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Differential electrolytic potentiometry (DEP) with twin silver–silver sulphide membrane electrodes in micro titration of quaternary ammonium compounds*

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Introduction

In a previous paper [1] a new technique for preparing a solid-state membrane electrode from a mixture of silver powder and silver sulphide was described and the electrode was applied to the zero-current potentiometric assay of thiols, cationic surfactants and halides with the three different titrants, mercury(II), tetraphenylborate and silver(I), respectively. The high conducting properties of this type of pellet electrode, lacking an inner reference electrode, are exploited for titrations based on differential electrolytic potentiometric (DEP) detection of the end-points in the present work. The DEP technique affords a very exact method for the location of a titrimetric end-point [2] (being the titration curve a sharp positive-going peak) and is judged superior to zero-current potentiometry [3]. DEP has been applied to all types of ion-combination and oxidation–reduction reactions in aqueous [3–5] and non-aqueous media [6–8] employing various metal electrodes. The use of graphite-supported ion-selective electrodes for complexiметric titrations of metal ions [3] is the only reported case of DEP application with a pair of polarised membrane electrodes.

This paper reports the results of a study on the applicability of DEP to cationic surfactants microtitrations with a pair of solid-state polarised membrane electrodes (silver–silver sulphide) and tetraphenylborate as titrant. Potentiometric titrations based on ion-pair formation between cationic or anionic species and oppositely charged titrants are widely used and have been recently reviewed [9]. The work reported here is the first example of using the DEP technique for the determination of organic compounds of pharmaceutical interest as authentic samples or in dosage forms.

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Experimental

Reagents

Solutions were prepared with bidistilled water from analytical grade materials. 0.0002–0.001 M sodium tetraphenylborate (TPB, E. Merck) stabilised at pH 8–9 by adding a little 1 M sodium hydroxide and 0.33 M phosphate buffer (pH 7.0) were used. Standard solutions of quaternary ammonium compounds were prepared from samples of the highest purity available used as received. Commercial pharmaceutical preparations were obtained from local drug stores.

Apparatus

Twin silver–silver sulphide electrodes were assembled as shown in Fig. 1. The area of each semicircular pellet was 0.3 cm^2. The single electrode preparation was previously reported [1]. In the present work the sensor lifetime was improved by adding a sintered silver–silver iodide layer between the silver–silver sulphide and the silver layers to avoid their possible disjunction during the experiment and causing a loss of conductivity. The metallic silver and the silver halide were chemically prepared in a very finely divided form as previously described [10]. The twin electrodes were kept in air when not in use.

The d.c. DEP circuitry, permitting polarisation of the twin pellets with a small heavily stabilised current, was made in-house with operational amplifiers. DEP volume–potential graphs were recorded by means of a Metrohm 636-Titroprocessor. To study the behaviour of the individual electrodes, a third silver–silver sulphide electrode was used as indicator in a zero-current mode referring the potential to a mercury(I) sulphate electrode. The zero-current graph was then compared with those (S-shaped) of the anode and cathode by measuring the anode-reference and cathode-reference potentials.

Current density and supporting electrolyte concentration

These parameters were studied in order to establish the values giving the sharpest

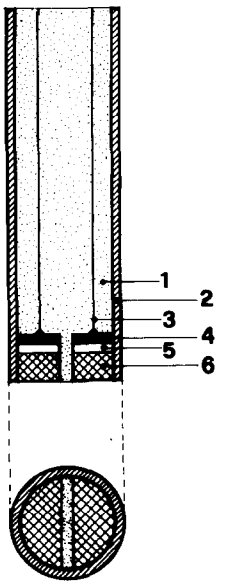

Figure 1
Twin electrodes assembly for DEP, with bottom electrode cross-section: 1, epoxy resin; 2, plastic electrode body (PVDF); 3, welded silver lead; 4, sintered silver layer; 5, sintered silver–silver iodide layer; 6, heterogeneous solid-state membrane (sintered silver–silver sulphide pellet).

peaks. A current density of 30 μA cm^{-2} and 0.033 M phosphate buffer final concentration gave suitable results and were therefore utilised throughout this work.

Microtitration procedure

Prior to each titration, the surfaces of the twin indicating electrodes were renewed by polishing them with a suede cloth impregnated with chromium(III) oxide. Titrations were done at ambient temperature with constant magnetic stirring. The titration cell was a 2 cm diameter Pyrex-glass test tube into which a suitable and accurately measured aliquot of an aqueous working solution of the drug was placed, 0.2 ml of the phosphate buffer were added and the volume made up to 2 ml with water. The automatic titrator was programmed to deliver 85% of the theoretically necessary titrant volume from a 1-ml auto-burette, then equal increments of 5–10 μl, each 10–20 s, were added until the end-point was passed.

Each ml of 0.001 M TPB is equivalent to 0.3650 mg of benzalkonium chloride, 0.4481 mg of benzethonium chloride, 0.4000 mg of benzyldodecylbis(2-hydroxyethyl)-ammonium chloride, 0.3364 mg of cetrimide, 0.3580 mg of cetylpyridinium chloride and 0.2638 mg of dequalinium chloride.

In the analysis of cationic surfactant antiseptic paint or solutions (Table 1) a volume corresponding to 0.2–0.3 mg of active ingredient was taken and the procedure thereafter was identical to that described above. Cetylpyridinium chloride lozenges were assayed by dissolving five lozenges in 30 ml of water. The slightly turbid solution was made up to volume in a 50-ml volumetric flask. To 2 ml of this solution, placed in the test tube cell, 0.2 ml of the phosphate buffer were added and the titration was automatically recorded as above.

Results and Discussion

The results obtained for some quaternary ammonium compounds in commercial preparations and in aqueous solutions are listed in Tables 1 and 2 respectively. The relative standard deviation at the 0.1 μmol level (Table 2) ranged from 0.2 to 1.9%

Table 1
DEP analyses on four separate samples of the same lot of commercial dosage forms

Preparation	Quantity taken (mg)	Average recovery, % (RSD)	Average recovery by alternative method, % (RSD)
Benzalkonium chloride contact lens soln, 0.01% (Soquette§)	0.2	100.2 (1.5)	101.0 (1.6)‡
Benzethonium chloride disinf. soln. 0.1% (Sterilix§)	0.3	96.9 (0.6)	97.4 (0.2)‡
Benzyldodecylbis(2-hydroxyethyl)-ammonium chloride disinf. soln. 0.1% (Bialcol§)	0.3	106.3 (0.7)	105.6 (0.5)†
Cetylpyridinium chloride lozenges, 1.42 mg Neo Cepacol§)	0.3	100.5 (0.8)	101.1 (1.2)*
Dequalinium chloride paint, 0.5% (Dequadin§)	0.2	96.6 (0.7)	96.3 (0.3)†

*FAB mass spectrometry [12].
†Zero-current potentiometry (mercury electrode) [11].
‡Zero-current potentiometry (Ag–Ag_2S electrode) [1].
§Registered trade mark.

Table 2
Titration (six replicates) of quaternary ammonium compounds with 0.0002–0.001 M sodium tetraphenylborate and DEP end point location

Compound	Mean quantity taken (mg)	Mean concentration (10^{-4}M)	Average recovery, % (RSD)
Benzalkonium chloride	0.040	0.55	98.7 (0.2)
	0.262	3.6	101.4 (1.2)
Benzethonium chloride	0.050	0.56	101.3 (1.6)
	0.249	2.8	99.0 (0.7)
Benzyldodecylbis(2-hydroxyethyl)-ammonium chloride	0.046	0.57	99.1 (1.9)
	0.240	3.0	99.2 (0.9)
Cetrimide	0.058	0.80	97.7 (1.0)
	0.247	3.4	99.2 (1.3)
Cetylpyridinium chloride	0.051	0.71	98.5 (1.9)
	0.250	3.5	100.0 (1.5)
Dequalinium chloride	0.100	0.95	96.4 (0.8)
	0.201	1.9	96.7 (1.4)

(n = 6). The sensitiveness of the DEP method compares favourably with classical potentiometry [1] and, by virtue of the sharpness of the end-points, shows an improvement of at least five-fold. There was good agreement (Table 1) between the recoveries for dosage forms, obtained by the present DEP method, and those previously described by means of zero-current potentiometry [1, 11] and FAB mass spectrometry [12].

Due to the small drug quantity assayed and to avoid possible loss of cationic compound activity by a surface adsorption process [13, 14], plastic and soft glass titration cells should not be used, while a type I neutral glass cell was the container of choice. Cationic surfactants react with TPB ions in stoichiometric proportions to form slightly soluble ion-pairs. Commercial dosage forms were assayed without extraction procedures, or interferences from other common ingredients; obviously the DEP method cannot differentiate between quaternary ammonium compounds present in mixtures and any ion that precipitates tetraphenylborate will cause positive errors.

A typical sharp peak of a DEP curve for the assay of cetylpyridinium chloride is presented in Fig. 2. From a study of electrode behaviour (a pair of silver wires) in DEP applied to argentimetry [15], it was found that, at the anode a small amount of titrant was coulometrically generated so that for this electrode the normal zero-current curve was slightly advanced along the volume axis, whereas for the cathode a small amount of titrant was coulometrically consumed, so retarding the titration curve back along the volume axis. The result was that the difference in potential of the two electrodes followed the first differential of the zero-current potentiometric curve.

In our case the study of the behaviour of the individual electrodes showed that the cathode led and the anode lagged with respect of the zero-current indicator electrode, giving rise to peak-shaped titration curves. The anodic reaction might be considered to be the coulometric stripping of silver ion from the silver–silver sulphide electrode with consequent small enhancement of the titrant consumption (the solubility product of silver tetraphenylborate was found to be very small [16]). At the cathode a small amount of sulphide ions could be generated with consequent slight advance of the end-point (the response of the silver–silver sulphide electrode to the sulphide or tetraphenylborate levels was Nernstian [1]).

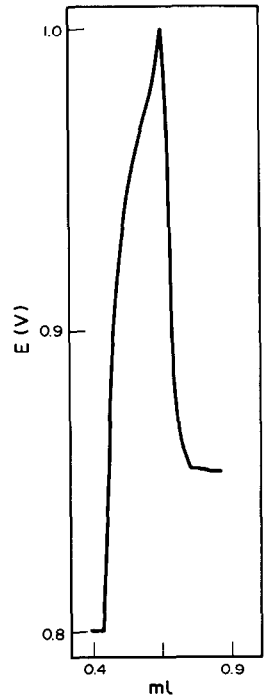

Figure 2
Direct current DEP curve with twin silver–silver sulphide electrodes. Determination of cetylpyridinium chloride (0.65 μmol) with 0.001 M sodium tetraphenylborate. Abscissa: titrant volume; ordinate: differential potential.

The twin electrodes employed in this work proved to be very rugged and their lifetime was very long: two pairs of pellets gave reproducible end-point potentials over 30 months. The proposed DEP procedure is simple, rapid (the rate at which the potentials reached equilibrium was very fast), precise, accurate and sensitive and can be regarded as an attractive alternative to the number of titrimetric, colorimetric and zero-current potentiometric techniques for quality control of quaternary ammonium compounds.

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