

Surface analysis of new chlorpromazinium plastic membrane electrodes

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Abstract

New chlorpromazinium (Cp) plastic membrane electrodes of the conventional type were constructed and characterized. They are based on incorporation of Cp-reineckate (CpRn) ion pair, Cp-phosphotungstate (Cp₃PT), or Cp-phosphomolybdate (Cp₃PM) ion associate into poly(vinyl chloride) membrane. The electrodes exhibited calibration graph slopes of 49.83, 52.87, and 61.30 mV/Cp concentration decade over life spans of 1, 5, and 3 days, respectively. All electrodes proved to be selective for Cp and have been applied to the assay of a pharmaceutical preparation. Energy dispersive spectroscopy (EDS) and X-ray photoelectron spectroscopy (XPS), as well as scanning electron microscopy (SEM) showed that the limitation of the lifetime of the electrodes is attributed to leaching of the ion exchanger from the membrane into the test solution in addition to deformation of the surface.

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1. Introduction

Ion-selective electrodes are the chemical sensors with the longest history and probably with the most frequent applications [1]. Polymeric membrane-based electrodes are the most versatile [2,3]. However, one of the main drawbacks of potentiometry using ion-selective electrodes had been and still is the limitation of the lifetime of these electrodes [4]. This was attributed to leaching of the ion exchanger from the lipophilic matrix of the membrane to the aqueous side of the inter-junction separating the two phases. The leaching from the membrane surface was traced by chronoamperometric technique [5,6]. In another study, it was found [7,8] that the extent of this leaching, in addition to the hydrophilicity of the exchanger, affects the value of the detection limit of the electrode. Because leaching is a surface phenomenon, it is important to analyze the material electronic structure of the membrane surface in correlation to soaking of the electrode in the bathing solution. This has been done in a previous work [9] where X-ray, as primary beam, was used to monitor the elemental composition change of the surface; electron microscopy was also employed to detect the

corresponding physical change associated with prolonged soaking. The results revealed that membrane surface deformation associates leaching and may be a factor enhancing it. However, X-ray photoelectron spectroscopy, though powerful technique, has the limitation that its sampling depth is only 0.5–5.0 nm; investigating deeper layers requires the use of an Ar ion gun [9]. On the other hand, energy dispersive spectroscopy (EDS) has corresponding depth of 1–2 μm. Therefore, analyzing the surface of the membrane using both techniques would lead to more interpretable results. In the present work the surfaces of new chlorpromazinium-responsive electrodes, based on ion-exchangers of different lipophilicity, were analyzed by probing with highly energetic electrons (EDS) and by X-rays (XPS). Moreover, secondary electrons' imaging has been applied to test the change in morphology of the surface that associates the leaching process.

Chlorpromazinium chloride (CpCl) is a very important drug that is used for treatment of psychotic disorder. Several methods have been reported for the determination of CpCl including spectrophotometry [10–12], chromatography [13–16] and fluorometry [17]. Although potentiometry using ion-selective electrodes are simple, cheap, applicable to samples of different natures, and usable with automated systems, very little had been reported about application of the technique to Cp-determination. A liquid membrane Cp-selective electrode was constructed

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[18] based on Cp salt with eosin and tetraphenylborate; the electrode showed near Nernstian response, in acidic medium, over a limited concentration range (6×10^{-3} to 4×10^{-5} M). Electrodes based on ion pairs of the drug with tetraphenylborate and dinonylnaphthalenesulphonate were constructed [19]. Although the electrodes exhibited near Nernstian responses, their response time was about 60 s; no studies for the effect of soaking on the life span of the electrodes were conducted. The drug was also determined [20] by potentiometric titration using sodium tetraphenylborate as titrant and fluoroborate ion-selective electrode as indicator. The present work describes new plastic membrane electrodes of the conventional type, for the determination of CpCl in pure solution and in pharmaceutical preparations. The electrodes are based on incorporation of Cp-reineckate (Rn^-) ion pair, Cp-phosphotungstate (PT^{3-}) or Cp-phosphomolybdate (PM^{3-}) ion associate in poly(vinyl chloride) membranes. They showed, in general, wider concentration ranges and faster response than the electrodes previously reported [18,19].

The novelty of the work originates in introducing the strong techniques, EDS, XPS and SEM to investigate the cause of limitation of the life span of plastic membrane electrodes and in presenting new sensors for the very important pharmaceutical compound, chlorpromazine.

2. Experimental

2.1. Reagents and materials

All chemicals used were of analytical grade. Chlorpromazinium chloride (chlorpromazine hydrochloride) (Sigma), poly(vinyl chloride) (PVC) of high molecular weight (Fluka), dioctyl phthalate (DOP) (Fluka), ammonium reineckate (Aldrich), phosphomolybdic acid (PMA) (Fluka), and phosphotungstic acid (PTA) (Fluka) were used. The Cp-containing tablets, Neurazine (100 mg Cp/tablet) were from Misr Co. for pharmaceuticals, Egypt. Ten tablets were ground into fine pow-

der, from which replicate samples were taken. All solutions and reagents were prepared in bi-distilled water. The CpRn ion pair and Cp_3PT and Cp_3PM ion-associates were prepared as previously described [21]. The elemental analysis of the produced ion-exchangers, carried out in ANALAB, Faculty of Science, Kuwait University, confirmed the stoichiometries: (1:1) (Cp:Rn), (3:1) (Cp:PT) and (3:1) (Cp:PM).

2.2. Construction of the electrodes

The electrodes were prepared, as previously described [9,22], using membranes of different compositions (Table 1). The internal solution in all electrodes was 1.00×10^{-3} M in CpCl and 1.00×10^{-1} M in KCl.

2.3. Potentiometric measurements and construction of the calibration graphs

Potentiometric measurements were carried out with an Orion, Model 420 A pH/mV meter. A Caron circulator thermostat was used to control the temperature of the test solution. The electrochemical system employed and the method of constructing the calibration graphs were similar to those described previously [9].

2.4. Selectivity

The selectivity coefficients of the Cp-selective electrode ($K_{Cp, j^{z+}}^{pot}$) towards different cationic species, j^{z+} , were determined by the separate solution (SSM) [23] and matched potential method (MPM) [24].

2.5. Energy dispersive X-ray spectroscopy

The electrode's membrane was loaded in JEOL'S, Japan, JSM-6300 scanning electron microscope and examined at 20 kV. Elemental X-ray microanalysis was done by Rontec's

Table 1
Effect of membrane composition on Cp-electrode performance

Ion pair (%)	Ion pair (mg)	DOP (%)	DOP (mg)	PVC (%)	PVC (mg)	Concentration range (M)	Slope ^a
3.0	6.4	48.0	102	49.0	104	8.32×10^{-3} to 1.78×10^{-5b}	47.47
						5.62×10^{-2} to 2.44×10^{-5c}	52.87
						1.40×10^{-2} to 2.37×10^{-5d}	61.30
4.0	8.6	47.5	102	48.5	104	8.91×10^{-3} to 1.00×10^{-4b}	49.83
						1.99×10^{-4} to 6.92×10^{-5c}	28.46
						1.97×10^{-3} to 6.92×10^{-5d}	45.87
5.0	10.9	47.0	102	48.0	104	1.10×10^{-2} to 1.78×10^{-5b}	38.00
						1.35×10^{-3} to 6.92×10^{-5c}	24.86
						1.97×10^{-3} to 6.92×10^{-5d}	50.71
7.0	15.5	46.0	102	47.0	104	1.10×10^{-2} to 1.78×10^{-5b}	46.00
						1.99×10^{-3} to 6.92×10^{-5c}	36.90
						1.99×10^{-3} to 6.92×10^{-5d}	49.70

^a mV/concentration decade.

^b CpRn.

^c Cp_3PT .

^d Cp_3PM .

(Germany) EDS system with detector resolution of 129 eV. Qualitative and standard-less quantitative examination was done for each sample; PUzaf package, from Rontec was used to apply Zaf-correction [25].

2.6. X-ray photoelectron spectroscopy (XPS)

X-ray photoelectron spectra were recorded on a model VG ESCALAB 200 (UK) spectrometer using Mg K α radiation (1253.6 eV) operating at 300 W (15 kV, 20 mA). The spectra acquisition and processing were carried out by means of an Eclipse V 2.1 data system (UK). Plastic membrane of the electrode was carefully cut out and introduced into the preparation chamber with the sample holder and degassed until high vacuum is achieved, then it was transferred into the analysis chamber where the pressure is reduced to 10^{-9} to 10^{-10} Torr. The analyses were carried out with the parameters: step size 0.1 eV, Dwell time 100 ms, and pass energy of 20 eV. All binding energy values were determined with respect to C1s line (284.6 eV) originating from adventitious carbon.

2.7. Scanning electron microscopy (SEM)

The morphology of the surfaces of freshly prepared and expired electrodes' membranes was studied by a JEOL scanning electron microscope model JSM-6300.

3. Result and discussion

3.1. Composition of the membrane

Four membrane compositions containing 3.0, 4.0, 5.0, and 7.0% (w/w) ion exchanger were tried (Table 1). Electrodes made by using membranes containing 4.0%, 3.0% and 3.0% of CpRn, Cp₃PT and Cp₃PM, respectively, exhibited the best responses over relatively wide ranges of CpCl concentration (Table 1). The response time was always less than 10 s. Electrodes containing the above mentioned percentages of the ion exchangers were used for further studies.

3.2. Life span of the electrodes

The performance characteristics of the electrodes were investigated as a function of soaking time. For this purpose the electrode was soaked in a solution that is 1.0×10^{-3} M in CpCl and 1.0×10^{-1} M in KCl and the calibration graphs (pCp vs. *E*, mV) were constructed after different intervals.

3.2.1. Electrodes based on CpRn ion pair

The average calibration graph slope was 49.83 mV/Cp concentration decade after 30 min conditioning time and remained constant for 24 h, over the concentration range 8.91×10^{-3} to 1.0×10^{-4} M, after which it decreased gradually. This poor performance of the electrode may be attributed to the low lipophilicity of the CpRn ion pair that negatively affects the phase equilibrium state of Cp at the immediate vicinity of the membrane surface.

3.2.2. Electrodes based on Cp₃PT ion associate

The conditioning time required for activating the membrane surface was 30 min. The average calibration graph slope was 52.87 mV/Cp concentration decade over concentration range of 5.62×10^{-2} to 2.44×10^{-5} M CpCl. The electrode kept its performance for 5 days of continuous soaking; then the calibration graph slope decreased gradually.

3.2.3. Electrodes based on Cp₃PM ion associate

The conditioning time required for activating the phase boundary exchange process at the surfaces of the membranes was 30 min with average concentration range of 1.40×10^{-2} to 2.37×10^{-5} M CpCl. The electrode proved reasonable activity throughout a period of 3 days (average calibration graph slope of 61.3 mV/Cp concentration decade). On soaking the electrode for longer than 3 days, the calibration graph slope decreased gradually.

3.3. Effect of pH

The pH of the test solution was altered by the addition of small volumes of HNO₃ and/or NaOH (0.1–1.0 M each). The results showed that the pH has a negligible effect on the potential reading within pH-ranges 2.5–8.3, 1.8–7.1 and 2.2–7.0 in case of the CpRn-, Cp₃PT-, and Cp₃PM-based electrodes, respectively. In these ranges the electrodes can be safely used for Cp determination without interference of neither hydronium nor hydroxyl ions.

3.4. Selectivity

The selectivity of the Cp-responsive electrodes has been studied by applying the separate solution [23] and matched potential methods [24]. The selectivity coefficients towards the biologically important cations, Na⁺, K⁺, Mg²⁺ and Ca²⁺, as obtained by the two methods (Table 2) reflect high selectivity of the investigated electrodes for the chlorpromazinium cation. It is noticeable

Table 2
Selectivity coefficients $K_{\text{Cp},j^{z+}}^{\text{pot}}$ of Cp-responsive electrodes

Interfering ion	Separate solution method	Matched potential method
Na ⁺	5.50×10^{-3a}	2.70×10^{-3a}
	1.29×10^{-2b}	9.53×10^{-3b}
	1.25×10^{-2c}	1.84×10^{-2c}
K ⁺	4.84×10^{-3a}	1.83×10^{-3a}
	1.43×10^{-2b}	9.58×10^{-3b}
	1.91×10^{-2c}	1.57×10^{-2c}
Mg ²⁺	2.33×10^{-3a}	3.61×10^{-3a}
	1.19×10^{-2b}	3.73×10^{-3b}
	1.02×10^{-2c}	5.86×10^{-2c}
Ca ²⁺	2.49×10^{-3a}	8.67×10^{-4a}
	1.48×10^{-2b}	3.81×10^{-3b}
	1.37×10^{-2c}	8.70×10^{-3c}

^a CpRn.

^b Cp₃PT.

^c Cp₃PM.

Table 3

Applying the Cp-responsive electrodes to determination of Cp in its pure solutions and in the pharmaceutical tablets, Neurazine, using the standard addition method

Ion exchanger	Sample	mg taken	mg found (mean) ^a	<i>s</i> ^b	<i>s_R</i> ^c (%)	Recovery (%)	<i>F</i> ^d value
CpRn	Pure solution	1.7765	1.6708	0.175	10.5	94.1	1.275
CpRn	Tablets	1.7765	1.5250	0.155	10.2	85.8	
Cp ₃ PT	Pure solution	1.7765	1.7860	0.0370	2.1	100.5	8.36
Cp ₃ PT	Tablets	1.7765	1.8260	0.107	5.9	102.7	
Cp ₃ PM	Pure solution	1.7765	1.6717	0.0358	2.1	94.1	5.03
Cp ₃ PM	Tablets	1.7765	1.6788	0.0803	4.8	94.5	

^a Four measurements.^b Standard deviation (four measurements).^c Relative standard deviation.^d $F_{\text{theo.}} = 9.28$ (degrees of freedom $\nu_1 = 3$ and $\nu_2 = 3$).

that the values obtained by the two methods differ slightly, in most cases. This may be attributed to the fact that SSM, in contrast to MPM, is based on Nikolsky equation [26,27], which assumes a Nernstian behavior of the interfering ion. However, the results as obtained by the two techniques, revealed high selectivity of the electrodes for Cp towards different cationic species.

3.5. Analytical application

The standard addition method was applied, to determine CpCl in pure solution and in the pharmaceutical preparation, Neurazine tablets, using the electrodes as sensors (Table 3). In this method small aliquots of standard solution, 0.1 M, of CpCl were added to pure or tablet sample solution, the ionic strength of the solution was kept constant at about 0.01 M with NaNO₃. The sample content of Cp was calculated from the difference in potential before and after the standard addition.

The *F*-significance test [28] was applied to compare the precision of the proposed method in case of pure solution with that in case of tablet solution, i.e. in absence and presence of matrix effect, respectively. The *F* values (s_1^2/s_2^2), where $s_1 > s_2$, obtained in all the three types of electrodes were less than the theoretical value at 95% probability level [28] (Table 3). This indicates that the matrix of the tablet's solution has negligible effect on the magnitude of the random error associating the application. Nevertheless, the three electrodes exhibited differences in the relative standard deviation and recovery values depending on the type of exchanger.

Application of the official method to the assay of Neurazine tablets [29] showed standard deviation of (± 0.765 , five determinations). Comparing this value with the corresponding values obtained by the present method (Table 3), using *F*-test, prove that there is a significant difference, in favor of the present method ($F_{\text{cal.}}$ in case of CpRn-, Cp₃PT- and Cp₃PM-based electrodes are 24.4, 36.6 and 91.4, respectively, in comparison to $F_{\text{theo.}} = 9.12$, for degrees of freedom $\nu_1 = 4$ and $\nu_2 = 3$ at 95% confidence level).

3.5.1. CpRn-based electrode

The obtained relative standard deviation and recovery values were (10.5% and 94.1%) and (10.2% and 85.8%) for measurements in pure and tablet solutions, respectively. This relatively

poor precision and accuracy of the results may be attributed to the low lipophilicity of the CpRn ion pair that weaken its interaction with the solvent mediator of the membrane and consequently weaken its adherence to the polymeric network.

3.5.2. Cp₃PT-based electrode

Relative standard deviation and recovery values of (2.1% and 100.5%) and (6.9% and 102.7%) were obtained for measurements in pure and tablet solutions, respectively. This reflects high precision and accuracy of the results.

3.5.3. Cp₃PM-based electrode

The relative standard deviation and recovery values were (2.1% and 94.1%) and (4.8% and 94.5%), for measurements in pure and tablet solutions, respectively. This indicates high precision and accuracy of the results, though less than those for Cp₃Pt-electrode.

3.6. Energy dispersive spectroscopy

Membrane's samples were obtained from two electrodes, one electrode was freshly prepared and the second was an expired electrode that has been soaked in 10⁻³ M solution of CpCl for 7 days. The spectra (X-ray energy vs. intensity counts) of the two membranes were compared. In all cases the comparison indicated leaching of the ion exchanger from the membrane to the test solution as a result of prolonged soaking. Representative

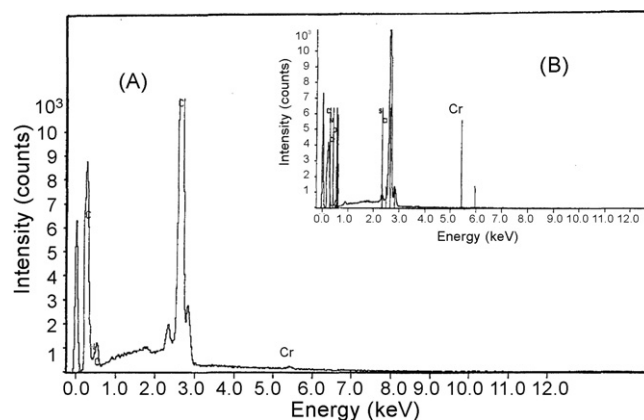


Fig. 1. Energy dispersive X-ray spectra of freshly prepared (A) and expired membranes (B) containing CpRn ion pair.

Table 4
Quantification of energy dispersive X-ray spectra of the surface layers of fresh and expired Cp-electrode based on CpRn ion pair

Element	Line	Peak area X-ray counts ^a ($\times 10^{-3}$) (fresh)	Atomic% (fresh)	Confidence interval (2 s) (fresh)	Peak area X-ray counts ^b ($\times 10^{-3}$) (expired)	Atomic% (expired)	Confidence interval (2 s) (expired)
C	K-ser	38.03	38.03	± 14.12	40.97	55.37	± 21.04
N	K-ser	14.11	14.11	± 7.28	9.64	11.18	± 8.07
O	K-ser	22.03	22.03	± 9.40	19.35	19.63	± 9.34
S	–	–	–	–	2.02	1.02	± 0.14
Cl	K-ser	25.58	25.58	± 2.56	27.78	12.72	± 1.29
Cr	K-alpha	0.24	0.24	± 0.12	0.23	0.07	± 0.04

^a Total counts 100.00×10^3 .

^b Total counts 100.00×10^3 .

Table 5
Quantification of X-ray photoelectron spectra of surface layers of fresh and expired Cp-ion-selective electrode based on Cp₃-PT ion associate

Energy level	Binding energy (eV) (fresh, expired)	SF ^a	Fresh membrane NPA ^b (counts)	Atomic%	Expired membrane NPA ^b (counts)	Atomic%
O1s	534.2, 533.7	2.93	157.55	24.793	108.47	13.168
N1s	401.9, 400.3	1.80	6.0044	0.94500	2.6825	0.32600
C1s	286.5, 286.2	1.00	393.12	61.862	635.33	77.130
Cl2p	201.8, 201.4	2.29	67.464	10.616	67.787	8.2290
W4f	36.52, 36.41	4.9	11.333	1.783	9.4412	1.1460

^a Sensitivity factor.

^b Normalized peak area.

results are shown in Fig. 1 and Table 4 for electrode containing CpRn. From the table, it is clear that the counts (peak area) due to K-emitted X-rays from N, O, Cl, and Cr cores, and consequently the corresponding atomic percentages, in case of the fresh membrane are higher than in case of the expired membrane. This may be attributed to leaching of the ion associate and of partially degraded PVC molecules to the test solution.

The decrease in the membrane content of the above mentioned elements led to an increase in the atomic percentage of carbon and sulfur.

3.7. XPS of the membrane's surface

Fresh and expired membranes' surfaces were scanned for different characteristic photoelectrons at a take-off angle of 35°. Table 5 includes representative results for quantification of the spectra for (Cp₃PT)-containing membranes (fresh and expired) (Fig. 2). The results revealed that the normalized peak areas of O1s, N1s, Cl2p and W4f photoelectron emissions and the atomic percentages of these elements decreased as a result of soaking. This confirmed the leaching of the ion associate together with some of degraded PVC into the bathing solution.

It was noticed in Fig. 2 that the W4f emission did not display the expected doublet band of W4f5/2 and W4f7/2 [30,31]; instead of this it exhibited broad band at about 36.5 eV for both the fresh (Fig. 2A) and the expired membranes (Fig. 2B). This merging of the doublet band is most plausibly due to interference from inelastic scattering of the emitted electron with plasma oscillation of the outer shell electrons (plasmon structure) and/or Auger transitions [32]. To remove this interference, Eclips 2.1

Table 6
Quantification of the peak-fitted W4f X-ray photoelectron spectral bands

Energy level	Binding energy (eV)	Sensitivity factor	Normalized peak area	Atomic%
W(VI) 4f5 (fresh)	37.62	1.00	12.603	42.94
W(VI) 4f7 (fresh)	35.87	1.00	16.745	57.06
W(VI) 4f5 (expired)	37.60	1.00	9.794	42.84
W(VI) 4f7 (expired)	35.72	1.00	13.072	57.16

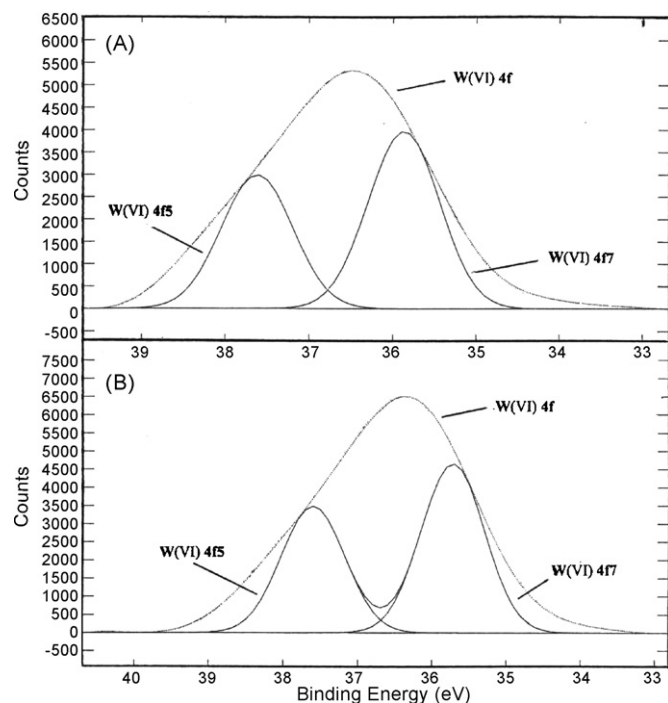


Fig. 2. XPS spectra of fresh (A) and expired membranes (B) containing Cp₃PT ion associate.

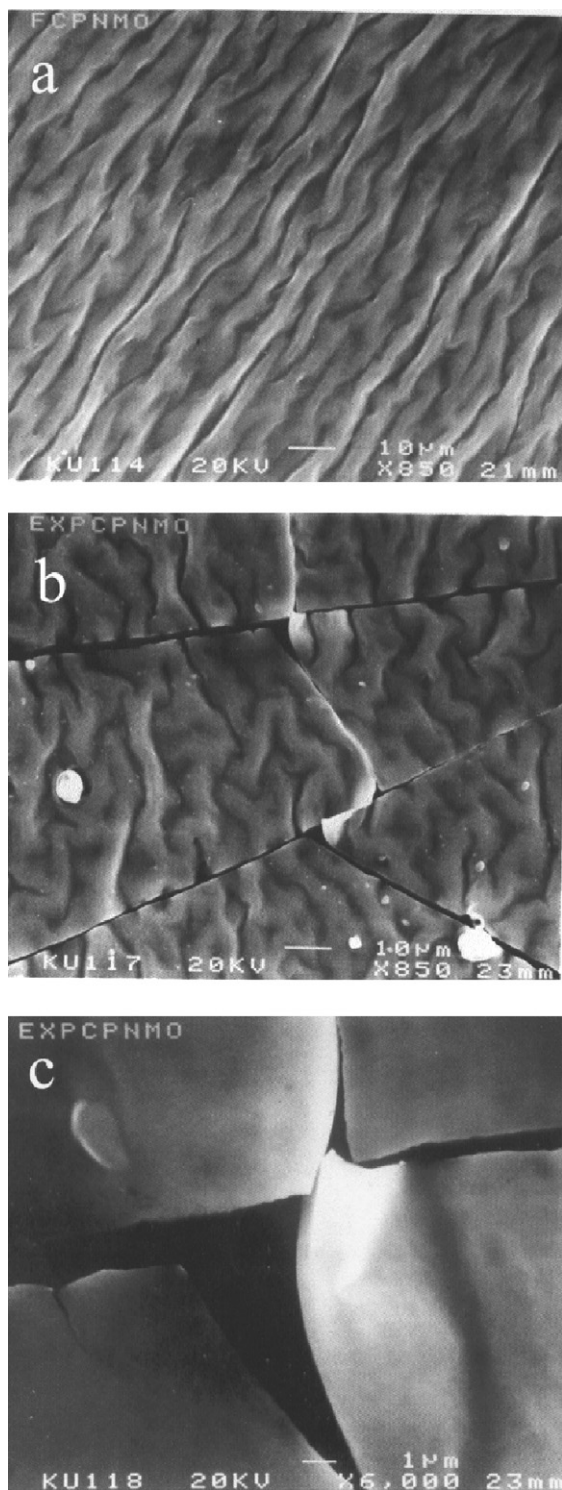


Fig. 3. High-resolution electron micrographs of a membrane surfaces containing Cp_3PM ion associate. (a) Fresh membrane (850-fold magnification), (b) expired membrane (850-fold magnification), and (c) expired membrane (6000-fold magnification).

peak-fitting program was applied to the spectral bands (Fig. 2). The results revealed the presence of $\text{W(VI)} 4f_{5/2}$ band at 37.62 and 37.60 and $\text{W(VI)} 4f_{7/2}$ band at 35.87 and 35.72 eV in case of the fresh and expired membranes, respectively. Quantification of the bands (Table 6) showed that the normalized peak area counts

due to both quantum numbers ($j = l \pm 1/2$) in case of the expired membrane are less than the corresponding area counts for the fresh membrane. This confirms the leaching of the Cp_3PT ion associate as a result of prolonged soaking of the electrode.

3.8. Effect of soaking on the morphology of the membrane's surface

The electron microscopy images of surfaces of fresh and expired electrodes were obtained by tracing the secondary electrons emitted from the membrane surface. The scattered electrons were not traced because such electrons provide information about the chemical nature of the surface rather than its physical feature. The results showed drastic changes in the morphology of the surfaces as a result of prolonged soaking of the electrodes; representative images for a membrane containing Cp_3PM ion associate are shown in Fig. 3. These morphological changes are, most plausibly, due to some sort of solvent/gel layer interaction leading ultimately to shrinking of the polymeric network and formation of cracks at the surface of the membrane [Fig. 3b and c]. The harm of these surface changes is that they generate unequal strains at the deformed areas and consequently produce asymmetry potentials [33]. These potentials interfere with the phase boundary equilibrium of Cp at the membrane surface, and negatively affect the performance of the sensor.

4. Conclusion

Ion associates of chlorpromazinium with phosphotungstate and phosphomolybdate are excellent ion exchangers for construction of chlorpromazinium ion-selective electrodes. Imaging and elemental surface analyses of fresh and expired membranes of plastic membrane electrodes proved that drastic physical changes at the electrode surface occur as a result of prolonged soaking. These changes in addition to leaching of the active ingredients lead to substantial inactivation of the sensor.

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