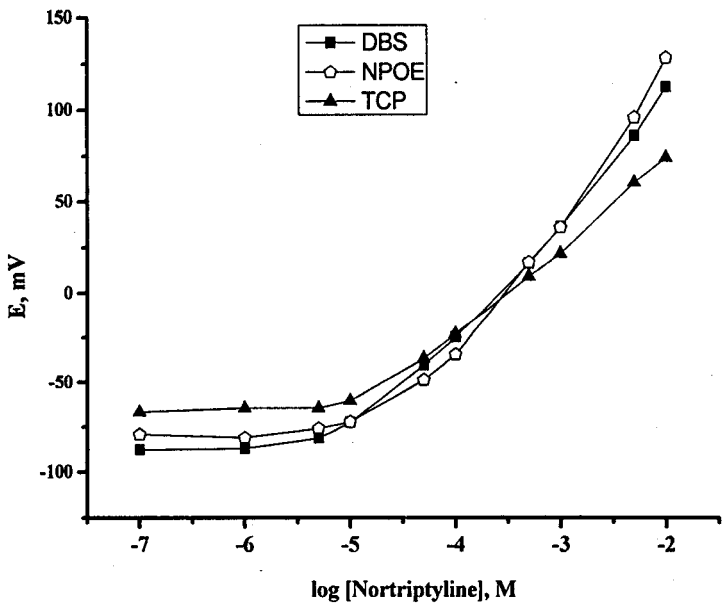

Fig. 2. Effect of the Nature of Plasticizer on the Response of NT Sensors at pH 7.0

Table (1)

Characteristic Performance of NT Sensors

Parameter	Sensor				
	DOP (I)	DOP KTpClPB (II)	DBS (III)	TCP (IV)	NPOE (V)
Slope/ mV decade^{-1}*	59.9 ± 0.5	61.4 ± 0.5	58.9 ± 0.7	48.8 ± 0.8	67.6 ± 1.4
Intercept/mV*	220.1 ± 0.2	240.5 ± 0.2	217.6 ± 1.45	161.9 ± 0.9	282.7 ± 1.1
Correlation coeficient, *r*	0.998	0.997	0.998	0.993	0.997
Lower limit of linear range/M	7 x 10^{-6}	1 x 10^{-6}	9 x 10^{-6}	1 x 10^{-5}	9 x 10^{-5}
Limit of detection/M	4 x 10^{-6}	9 x 10^{-7}	6 x 10^{-6}	8 x 10^{-6}	4 x 10^{-5}
Working pH range	5.5-7.8	5.5-7.8	5.5-7.8	5.5-7.8	5.5-7.8
Response time/s $\geq 10^{-4}$ M	10	10	10	10	10
Life span/week	8	8	8	6	4

*Average of ten measurements ± standard deviations of values

The response time of a sensor is fundamentally an important factor. The time required to reach a steady state potentials within ±1 mV of the final equilibrium after immersion of the sensors in NT solutions each having a 10-fold increase from 10^{-7} to10^{-2} M at pH 7.0 has been measured. The proposed sensors exhibit an average dynamic response time of 10 s for concentrations $\geq 10^{-4}$ M and 60s for concentrations $\leq 10^{-5}$ M.

borate and potassium tetrakis (p-chlorophenyl) borate as cation exchangers and DOP as plasticizer [20].

The results obtained by DOP plasticized membrane sensor (II) incorporating resistance-lowering anionic additive KTpClPB reflect the influence of the additive as compared with DOP plasticized sensor without additive. The sensor exhibits a near-Nernstian slope of 61.4 mV/decade over a wider linear range (1.0×10^{-6} to 1.0×10^{-2} M) and lower detection limit of 9.0×10^{-7} M NT. Indeed, the additive lowers the electrical membrane resistance as well as the activation barrier for the cation-exchange reaction at the membrane/solution interface resulting in the improvement of both the linear range and detection limit [21].

Meanwhile, the non-Nernstian response (slope 33.4 mV/decade) of a sensor with DOP plasticized membrane containing TDMAC cationic additive (Fig. 3) is probably due to the decrease of the concentration of free ion exchanger active site to some extent as a result of the formation of lipophilic ion-pairs $PM^-.TDMA^+$ in the membrane [22]. Generally, the linearity and sensitivity of ion exchanger based electrodes depend on the concentration of ion exchanger in the membrane phase [23].

the value of the electrode/solution distribution ratio of the particular C+A− ion-pair employed as an ion-exchanger [17].

In order to shed light on the influence of plasticizer, four plasticizers with different dielectric constants have been used; *o*-NPOE (ε = 23), DOP (ε = 5.1), DBS (ε = 4.5) and TCP (ε = 6.9). In addition to the role of plasticizers, the performance of DOP plasticized membrane sensors incorporating anionic or cationic lipophilic additives were examined and compared. The main analytical features and response characteristics of the proposed sensors at pH 7.0±0.05 at room temperature using the IUPAC recommendations [18] over a period of 10 weeks are summarized in Table 1. Typical calibration plots of NT-PM sensors are shown in Fig. 2 and Fig. 3. It is apparent from Table 1, Fig. 2 and Fig. 3 that, Nernstian response close to the expected theoretical value (59.9 and 58.9 mV/decade) over the concentration range from 7.0×10^{-6} to 1.0×10^{-2} M and 9.0×10^{-6} to 1.0×10^{-2} M are obtained for sensors plasticized with DOP (I) and DBS (III), respectively. The detection limit, as determined from the point of intersection of the two extrapolated segments of the calibration plot, are 4.0×10^{-6} M and 6.0×10^{-6} M for sensors (I) and (III), correspondingly. This is in good agreement with previous report showing that the response characteristics and selectivity of monovalent cations are favoured by low dielectric constant plasticizers [19]. However, a great decrease in sensitivity (slope 48.8 mV/decade) over relatively shorter concentration range (1.0×10^{-5} - 1.0×10^{-2} M) is displayed with TCP plasticized membrane sensor (IV) probably due to the low solubility or low distribution of the NT-PM ion pair complex in this solvent. The lower detection limit is 8×10^{-6} M. In contrast, membrane sensor plasticized with *o*-NPOE (V) presents a super-Nernstian behavior (slope 67.6 mV/decade) due to the excessive depletion of the primary ion in the sample/membrane boundary layer and at the same time, it is displayed a narrower linear range from 9.0×10^{-5} to 1.0×10^{-3} M.

It is noteworthy mentioned that both DOP and DBS plasticized membrane sensors afforded sensitivities, linear ranges, and detection limits much better than those obtained by electrodes using tetraphenyl

measurements, the unknown concentration is measured from the regression equation of the calibration plots.

2.5. Determination of nortriptyline in dosage form

Eight tablets (motival, 10 mg nortriptyline hydrochloride and 0.5 mg fluphenazine hydrochloride/tablet) were accurately weighted, powdered and the required weight equivalent to five tablets were dissolved in the minimum volume of 0.05 M Tris-HCl buffer solution. The solution was filtered into a 50-ml calibrated flask, and diluted to the mark with the buffer. A 1.0 ml aliquot of the drug test solution was added to 9.0 ml 0.05 M Tris-HCl buffer solution and potentiometrically measured as described above and the potential readings was compared with the calibration plot. Alternatively, the standard addition method [16] was used by measuring the potential displayed by the drug test solution before and after the addition of a 0.1 ml aliquot of 2.0×10^{-2} M standard nortriptyline solution. The change in the electrode potential (ΔE) was recorded and used to calculate the concentration of the drug using equation (1)

$$C_0 = C_s\left(\frac{V_s}{V_s+V_0}\right)\left[10^{\Delta E/S} - \left(\frac{V_0+V_s}{V_0}\right)\right]^{-1} \qquad (1)$$

Where, C_0 and V_0 are the concentration and the volume of the unknown, respectively, and C_s and V_s are the concentration and the volume of the standard solution, respectively and S is the slope of calibration plot.

3. Results and Discussion

3.1. Performance Characteristics

It has been reported that the performance characteristics of ion exchanger based polymeric membrane sensors depend not only on the nature of the used ion exchanger but also significantly depend on the properties of the plasticizer used. This is due to the influence of the plasticizer on the dielectric constant of the membrane phase, permittivity of the membrane and mobility of the ion-exchanger sites. In addition, the proper selection of the plasticizer allows one to control

precipitate was filtered, washed thoroughly with distilled water and dried at room temperature then grinded to fine powder. The predicted composition of the ion associate complex ($C_{57}H_{66}N_3PMo_{12}O_{40}$) has a molar ratio of 3(nortriptyline):1(phosphomolybdic) and was ascertained by elemental analysis calculated: C, 26.15; H, 2.52; N, 1.6%. found: C, 25.6; H, 2.75; N, 1.7%). The calculated and experimental elemental analysis data for the prepared ion-associate complex are in a good agreement with the proposed structure. This ion association complex was used as an electroactive material in the developed sensors. Plasticized membranes with the composition of 2-1 wt % NT-PM ion-pair, PVC/plasticizer (1:2) and 0-1 wt % of lipophilic additives were prepared by mixing these ingredients with THF (3 ml) and pouring the mixture into a 28- mm diameter glass ring placed on a glass plate. The solvent was left to evaporate freely, forming master membranes with ~ 0.1 mm thickness. Disks (~ 4 mm o.d.) were punched from the master membrane and glued with a PVC/THF slurry to a plasticized PVC tubing fixed onto a 1000-ml pipette tip. The tube was then filled with equal volumes of 1.0×10^{-2} M NT hydrochloride and 1.0×10^{-2} M KCl (internal solution) and an Ag/AgCl wire (~1 mm diameter) was immersed in this solution as an internal reference electrode. Before calibration, all fresh sensors were conditioning by soaking in 1.0×10^{-2} M nortriptyline hydrochloride solution for 1 h and kept dry in air when not in use.

2.4. Sensor Calibration

The sensors were calibrated by spiking with successive aliquots of NT hydrochloride standard solutions ($1.0 \times 10^{-6} - 1.0 \times 10^{-2}$ M) into a 9.0 ml 0.05 M Tris-HCl buffer solution at pH of 7.0 ± 0.05 Alternatively, the calibration was carried out by immersing the NT based membrane sensors in conjunction with a double-junction Ag/AgCl reference electrode into a 50-ml beaker containing 20 ml aliquots of $1.0 \times 10^{-7} - 1.0 \times 10^{-2}$ M NT solutions starting from low to high concentrations at constant pH. The emf values of the stirred solutions were recorded after stabilization to ±1.0 mV and plotted as a function of the logarithm of the NT concentrations. With the mean potential of five

tricresyl phosphate (TCP) were purchased from British Drug Houses, Poole, England. High molecular weight poly(vinyl chloride) (PVC), and tridodecylmethylammonium chloride (TDMAC) were obtained from Aldrich Chemical Co.(Milwaukee, WI.) Potassium tetrakis (p-chlorophenyl) borate (KTpClPB), and 2-nitrophenyl octyl ether (*o*-NPOE) were supplied from Fluka (Buchs, Switezerland). Fluphenazine was obtained as a kind gift from Bristol-Myers Squibb Egypt. Dosage forms containing nortriptyline hydrochloride were purchased from local drug stores. A stock solution of nortriptyline hydrochloride (0.01 M) was prepared by dissolving the calculated weight of pure drug in 100 ml 0.05 M Tris-HCl buffer solutions at pH 7.0 ± 0.05 or in doubly distilled water and dilute solutions (1.0×10^{-7} - 5.0×10^{-3} M) were prepared by successive dilutions of the stock solution. Solutions of interferences (0.01 M) were prepared by dissolving the appropriate weight of each compound in doubly distilled water. All of the working solutions were buffered at pH 7.0 ± 0.05 using 0.05 M Tris-HCl buffer solution. A solution of PMA (1.0×10^{-2} M) was prepared by dissolving an accurate weight of the reagent in a minimum volume of doubly distilled water, followed by filtration and dilution to 100 ml.

2.2. Apparatus

Potentiometric measurements were performed at 25 ± 1°C using an ORION model 420 A digital pH/mV meter and nortriptyline membrane sensors in conjunction with an Orion double-junction Ag/AgCl reference electrode (90-02) containing 10% (w/v) potassium nitrate in the outer compartment. An Orion Ross pH electrode (Model 81-02) was used for pH adjustment. The cell assembly was: Ag/AgCl/10^{-2} M KCl – 10^{-2} M NT hydrochloride at pH 7.0//sensor membrane//sample test solution/Orion double junction reference electrode with 10% KNO_3 in the outer compartment.

2.3. Membrane and Sensor Preparation

The ion-pair associate was prepared by adding 10 ml aqueous solution of 10^{-2} M phosphomolybdic acid to 30 ml of 10^{-2} M nortriptyline hydrochloride aqueous solution. The resulting ion-pair associated

associate complexes with tetraphenyl borate and potassium tetrakis (p-chlorophenyl) borate has been reported [14]. At the same time, the comparison of behavior of the membrane sensors incorporating another electroactive materials and the selectivity of sensors with respect to analogous compounds represent a significant interest.

The current work describes nortriptyline membrane sensors based on the use of phosphomolybdic acid ion exchanger. This acid belongs to the Keggin-type heteropoly acids which are very attractive choice as cation exchangers for use in the fabrication of the many polymeric membrane ion selective electrodes [15]. The present investigation presents a systematic study on the electrochemical properties; sensitivity, linear range, detection limit and selectivity of nortriptyline phosphomolybdic PVC based sensors. Effects of membrane plasticizers and the influence of lipophilic additive are discussed.

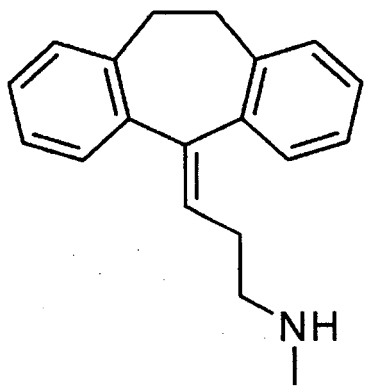

Fig. (1) Nortriptyline Chemical Structure (NT)

2. Experimental

2.1. Reagents and Materials

All chemicals used were of analytical reagent grade, unless otherwise specified and doubly distilled water was used throughout. Nortriptyline (NT) hydrochloride, phosphomolybdic acid (PMA) and dibutylsebacate (DBS) were obtained from Sigma Chemical Co., St. Louis, MO. Tetrahydrofuran (THF), dioctylphthalate (DOP) and

3-(10,11-dihydro-5H-dibenzo[a,d]cyclohept-5ylidene) propyl-methyl amine hydrochloride, belongs to tricyclic antidepressants (TCAs) one of the oldest drugs, developed in the 1950s, used frequently for the treatment of depression[2]. Also, current evidence-based guidelines recommend the use of TCAs as one of the first-line options for the treatment of neuropathic pain. The studies indicated that secondary-amine TCAs (nortriptyline, desipramine) is preferred because they are better tolerated than TCAs containing tertiary-amine (e.g., amitriptyline, imipramine) and have comparable analgesic efficacy [3]. Recent reports revealed that nortriptyline is an effective and well-tolerated drug for the treatment of addiction to smoking with success rates especially for smokers having a high dependence on nicotine, and without any significant side effects [4]. Along with its desired pharmacological effects, nortriptyline and other TCAs are dangerous in overdoses and they are notorious for many drug-related death due to their relatively narrow therapeutic window [5].

The pharmacological properties and potent toxicity of nortriptyline and other TCAs have resulted in generation of extensive literature concerning determination of this class of drugs including; high performance liquid chromatography [6], liquid chromatography-tandem mass spectrometry [7], gas chromatography [8], gas chromatography-mass spectrometry [9], electrophoresis [10], and spectrophotometry [11]. While these methods are often unsurpassed for accuracy, detection limit, linearity and selectivity, they are also often too expensive and tedious to be conducted with great regularity.

Besides, the advantages of the aforementioned methods, ion selective electrodes (ISEs) provide also simple design and operation, fast response, low cost, portability, applicability to colored and turbid solutions and possible interfacing with automated and computerized systems [12]. The development and applications of ion-selective electrodes (ISEs) continue to be of interest for pharmaceutical analysis [13]. Most of these applications rely mainly on the ability of pharmaceutical compounds to form ion-associates with lipophilic counter ions as electroactive materials immobilized in a PVC matrix.

In the best of our knowledge, only one work regarding the determination of nortriptyline using ISE based on nortrityline ion-

ELECTROCHEMICAL RESPONSE CHARACTERISTICS AND ANALYTICAL APPLICATION OF NORTRIPTYLINE-SELECTIVE POLYMERIC MEMBRANE SENSORS

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The performance of polymeric membrane nortriptyline selective sensors based on phosphomolybdic acid (PMA) as an ion exchanger has been studied. The effects of various kinds of plasticizers (e.g., dioctyl phthalate (DOP), dibutyl sebacate (DBS), tricesyl phosphate (TCP) and 2-nitrophenyl octyl ether (NPOE) and lipophilic additives are investigated. Regarding sensitivity, linear range and lower limit of detection, membrane sensors plasticized with DOP (I) and DBS (III) show the best potentiometric responses; slope of 59.9 and 58.9 mV/decade and detection limits of: 4.0×10^{-6} M and 6.0×10^{-6} M for sensors (I) and (III), respectively. Contrastingly, membrane sensor incorporating TCP plasticizer (IV) exhibits a sub-Nernstian slope (48.8 mV/decade) and NPOE plasticized membrane (V) displays a super-Nernstian behavior (slope 67.6 mV/decade) and a higher detection limit 4×10^{-5} M. Sensors (I), (III) and (IV) present remarkable selectivity over many organic compounds and inorganic salts compared with sensor (V). Fortunately, the sensors exhibit high selectivity over fluphenazine which formulated in combination with nortriptyline in the dosage forms. This permits determination of nortriptyline without any pretreatment. The relative standard deviation values range from 0.43 to 0.99 % and the recoveries are from 101.43± 0.44% to 97.48± 0.57 % to for sensors (I) and (III), respectively.

1. Introduction

Depression is one of the most common diseases of the human race, related to decrease quality of life and its burden on society and economy is really impressive. It alone ranks as the third leading contributor to the global burden of diseases [1]. Nortriptyline HCl;

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