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A novel naphazoline-selective membrane sensor and its pharmaceutical applications

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Abstract

New naphazoline (NPZ) ion selective membrane electrodes of both conventional and coated graphite types were prepared based on the ion-pair of naphazoline tetraphenylborate (NPZ–TPB). The conventional type electrode was fully characterized in terms of membrane composition, life span, pH, ionic strength and temperature. The electrode exhibited a Nernstian response for naphazoline in the concentration range 1.0×10^{-5} to 5.0×10^{-2} and 5.0×10^{-6} to 5.0×10^{-2} M with a slope of 58.4 ± 1.1 and 57.0 ± 0.1 mV/concentration decade and a limit of detection of 4.0×10^{-6} and 2.5×10^{-6} M for conventional and coated graphite types, respectively. It could be used in the pH range 3.0–8.0. It was applied to potentiometric determination of naphazoline in pure state and pharmaceutical preparation under batch conditions. The selectivity of the electrode toward a large number of inorganic cations, sugars and amino acids was tested. The solubility product of the ion-pair and the formation constant of the precipitation reaction leading to the ion-pair formation were determined conductometrically.

Keywords: Ion-selective electrode; Naphazoline hydrochloride; Coated wire

1. Introduction

Naphazoline hydrochloride (NPZ-HCL) [2-(naphthalene-1-yl-methyl)-4,5-dihydro-1*H*-imidazole hydrochloride] is a decongestant, which acts on alpha-adrenergic receptors in the arterioles of the conjunctiva to produce vasoconstriction, resulting in decreased conjunctival congestion. Its chemical structure is demonstrated in Fig. 1.

A number of studies have been reported for the determination of NPZ including micellar electrokinetic chromatography [1], phosphorimetry [2,3], spectrophotometric [4]. In 1985, a PVC membrane electrode based on the salt of naphazoline with tetraphenylborate as ion-exchanger for the potentiometric determination of naphazoline was reported to have a usable concentration range of 1.0×10^{-5} to 1.0×10^{-2} M [5].

Compared with the previously naphazoline-selective membrane electrode, the prepared membrane electrodes in this project were more stable and had a longer lifetime, the more extensive usable concentration range and the lower detection limit, in particular, with a coated graphite electrode, which contained no solution to evaporate or leak away into the test solution. Thus it could be used continuously without any significant change of response. Also, in this work, all of the parameters affecting the electrode response (pH, temperature, ionic strength, effect of soaking and plasticizer) were studied.

In recent years, the potentiometric membrane sensors have been widely used in pharmaceutical analysis [6–8]. This is mainly due to simple design, low cost, adequate selectivity, low detection limit, high accuracy, wide concentration range and applicability of the selective electrodes to colored and turbid solutions.

Potentiometric titrations were suitable for the determination of a relatively large amount of the drugs. The apparatus required for making potential measurements and performing titrations are generally inexpensive and basically simple in details. For this reason, the potential measurements find wide acceptance in industry as an analytical tool, both in the

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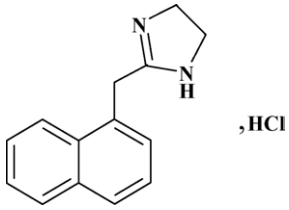

Fig. 1. Structure of naphazoline hydrochloride.

laboratory and in the process and quality control for routine analyses [9,10].

It is noteworthy that most previously reported works using poly(vinyl chloride) membrane selective electrodes for the determination of species of pharmaceutical and/or medical importance have been carried out at only one temperature, mainly 20 or 25 °C. Less attention has been paid to the higher temperature ranges (e.g. 25–65 °C), although many potentiometric measurements concerning biological media and fluids are made at such temperatures [11]. Here, the effect of the temperature of the test solution on the performance characteristics of the proposed conventional electrode is reported.

2. Experimental

2.1. Apparatus

Potentiometric measurements were carried out with an Orion model 162 a digital pH/mV-meter. A Tamson circulator thermostat model T-1000 was used to control the temperature of the test solution.

The electrochemical system was as follows:

Ag/AgCl/filling solution/membrane/test solution//KCl salt bridge//SCE.

The potentials of the ISE were measured against a calomel reference electrode (SCE) as an external reference electrode under open circuit conditions at the experimental temperature.

Conductometric measurements were carried out with a metrohm 644 conductometer.

2.2. Reagents and materials

All chemicals used were of analytical reagent grade unless otherwise stated and doubly distilled water was used throughout. Pharmaceutical grade NPZ powder (purity 100%) and NPZ dosage forms were supplied by Sina Daru Co., Tehran, Iran. Carboxylated 1.8% PVC powders with high molecular weight was obtained from Aldrich Chemical Company. Dibutylphthalate (DBP), bis (2-ethylhexyl) phthalate (BEHP), sodium tetraphenylborate (minimum purity 99.5%) and tetrahydrofuran (THF) of purity >99% were obtained from Merk Chemical Company.

A stock standard solution of 0.05 M naphazoline hydrochloride was prepared by dissolving 0.30843 g of pure drug in 25 ml water. The working solutions were prepared by appropriate dilution of the stock solution with water.

Table 1
Composition of the different NPZ–TPB representative membranes and slopes of the corresponding calibration graphs[a]

Membrane	Composition (mg)				Slope (mV/decade)	R.S.D.[b] (%)
	Ion-pair	DBP	BEHP	PVC		
I	9	150	–	150	58.4	1.1
II	3	400	–	200	57.6	1.6
III	6	400	–	200	61.0	1.2
IV	12	150	–	150	55.2	2.1
V	6	–	400	200	57.0	1.7
VI	3	–	400	200	52.8	1.0
VII	9	–	150	150	57.8	1.3
VIII	12	–	150	150	52.2	0.1

[a] The measurements were carried out in bidistilled water.
[b] Relative standard deviation (four determinations).

2.3. Preparation of the ion exchanger

The ion exchanger, naphazoline tetraphenylborate (NPZ–TPB) was prepared by mixing 20 ml of 1.0×10^{-2} mol l^{-1} naphazoline hydrochloride with 20 ml of 1.0×10^{-2} mol l^{-1} sodium tetraphenylborate. The white precipitate formed, after digestion over night, was filtered, washed by double distilled water until chloride free and dried at room temperature.

2.4. Preparation of conventional and coated graphite types electrodes

The conventional electrode was constructed by varying the percentages (w/w) of the ion exchanger, PVC and plasticizer (DBP and BEHP) until optimum characteristics were reached (Table 1). The membranes were prepared by dissolving the required amount of ion exchanger, plasticizer and PVC in about 6 ml tetrahydrofuran. The solution mixture was poured into a 5.5 cm Petri dish and left to dry in air. A 12 mm diameter disk was cut out from the membrane and glued to the polished end of a plastic cap attached to a polyethylene tube. The electrode body was filled with a solution that was 10^{-1} mol l^{-1} in NaCl and 1.0×10^{-3} mol l^{-1} in NPZ-HCl. An Ag/AgCl wire was immersed in the internal solution of the electrode to act as an internal reference.

The coated graphite electrode was prepared using a graphite bar (2 cm length, 3 mm diameter). One of the two ends of the bar was used for the connection, while the other, about 1 cm length, was dipped in a solution of the same optimum membrane composition used for the conventional type and left to dry in air. The process was repeated several times until a layer of proper thickness was formed covering the terminal of the graphite bar.

2.5. Conductometric determination of the solubility product and the formation constant of NPZ–TPB ion-pair

The solubility product and the formation constant of NPZ–TPB ion-pair were conductometrically determined [12]. For this purpose, a series of solutions of different concentration ($C = 1.0 \times 10^{-4}$ to 1.0×10^{-2} mol l^{-1}) were prepared for both NPZ-HCl and NaTPB. The measured conductivities of these solutions at 25 °C were used to calculate the specific conductivities (K), corrected for the effects of the solvent and dilution then the equivalent conductivities (λ) of the solutions ($\lambda = 1000K/C$) were obtained.

Straight-line plots of λ versus $C^{1/2}$ were constructed and the equivalent conductance at infinite dilution (λ_0) values was determined for both NPZ-HCl ($\lambda_{0,\,\text{NPZ-HCl}}$) and NaTPB ($\lambda_{0,\,\text{NaTPB}}$) from the intercept of respective lines with the λ-axis. The activity coefficients of the ions employed were taken as unity because all the solutions were sufficiently dilute; moreover, all the ions under study were univalent and, consequently, they were less affected by changes in the ionic strength of the solution [13]. $\lambda_{0,\,\text{NPZ–TPB}}$ was calculated from Kohlrausch's law of independent migration of ions using $\lambda_{0,\,\text{NPZ-HCl}}$ and $\lambda_{0,\,\text{NaTPB}}$ values. The solubility (S) and solubility product (K_{sp}) of the ion-pair were obtained applying the following equations:

$$S = K_s \times 1000/(\lambda_{0,\,\text{NPZ-TPB}}), \quad K_s = S^2$$

where K_s is the specific conductivity of a saturated solution of NPZ–TPB determined at 25 °C and corrected for the effect of the solvent. Stirring a suspension of the ion-pair of the saturated solution precipitate in distilled water for 4 h made.

3. Results and discussion

3.1. Construction of the calibration graphs

The sensors were calibrated by transferring 20 ml aliquots of 1.0×10^{-7} to 1.0×10^{-1} mol l^{-1} aqueous solutions of naphazoline hydrochloride to 50 ml beakers, followed by immersing the naphazoline-selective membrane sensors in conjunction with a calomel reference electrode in the solution. The potential readings were recorded after stabilization to ±1 mV and the e.m.f. was plotted as a function of the logarithm of the naphazoline concentration (Fig. 2). The calibration graph was used for subsequent determination of unknown naphazoline concentrations.

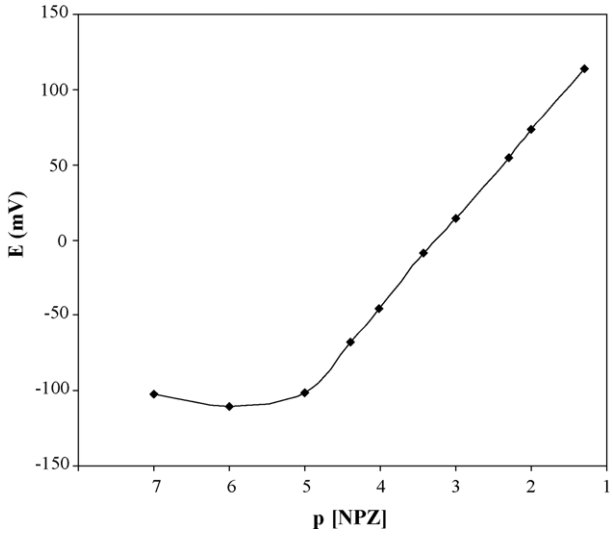

Fig. 2. Calibration curve for the naphazoline-selective electrode.

3.2. Optimization of the ISE response in conventional and coated graphite type

3.2.1. Composition of the membrane

Several different membrane compositions that contained 2.9% (I), 0.5% (II), 1% (III) and 3.8% (IV) of the ion-pair were investigated. The slopes of their calibration plots were found to be 58.4, 57.6, 61.0 and 55.2 with relative standard deviation (R.S.D.) 1.1, 1.6, 1.2 and 2.1 for compositions I, II, III and IV, respectively. The preparation process was fairly reproducible as indicated by the small values of the R.S.D.s. Electrodes made by using the membrane composition (I) showed the nearest performance characteristic to the Nernstian behaviour (slope = 58.4 and 57.0 mV/concentration decade, at 25 °C for the conventional and coated graphite type electrode, respectively). The usable concentration range was found to be 1.0×10^{-5} to 5×10^{-2} and 5×10^{-6} to 5×10^{-2} mol l^{-1} NPZ-HCl in case of conventional and coated graphite type, respectively. The smaller concentration range in case of the conventional type may be attributed to the difference in the physical and mechanical parameters of the membrane of the conventional type and those of the layer on the coated graphite type, in addition to the absence of an internal solution in the coated electrode, which might increase the sensitivity of the membrane. In all the subsequent studies, electrodes made of membrane I were used. The critical response characteristics of the electrodes are summarized in Table 2.

3.2.2. Effect of plasticizer

The major membrane component of the naphazoline-selective membrane electrode was the plasticizer, which

Table 2
Response characteristics of naphazoline PVC membrane sensors at 25 °C

Parameter	Conventional type	Coated graphite type
Slope (mV/decade)[a]	58.4 ± 1.1	57.0 ± 0.1
Intercept (mV)	189.6 ± 1.6	448.4 ± 1.6
Usable range (M)	1.0×10^{-5} to 5×10^{-2}	5.0×10^{-6} to 5×10^{-2}
Correlation coefficient, r	0.9999	0.9998
Detection limit (M)	4×10^{-6}	2.5×10^{-6}
Working pH range	3.0–7.5	3.0–7.5
Response time for 1.0×10^{-3} M (s)	20	10
Life time (days)	30	60

[a] Average of four measurements.

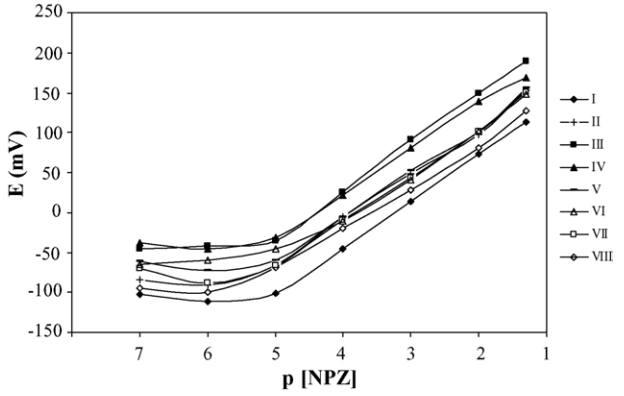

Fig. 3. The calibration curves and effect of plasticizers on potentiometric response for compositions mentioned in Table 1 at 25 °C.

ensured the mobility of free and complexed ionophores, set the dielectric constant and provided a suitable mechanical property of the membrane.

As mentioned in Section 2.4 and Table 1, two plasticizers were tested to evaluate their effects on the response. The better results (the better slopes) were obtained with DBP plasticizer (Fig. 3). To our knowledge, this may be because the DBP has a greater polarity and a less lipophilicity that make it more suitable for the naphazoline-selective membrane electrode.

3.2.3. Effect of soaking

Freshly prepared electrodes can be used without preconditioning where the mean slopes of the calibration graphs constructed in doubly distilled water is 58.4 mV/concentration decade for the conventional electrode with composition I and 57.0 mV/concentration decade for the coated graphite electrode with the same composition. The electrode was then soaked in 1.0×10^{-3} mol l^{-1} NPZ-HCl at room temperature. It was found that the continuous soaking affect negatively on the response of the electrode due to the leaching of the active ingredients (ion-exchanger and plasticizer) to the bathing solution [14].

3.2.4. Effect of temperature of the test solution

Calibration graphs (electrode potential (E_{elec}) versus p[NPZ]) were constructed at different test solution temperatures (25, 30, 40, 50, 60 and 65 °C). For the determination of the isothermal coefficient (dE^0/dt) of the electrode, the standard electrode potentials (E^0) against the normal hydrogen electrode at the different temperatures were obtained from calibration graphs as the intercepts at p[NPZ] = 0 (after subtracting the values of the standard electrode potential of the calomel electrode at these temperatures) and were plotted versus ($t - 25$), where t was the temperature of the test solution in °C (Fig. 4).

A straight-line plot is obtained according to Antropov's equation [15]:

$$E^0 = E^0_{(25)} + (dE^0/dt)(t - 25)$$

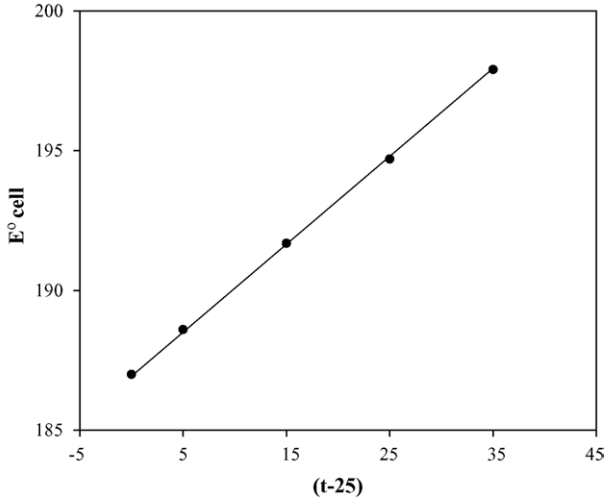

Fig. 4. Variation of the cell e.m.f. with the temperature for the NPZ electrode.

where $E^0_{(25)}$ is the standard electrode potential at 25 °C, the slope of the straight-line obtained represents the isothermal coefficient of the electrode (0.003 V/°C). The value of the obtained isothermal coefficient of the electrode indicates that the electrode has a fairly high thermal stability within the investigated temperature range. The investigated electrode was found to be usable up to 60 °C without noticeable deviation from the Nearnestian behaviour.

3.2.5. The effect of pH

The pH effect of the test solutions on the electrode potentials was studied. The variation in potential with pH change was followed by the addition of small volumes of HCl and NaOH (0.01–0.3 mol l^{-1}) to the test solution (1×10^{-2}, 1×10^{-3}, and 1×10^{-4} mol l^{-1} NPZ-HCl). For each pH value, the potential was recorded and thus the potential-pH curves for three NPZ-HCl concentrations were constructed (Fig. 5). As is obvious, within the pH range 3–8.0, the elec-

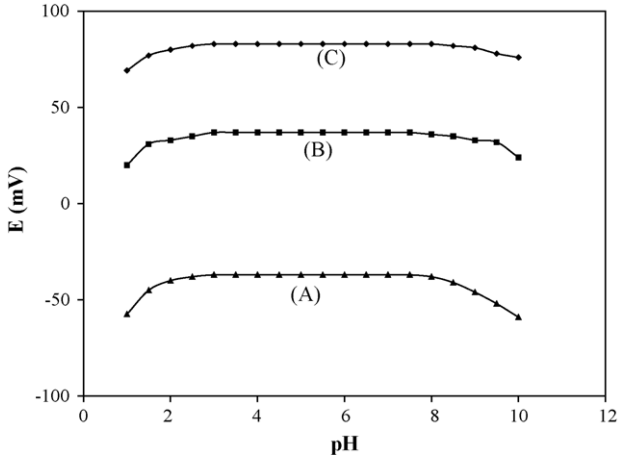

Fig. 5. Effect of pH of the test solution on the potential reading: (A) 1.0×10^{-4} mol l^{-1}; (B) 1.0×10^{-3} mol l^{-1}; (C) 1.0×10^{-2} mol l^{-1} NPZ-HCl solution at 25 °C using NPZ–TPB electrode.

trode potential is practically independent of pH, and in this range, the electrode can be safely used for naphazoline determination. The decrease in mV readings at pH < 3 may be due to interference of hydronium ion and penetration of H_3O^+ into the membrane surface or a gradual increase of protonated species and dependence of the e.m.f. on the pH of the solution. At higher pH values (pH > 8.0), free-base precipitates in the test solution and consequently, the concentration of unprotonated species gradually increased. As a result, lower e.m.f. readings were recorded. The decrease in potential readings at pH > 8.0, on the other hand, can be probably attributed to penetration of OH^- ions into the gel layer of the membrane.

3.2.6. Effect of ionic strength

Calibration graphs were constructed at different concentrations of NaCl (1.0×10^{-4} to 1.0×10^{-1} mol l^{-1}). It was found that the slope of the electrode increased gradually from 58.4 mV/concentration decade in doubly distilled water to reach its maximum value 59.1 mV/concentration decade in 1.0×10^{-4} mol l^{-1} of NaCl and then decreased in higher concentration of NaCl to reach 57.7 mV/concentration decade in 1.0×10^{-3} mol l^{-1} NaCl, 55.3 mV/concentration decade in 1.0×10^{-2} mol l^{-1} NaCl, and 50.5 mV/concentration decade in 1.0×10^{-1} mol l^{-1} NaCl which may be attributed to the interference of high concentration of Na^+ ions.

3.3. Selectivity of the electrode

The selectivity of the ion-pair associates based membrane electrodes depends on the selectivity of the ion-exchange process at the membrane–test solution interface and the mobilities of the respective ions within the membrane.

Selectivity coefficients were determined by the separate solution method [16,14] in which the following equation was applied:

$$\log K^{\text{pot}}_{\text{NPZ},\, j^{z+}} = (E_2 - E_1)/S + \log[\text{NPZ}] - \log\,[j^{z+}]^{1/z}$$

where E_1 is the electrode potential in a 1.0×10^{-3} mol l^{-1} NPZ-HCl solution; E_2 the potential of the electrode in a 1.0×10^{-3} mol l^{-1} solution of the interferent ion (j^{z+}) and S the slope of the calibration plot. The influence of some inorganic cations, sugars and amino acids on the electrode response was investigated.

This method is considered to be the simplest way to evaluate the degree of interference that might be taking place and is used to perform measurements in important biological samples such as blood [17].

The selectivity coefficients obtained by this method (Table 3) showed that the proposed electrode was highly selective toward NPZ^+ ion. The inorganic cations did not interfere due to the differences in their mobilities and permeabilities as compared with NPZ^+. In the cases of sugars and amino acids, the high selectivity is mainly attributed to the difference in polarity and lipophilic character of their molecules relative to NPZ-HCL.

Table 3
Selectivity coefficients for the naphazoline electrode[a]

Interferent	$K^{\text{pot}}_{\text{NPZ},\, j^{z+}}$
Na^+	3.81×10^{-3}
K^+	4.64×10^{-3}
NH_4^+	1.35×10^{-3}
Ba^{2+}	2.34×10^{-4}
Cu^{2+}	1.55×10^{-4}
Co^{2+}	1.80×10^{-4}
Ni^{2+}	2.15×10^{-4}
Hg^{2+}	2.4×10^{-2}
Al^{3+}	9.64×10^{-5}
Zr^{4+}	2.46×10^{-4}
Glucose	4.75×10^{-3}
Sucrose	2.91×10^{-3}
Urea	3.2×10^{-3}
L-Cystine	3.59×10^{-3}
Citric acid	5.03×10^{-3}
Phenylephrine	0.25
Betaxolol	0.14

[a] Four determinations.

3.4. Lifetime and reproducibility

Plotting the calibration curve periodically with standard solutions and calculating the response slopes investigated the lifetime of electrodes. It was indicated that the conventional and coated graphite electrodes could be used continuously for about 1 and 2 months, respectively, without considerable decrease in its slope values. This kind of the membrane electrodes do not require any pre-conditioning in the solutions of corresponded drugs or maintenance before use. The membranes of electrodes were washed with water after each application and stored in a desicator under atmospheric condition and kept far from the light.

The reproducibility of this sensor was evaluated by constructing replicate calibration graphs. The potential displayed by the proposed sensors for consecutive measurements in the previously mentioned concentration range of NPZ solutions in the same day did not vary by more than ±1 mV ($n = 4$).

3.5. Response time

The time required for the prepared electrodes to reach steady potential values, after successive immersion of the electrode in different concentrations of naphazoline hydrochloride solutions each having a 10-fold difference in concentration has been measured.

The average static response time [18] was found to be short ranging from 20 s for concentration $\geq 1.0 \times 10^{-4}$ mol l^{-1} to 30 s for concentration 1.0×10^{-5} mol l^{-1} for the conventional electrode, and 10 s for concentration $\geq 1.0 \times 10^{-5}$ mol l^{-1} for the coated graphite electrode.

3.6. Determination of solubility product of the NPZ–TPB ion pair

The determination of the solubility product of the ion-pair is important since its reciprocal is approximately equal

Table 4
Determination of NPZ-HCl by applying the potentiometric titration and standard addition method

Pure solutions				Naprivin (naphazoline 0.1%)			
Taken (mg)	Found (mg)	Recovery (%)	R.S.D.[a] (%)	Taken (mg)	Found (mg)	Recovery (%)	R.S.D. (%)
Standard addition method							
0.493	0.489	99.2	6.1	1.998	1.976	98.9	9.6
0.864	0.865	100.1	4.6	3.498	3.424	97.9	15.2
1.234	1.274	103.2	6.3	4.996	5.006	100.2	18.0
Potentiometric titration method							
0.493	0.481	97.6	4.0	1.998	1.969	98.5	2.6
0.864	0.873	101.0	1.1	3.498	3.463	99.0	3.2
1.234	1.228	99.5	3.2	4.996	5.086	101.8	1.5

[a] Four determinations.

to the formation constant of the ion-pair, which is tightly related to the degree of hydrophobicity of ion-pair. Therefore, as the hydrophobicity of the ion-pair (NPZ–TPB) increases, the leaching process of it to the aqueous bathing solution, which is the main determining factor to decrease the lifetime of the electrode membrane. The solubility product of the NPZ–TPB was determined conductometrically as described in the experimental part and was found to be 2.55×10^{-9}, indicating a very low solubility of the ion pair (5.1×10^{-5} mol l^{-1}). Consequently, the formation constant of the reaction NPZ + TPB $\leftrightarrow$ NPZ–TPB was 3.9×10^{8}. In the above equilibrium, the solubility of the undissociated ion-pair in water (i.e. the intrinsic solubility) was omitted as it provided too small contribution to the total solubility.

3.7. Analytical application

The prepared electrode has been successfully used for the determination of naphazoline in aqueous solutions and in pharmaceutical preparations (i.e. Naprivin) by using the standard addition and potentiometer titration method, and the results are summarized in Table 4.

In the potentiometric titration method, different volumes of 1.0×10^{-3} mol l^{-1} of pure NPZ-HCl and 4.0×10^{-3} mol l^{-1} of its pharmaceutical preparation were taken (2, 3.5 and 5 ml) and completed to 20 ml with doubly distilled water (at pH 6). The naphazoline-selective sensor in conjunction with a calomel reference electrode was immersed in the solution and titrations were carried out with standard 1.0×10^{-3} mol l^{-1} NaTPB. The e.m.f. was recorded after potential stabilization. The end point was determined by the plotting potential versus added titrant volume. The typical titration curves are shown in Fig. 6.

The standard addition method was applied by adding a small portion (0.1 ml) of 1.0×10^{-2} mol l^{-1} standard NPZ-HCl solution to 20 ml aliquot samples of various pure and formulation drug concentrations (4.0×10^{-3} to 1.0×10^{-3} mol l^{-1}). The change in potential readings (at a constant temperature of 25 °C) was recorded after each addition and used to calculate the concentration of NPZ-HCl sample solutions [19] by the following equation:

$$C_x = C_s V_s / [(V_x + V_s) \times 10^{n(\Delta E/S)} - V_x)]$$

where C_x and V_x are the concentration and the volume of the unknown sample, respectively. C_s and V_s are the concentration and the volume of the standard, respectively. S is the slope of the calibration graph and ΔE is the change in mV due to the addition of the standard. So the determination of the concentration depends mainly on ΔE, hence to obtain noticeable ΔE we need to prepare higher concentration of the standard.

For sampling of Naprivin sterile eye drops (0.1% naphazoline), the content of 10 droppers was poured in a 100 ml flask, and used as a stock solution. The required volumes for the preparation of different concentrations were taken and diluted to 20 ml with doubly distilled water.

The mean recovery of the amounts taken (0.5–5 mg) in the proposed method ranged from 97.6 to 103.2% for pure solutions and droppers.

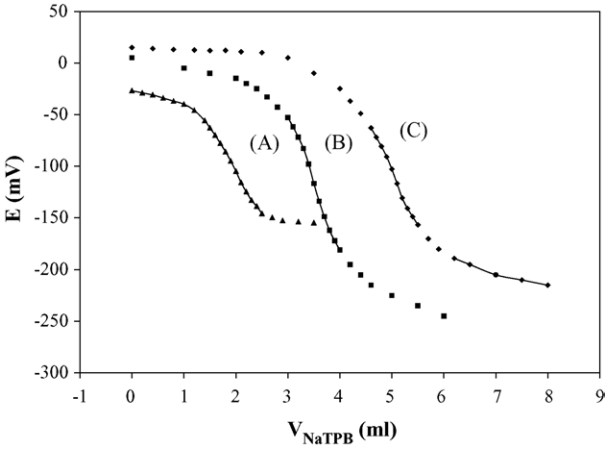

Fig. 6. Typical potentiometric titration curves for (A) 2.0 ml, (B) 3.5 ml, and (C) 5.0 ml of 1.0×10^{-3} mol l^{-1} of NPZ with 1.0×10^{-3} mol l^{-1} NaTPB using NPZ-selective membrane sensor.

4. Conclusion

The results presented herein led us to conclude that despite the accuracy of the previously reported methods for naphazoline determination, the proposed potentiometric sensors provide a simple low-cost method, which offers a direct selective determination of NPZ in pure solutions and in its pharmaceutical formulation without prior separation or derivatization steps with high accuracy, precision and sensitivity.

The elimination of the inner reference solution contributed to the greater reproducibility and most especially to a considerably significant increase in the lifetime of the electrodes.

It is inferred that the electrode based on the NPZ–TPB ion-pair, without an inner reference solution, provides a rapid, sensitive, inexpensive and reliable method for NPZ determinations in pharmaceutical analysis with minimal sample pre-treatment. It is also better than previously reported potentiometry method in the literature in 1985.

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References

[1] J.M.L. Gallego, J.P. Arroyo, Determination of prednisolone, naphazoline, and phenylephrine in local pharmaceutical preparations by micellar electrokinetic chromatography, J. Sep. Sci. 26 (2003) 947–952.
[2] A.S. Carretero, C.C. Blanco, B.C. Diaz, A.F. Gutierrez, Room-temperature phosphorimetric method for the determination of the drug naphazoline in pharmaceutical preparations, Analyst 123 (1998) 1069.
[3] A. Salinas-Castillo, A.S. Carretero, A. Fernandez-Gutierrez, Sensitive and simple determination of the vasodilator agent dipyridamole in pharmaceutical preparations by phosphorimetry, Anal. Bioanal. Chem. 376 (2003) 1111–1114.
[4] H.C. Goicoechea, A.C. Olivieri, Theoretical and experimental study involving the spectrophotometric analysis of multicomponent mixtures, Analyst 126 (2001) 1105–1112.
[5] Y. Liang, Q. Huang, A naphazoline selective electrode, Yaowu Fenxi Zazhi 5 (1985) 81.
[6] M. Shamsipur, F. Jalali, S. Haghgoo, Preparation of a cimetidine ion-selective electrode and its application to pharmaceutical analysis, J. Pharm. Biomed. Anal. 27 (2002) 867–872.
[7] V.V. Cosofret, R.P. Buck, Pharmaceutical Applications of Membrane Sensors, CRC Press, Boca Raton, FL, 1992.
[8] D.G. Peter, J.M. Hayes, G.M. Hieftje, Chemical Separation and Measurements, Saunders, Philadelphia, PA, 1974.
[9] K. Vitras, Potentiometry, in: J. Swarbric, J.C. Boylan (Eds.), Encyclopedia of Pharmaceutical Technology, vol. 12, Marcel Dekker, New York, 1995, p. 347.
[10] H.H. Bauer, G.D. Christian, J.E. O'Reilly (Eds.), Instrumental Analysis, Allyn and Bacon Inc., Boston, 1978, p. 117.
[11] G. Nagy, J. Tarcall, K. Toth, R.N. Adams, E. Pungor, Proceedings of the Fourth Symposium on Ion-selective Electrodes, Matrafured, Hungary, 1984, p. 567.
[12] A.F. Shoukry, N.T. Abdel Ghani, Y.M. Issa, H.M. Ahmed, Plastic membrane selective electrode for cetirizinium ion based on cetirizinium–tetraphenylborate ion-pair, Electroanalysis 11 (1999) 443.
[13] Y.M. Issa, A.F. Shoukry, R.M. El-Nashar, Conductimetric determination of reproterol HCl and pipazethate HCl and salbutamol sulfate in their pharmaceutical formulations, J. Pharm. Biomed. Anal. 26 (2001) 379–386.
[14] E. Linder, K. Toth, E. Pungor, Dynamic Characteristics of Ion Selective Electrodes, CRC Press, Boca Raton, FL, 1988.
[15] L.I. Antropov, Theoretical Electrochemistry, Mir Publisher, Moscow, 1977.
[16] Y. Umezawa, P. Buhlmann, K. Umezawa, K. Tohda, S. Amemiya, Potentiometric selectivity coefficient of ion-selective electrodes, Pure Appl. Chem. 72 (2000) 1851–2082.
[17] N.T. Abdel-Ghani, S.H. Hussein, Determination of ambroxol hydrochloride in pure solutions and some of its pharmaceutical preparations under batch and FIA conditions, Il Farmaco 58 (2003) 581–589.
[18] C. Maccà, Response time of ion-selective electrodes, current usage versus IUPAC recommendations, Anal. Chim. Acta 512 (2004) 183–190.
[19] R.P. Buck, E. Lindner, Recommendations for nomenclature of ion selective electrodes, Pure Appl. Chem. 66 (1994) 527–536.

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