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CONSTRUCTION AND PERFORMANCE CHARACTERISTICS OF NEW TETRAMISOLE SELECTIVE PLASTIC MEMBRANE ELECTRODES

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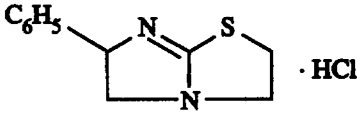
Summary—New tetramisole (Tm) ion selective PVC membrane electrodes are constructed based on either the ion-pair complex Tm TPB (Electrode I) where TPB is tetraphenylborate or the ion associate Tm_3 PT (Electrode II) where PT is phosphotungstate. The rectilinear concentration ranges of Electrodes I and II are 4×10^{-5}–$10^{-2}M$ (average slope = 55.7 mV/concentration decade) and 5×10^{-5}–$10^{-2}M$ TmCl (average slope = 57.0 mV/concentration decade), at 25°C, respectively. The life time of the two Electrodes I and II are 14 and 49 days of continuous working, respectively. The change in pH does not affect the electrodes performance within the range 3.0–5.5, 3.0–6.0 and 3.0–7.0 for Tm concentrations 10^{-2}, 5×10^{-3} and $10^{-3}M$, respectively. The isothermal coefficients of Electrodes I and II are found to be 0.000667 and 0.001164 V/°C, respectively. The electrodes proved to be highly selective for TmCl towards inorganic cations, sugars and amino acids. The standard addition method and potentiometric titration are used to determine Tm in pure solutions and in tetramisole 10% oral solution. Regeneration process for the exhausted Electrodes I and II is applied successfully by soaking them in a solution of NaTPB and PTA, respectively.

Tetramisole hydrochloride (TmCl) is an anthelmintic for intestinal nematode worms, round worm infection (ascariasis) and hook worm infections (ancylostomiasis and necatoriasis). It is also an immunostimulant for T-cell, and used in case of aphthous stomatitis, bacterial infections, malignant neoplasms, renal and rheumatic disorders.[1]



Tetramisole Hydrochloride

TmCl was determined by several techniques including spectrophotometry using different chromophoric reagents, *e.g.* fast green, orange II,[2] 7,7,8,8,-tetracyanoquinodimethane, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone and 2,4,5,7-tetranitrofluoren-9-one,[3] and other dyes.[4] It has also been determined by forming coloured compounds with cobalt thiocyanate[5] and sodium nitroprusside.[6] The drug was assayed by HPLC using μ-Bondapak C_{18} column with methanol–water–anhydrous acetic acid-triethylamine (600:1400:40:1) as mobile phase and detection at 254 nm,[7] or using Lichrosorb RP-8 with 1% of concentrated H_2SO_4 in H_2O–acetonitrile (4:1) as mobile phase and detection at 254 nm.[8] Tetramisole has been identified by X-ray diffraction employing a Debye–Scherrer camera.[9]

In the present work, two new plastic membrane electrodes selective for tetramisole cation were constructed and their performance characteristics were studied. The electrodes are based on incorporation of tetramisole tetraphenylborate ion pair (Tm^+ TPB^-) and tetramisole phosphotungstate ion associate $(Tm^+)_3PT^{3-}$ in a poly vinylchloride (PVC) membrane plasticized with dioctylphthalate (DOP). The electrodes have been used successfully as potentiometric sensors for the determination of TmCl in pure solutions and in tetramisol 10% oral solution for veterinary use (El Nasr Pharm. Chem. Co., Egypt "ADWIC"). The present method has the following advantages over the previously reported techniques: (a) the preparation of the electrode is at low cost, (b) no sophisticated instruments are required and (c) the method is simple, and not time consuming. The work

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also includes a method for the regeneration of the exhausted electrodes.

EXPERIMENTAL METHODS

Reagents and materials

All chemicals used were of analytical grade. Twice distilled water was used throughout all experiments. Pure grade TmCl was supplied by El Nasr Pharm. Chem. Co. (ADWIC), Egypt. The veterinary preparation of tetramisol 10% oral solution was provided by ADWIC (Cairo, Egypt).

The ion-pair, Tm^+ TPB^-, were precipitated from aqueous medium by adding portion-wise 100 ml $10^{-2}M$ TmCl solution to 100 ml $10^{-2}M$ NaTPB solution with continuous stirring, while Tm_3PT was precipitated by mixing and stirring 150 ml of $10^{-2}M$ TmCl with 50 ml $10^{-2}M$ PTA solution. The white precipitates obtained were filtered, washed thoroughly with distilled water and dried at room temperature. The composition of precipitates was identified by IR, conductimetry and elemental analysis (Table 1).

The electrodes

Different membrane compositions were tried as given in Table 2. The membranes were prepared by dissolving Tm TPB in tetrahydrofuran or Tm_3PT in acetone, the resultant solution was added to a solution of PVC in tetrahydrofuran, then the required amount of DOP was added with continuous stirring. The obtained solution mixture was poured into 7.5 cm Petri dish and left to dry in air. A 12-mm diameter disc was cut out from the prepared membrane and glued to the polished end of a plastic cap attached to a glass tube. The electrode body was filled with a solution that is $10^{-1}M$ in NaCl and $10^{-2}M$ in TmCl. In this solution, an Ag/AgCl wire is immersed in order to act as internal reference electrode. The electrode is preconditioned by soaking in $10^{-2}M$ TmCl solution.

Table 1. Elemental analysis of the ion-pairs of TmCl with Na–TPB and PTA

	Tm–TPB		Tm_3–PT	
Element	Calculated	Found	Calculated	Found
C	80.1	78.5	11.3	11.9
H	6.3	5.2	1.1	1.5
N	5.3	5.9	2.4	2.4

Table 2. Composition of the different membranes and slope of the corresponding calibration graphs at 25 ± 1°C*

Ion exchanger	Composition % (W/W)			Slope (mV/decade)	Mean value *S*† (%)
	Ion pair	DOP	PVC		
Tm TPB	5.0	47.50	47.50	54.4	0.34
	7.5	46.25	46.25	50.6	0.40
	10.0	45.00	45.00	55.7	0.29
	15.0	42.00	42.50	52.1	0.13
	20.0	40.00	40.00	—	—
Tm_3PT	5	47.5	47.5	57.0	0.75
	10	45.0	45.0	48.0	0.82
	15	42.5	42.5	38.0	0.68
	20	40.0	40.0	53.7	0.73

*Thirty minutes of soaking in $10^{-2}M$ TmCl.

†Relative standard deviation mean value (four preparations).

Potentiometric studies and electrochemical system

Potentiometric measurements were carried out with a titroprocessor 682 (Metrohm, Swiss made). A Techne circulator thermostat, model C-100, 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//saturated calomel electrode.

Selectivity

The selectivity coefficients, $K^{Pot.}_{Tm^+, J^{z+}}$ of the electrodes toward different cationic species, J^{z+}, were determined by the separate solution method.[10]

Potentiometric determination of TmCl

The standard addition method, in which small increments of a standard solution (0.1M) of TmCl were added to 50 ml samples containing 10–100 mg TmCl, was used. The change in the mV-reading was recorded after each addition and used to calculate the concentration of the TmCl sample solution.

For the analysis of the Tm-containing formulation, aliquots of 0.1–1 ml of the oral solution were quantitatively transferred into 100 ml beakers, each containing 50 ml of distilled water and the standard addition technique was applied as described above.

Potentiometric titration of TmCl

An aliquot of the Tm solution containing 2–10 mg TmCl in the case of Electrode I and

10–35 mg TmCl in the case of Electrode II, was transferred into 100-ml beaker and dissolved in 50 ml distilled water then titrated with 0.01*M* of NaTPB or PTA solution using the respective membrane electrode as the sensor.

For Tm-oral solution, 0.02–0.1 ml and 0.1–0.35 ml aliquots of the pharmaceutical preparation, in case of Electrodes I and II, respectively were transferred into 100-ml beakers, each containing 50 ml water and titrated as above.

RESULTS AND DISCUSSION

Composition of the membrane

Table 2 comprises the different membrane compositions investigated. For each composition, the electrode was repeatedly prepared four times, the relative standard deviation values of the obtained calibration curve slopes show that the preparation process is highly reproducible. The results also reveal that the use of the composition (20% Tm TPB, 40% DOP and 40% PVC) in preparing Tm TPB-based electrode leads to poor results. This is most probably due to oversaturation of the ion pair in the solvent mediator resulting in a hard membrane with poor physical properties. The results given in Table 2 show that the best membrane composition for electrodes based on Tm TPB and Tm_3 PT are (10% Tm TPB, 45% DOP and 45% PVC) and (5% Tm_3PT, 47.5% DOP and 47.5% PVC), respectively. These membrane compositions lead to electrodes having the following performance characteristics, respectively: (slope 55.7 mV/decade at 25°C, usable concentration range 4×10^{-5}–$10^{-2}M$ TmCl with instantaneous response) and (slope 57 mV/decade at 25°C, usable concentration range 5×10^{-5}–$10^{-2}M$ TmCl and response time of a few seconds).

In all subsequent studies, electrodes made of membranes having the above mentioned two compositions are used and referred to as Electrodes I and II, respectively.

Life time of the electrodes

Calibration plots (*p*Tm *vs E*,mV) were obtained after electrode soaking in $10^{-2}M$ TmCl for 0.5, 1, 1.5, 2 and 24 hr; and 7, 14, 21, 28 and 49 days, in case of Electrode I, and for 0.5, 1, 2 and 24 hr; and 14, 35, 49, 56, 70, 84 and 91 days in case of Electrode II. Figure 1 includes representative calibration curves exhibiting the effect of soaking on electrode performance. The results show that, in general, the slope at higher

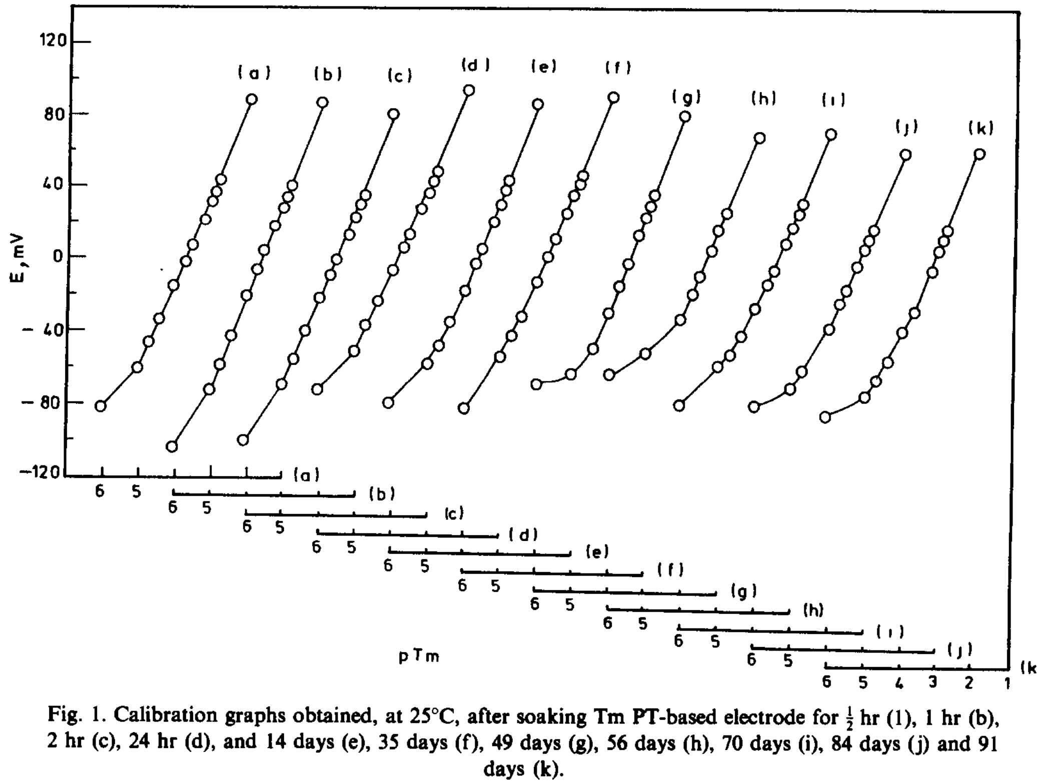

Fig. 1. Calibration graphs obtained, at 25°C, after soaking Tm PT-based electrode for $\frac{1}{2}$ hr (1), 1 hr (b), 2 hr (c), 24 hr (d), and 14 days (e), 35 days (f), 49 days (g), 56 days (h), 70 days (i), 84 days (j) and 91 days (k).

concentrations is closer to the Nernstian value than the slope at lower concentrations beyond the detection limit. In case of Electrode I, the calibration graph slope remains constant at 54 mV/decade for 14 days of continuous soaking, then it decreases gradually reaching 43.4 mV/decade after 49 days with a clear change in detection limit from 4×10^{-5} to 1×10^{-5}. In the case of Electrode II, up to 49 days, the slope is almost constant at 57 mV/decades then it decreases gradually to 49.9 mV/decade after 91 days, while the detection limit remains constant at $1 \times 10^{-4} M$ TmCl after 2 hr soaking and up to 91 days. However, when the electrodes are kept dry in a refrigerator, they maintain their characteristic slope even after three months. Therefore, it is recommended to keep the electrodes in a refrigerator while not in use. Nevertheless, the exhausted Electrode I or II are regenerated successfully by soaking the electrode in $10^{-2} M$ NaTPB or PTA solution, respectively, for 24 hr followed by soaking for 30 min in $10^{-2} M$ TmCl solution. In all cases, the calibration graph slope restores a value very close to the Nernstian one. Representative curves are shown in Fig. 2. The mean life spans for the regenerated electrodes were 3 and 10 days for the two Electrodes I and II, respectively. The presented regeneration process is similar to that described in a previous work[12] for TPB^- anion-selective electrode based on ion pair of TPB^- with the cationic detergent, hexadecylpridinium bromide.

Effect of temperature of the test solution

Calibration graphs (electrode potential, E_{elec}, *vs p*Tm) are constructed at test solution temperatures of 25, 40, 50, 60 and 70°C. The slope, usable concentration range and standard electrode potential ($E°$) at each temperature are given in Table 3.

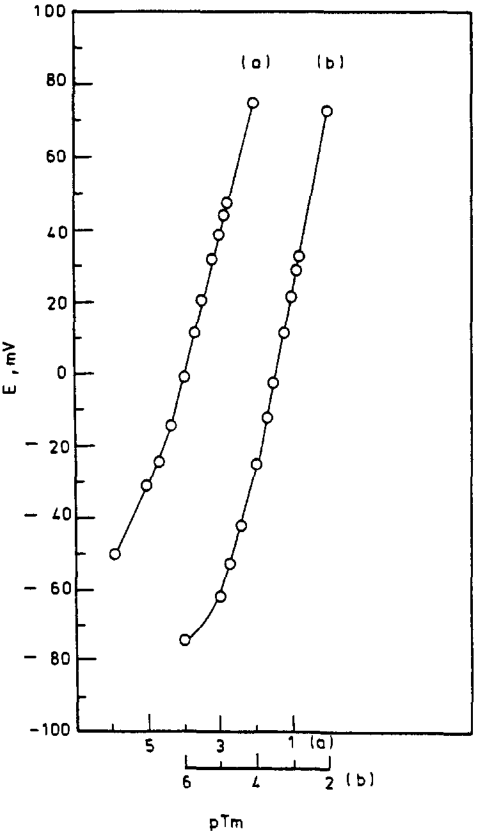

Fig. 2. Calibration curves of TmTPB-based electrode for exhausted electrode (a) and regenerated electrode (b).

The results show that within the temperature range investigated, the electrode responds, practically, to TmCl concentration with a nearly constant usable concentration range. The slopes deviate slightly and nearly constantly from the Nernstian values acquiring higher values over the whole temperature range and only above 35°C for Electrodes I and II, respectively. This deviation may be attributed to additional potential arising from disturbances in the mechanism of the ion exchange process occurring at the gel layer-test solution interface as a result of excessive thermal agitation.

Table 3. Performance characteristics of the electrodes at different temperatures

Electrode	Temperature (°C)	Slope (mV/decade)	Usable concentration range (*M*)	$E°$ (mV)
I	25	55.6	4.0×10^{-5}–1.0×10^{-2}	+209.3
	40	56.2	1.0×10^{-4}–1.0×10^{-2}	+211.2
	50	59.2	1.0×10^{-4}–1.0×10^{-2}	+219.2
	60	61.1	1.0×10^{-4}–1.0×10^{-2}	+223.5
	70	64.2	1.0×10^{-4}–1.0×10^{-2}	+231.8
II	28	57.1	5.0×10^{-5}–1.0×10^{-2}	+201.3
	40	62.4	1.0×10^{-4}–1.0×10^{-2}	+207.4
	50	68.4	1.0×10^{-4}–1.0×10^{-2}	+219.5
	60	74.3	1.0×10^{-4}–1.0×10^{-2}	+233.9
	70	76.0	1.0×10^{-4}–1.0×10^{-2}	+241.4

For the determination of the isothermal coefficients of the electrodes (dE°/dt), the standard electrode potentials (E°) are determined, at different temperatures, from the calibration graphs at different temperatures, as the intercepts of the plots at $p\text{Tm} = 0$ (Table 3) and plotted *vs* $(t - 25)$, where (t) is the temperature of the test solution. A straight line plot is produced according to:[13]

$$E^\circ = E^\circ_{25} + (dE^\circ/dt)(t - 25).$$

The slope of the straight line obtained represents the isothermal coefficient of the electrode. The values amount to 0.000667 V/°C for Electrode I and 0.001164 V/°C for Electrode II, revealing a fairly good thermal stability of the electrodes within the temperature range investigated.

Effect of pH

The effect of pH of the test solution (10^{-2}, 5×10^{-3} and $10^{3}M$ TmCl) on the electrode potential is investigated by following the variation in potential with change in pH by the addition of very small volumes of HCl and NaOH (0.1–1M each). Potential–pH curves of nearly the same pattern are obtained in each case, representative plots are shown in Fig. 3. It is clear that the change in pH has a negligible effect within the pH ranges 3–5.5, 3–6 and 3–7 for 10^{-2}, 5×10^{-3} and $10^{-3}M$, respectively for both Electrodes I and II. At pH less than 3, the potential readings decrease, which may be attributed to penetration of chloride ion in the membrane gel layer, or formation of diprotonated species. In alkaline medium, the potential value decreases sharply which may be due to formation of the free Tetramisole base in solution leading to a decrease in the concentration of the tetramisolium cation. It is noteworthy that the slope of this descending part of the curve is nearly Nernstian (≅54 mV/pH unit) pointing to a hydroxyl ion exchange at the membrane surface—test solution interfacial junction. The ion exchanger in the PVC network contacting the alkaline test solution is most probably tetramisole base molecules. This is in accordance with previous study[14] concerning the construction of hydroxyl

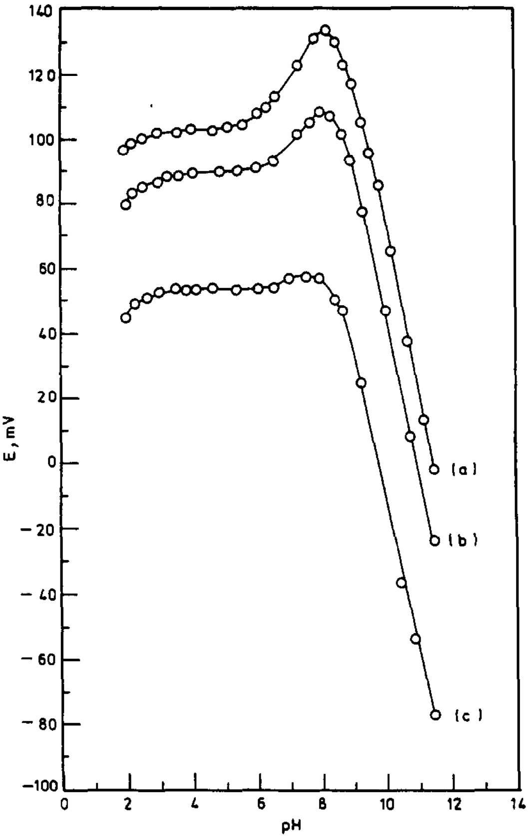

Fig. 3. Effect of pH of the test solution of concentrations $10^{-2}M$ (a), $5 \times 10^{-3}M$ (b), and $10^{-3}M$ (c) TmCl on the potential readings using Tm–TPB electrode.

Table 4. Selectivity coefficients, $K^{\text{Pot}}_{\text{Tm},\,J^{z+}}$, of the electrodes for Tm towards different species

	$K^{\text{Pot}}_{\text{Tm},\,J^{z+}}$ $(\times 10^{4})$			$K^{\text{Pot.}}_{\text{Tm},\,J^{z+}}$ $(\times 10^{-4})$	
Interferent	Electrode I	Electrode II	Interferent	Electrode I	Electrode II
Li^+	0.14	0.023	Dextrose	4.40	0.042
Na^+	6.60	0.100	Sucrose	3.10	0.031
K^+	8.20	2.100	Alanine	6.40	0.070
Zn^{2+}	0.48	0.056	Leucine	4.90	0.052
Co^{2+}	0.44	0.034	Treptophan	3.70	0.110
Ni^{2+}	0.40	0.056	Glycine	4.20	0.057
Mg^{2+}	0.31	0.083	Asparagine	3.30	0.520
Pb^{2+}	0.37	0.120	Tyrosine	3.90	0.680
Ba^{2+}	0.30	0.037	Cyctine	3.00	3.100
Sr^{2+}	0.25	0.053	Lycine	2.80	0.120
Cu^{2+}	0.37	0.032	Triethanolamine	0.15	0.003
Cd^{2+}	0.41	0.022	Hydroxylamine HCl	3.30	0.350

Table 5. Determination of tetramisole hydrochloride by Tm TPB-based electrode

	Standard addition method			Potentiometric titration		
Sample	Taken (mg)	Mean Recovery (%)	S* (%)	Taken (mg)	Mean Recovery (%)	S* (%)
Pure solution	10	98.6	0.06	2.0	98.6	0.02
	20	100.7	0.13	3.0	99.6	0.02
	30	97.7	0.28	4.0	98.2	0.04
	40	100.1	0.78	5.0	99.9	0.07
	50	99.4	0.81	6.0	99.3	0.11
	60	98.3	0.65	7.0	99.1	0.04
	70	99.5	0.49	8.0	98.3	0.08
	80	99.3	0.68	9.0	98.9	0.03
	90	98.9	0.59	10.0	98.8	0.03
	100	100.5	0.27			
Tetramisole 100% oral solution	10	102.7	0.03	2.0	105.7	0.03
	20	103.9	0.53	3.0	103.8	0.05
	30	103.7	0.53	4.0	102.2	0.18
	40	102.2	0.54	5.0	103.0	0.08
	50	103.0	0.29	6.0	103.1	0.07
	60	103.6	0.39	7.0	102.4	0.05
	70	102.1	0.44	8.0	102.1	0.12
	80	102.7	0.36	9.0	101.9	0.11
	90	102.6	0.34	10.0	102.4	0.10
	100	102.9	0.17			

*Relative standard deviation (four determinations).

ion-selective electrode using chloropromazine base as the ionophore.

Selectivity

The influence of some inorganic cations, sugars, amino acids and large organic cations on Electrodes I and II were investigated. The selectivity coefficient being determined by the separate solution method[10] (Table 4).

In this method the following equation is applied:

$$\log K^{\mathrm{Pot.}}_{\mathrm{Tm}^+,\, \mathrm{J}^{z+}} = (E_2 - E_1)/S + \log[\mathrm{Tm}^+] - \log[\mathrm{J}^{z+}]^{1/z}.$$

Table 6. Determination of tetramisole hydrochloride by $\mathrm{Tm}_3\mathrm{PT}$-based electrode

	Standard addition method			Potentiometric titration		
Sample	Taken (mg)	Mean Recovery (%)	S* (%)	Mean Taken (mg)	Recovery (%)	S* (%)
Pure solution	10	100.0	0.03	10	99.9	0.01
	20	98.3	0.20	15	99.8	0.20
	30	99.7	0.15	20	100.0	0.17
	40	99.8	0.53	25	99.7	0.03
	50	99.9	0.21	30	100.2	0.02
	60	99.4	0.89	35	99.8	0.02
	70	99.5	0.45			
	80	99.7	0.67			
	90	98.9	0.60			
	100	99.8	1.07			
Tetramisole 10% oral solution	10	103.4	0.08	10	100.5	0.03
	20	102.2	0.17	15	100.9	0.01
	30	102.0	0.17	20	100.8	0.03
	40	102.9	0.25	25	100.7	0.02
	50	101.9	0.42	30	101.3	0.01
	60	101.3	0.28	35	100.0	0.05
	70	101.2	0.43			
	80	103.5	0.36			
	90	102.6	0.47			
	100	100.7	0.39			

*Relative standard deviation (four determinations).

Where E_1 is the electrode potential in $10^{-3}M$ Tm solution and E_2 is the potential of the electrode in $10^{-3}M$ solution of the interferent J^{z+}. None of the investigated species was found to interfere as shown by the very small values of $K^{\text{Pot.}}_{\text{Tm}, J^{z+}}$. This reflects a very high selectivity of the investigated tetramisole electrodes. However, from Table 4, it is evident that Electrode II is generally more selective than I. This may be attributed to more favorable thermodynamic parameters controlling the ion-exchange process at the membrane-test solution interface and to a greater mobility of Tm cation through the polymeric network in case of the Tm_3PT-containing membrane.

Analytical application

The Tm TPB- and Tm_3PT-based electrodes are shown to be useful in the potentiometric determination of TmCl in pure solutions by the standard addition method and potentiometric titrations.

The tetramisole-containing veterinary preparation (Tetramisol 10% oral solution) has been assayed by the standard addition method and by potentiometric titration using such electrodes. Collective results are given in Tables 5 and 6. The obtained values for recovery and relative standard deviation reveal a high degree of accuracy and precision on using the present electrodes in the determination of TmCl either in pure solutions or veterinary preparations.

CONCLUSION

The ion-pair Tm TPB and the ion associate Tm_3PT are very efficient ion exchangers for the construction of Tm-plastic membrane ion selective electrodes. Such electrodes can be successfully used for the determination of TmCl in its pure solutions and a pharmaceutical preparation.

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