Table 2. Results of analysis of commercial tablets containing I and II*.

Compound	Present method** average recovery	Present method** % average recovery	B.P. method*** average recovery	B.P. method*** % average recovery
I	80·27 ±3·19	100·34 ±3·97	79·35 ±2·70	99·18 ±3·38
II	398·45 ±6·43	99·61 ±1·61	395·83 ±4·17	98·95 ±1·05

* Septrin tablets containing 80 mg of I and 400 mg of II.
** Average of ten tablets.
*** Average of five tablets.

The advantage of the present method over the official one lies in the simultaneous assay of both I and II without prior separation. This of value in the study of the dissolution rates of commercial preparations containing I and II, where samples with small volumes are taken at intervals and rapid and accurate assay is required.

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Potentiometric analysis with a silver electrode in stability control of quaternary ammonium salt disinfectant solutions during storage in plastic and glass containers

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Several workers have recently reported on the loss of quaternary ammonium compounds from their solutions due to interactions with plastic materials such as plasticized polyvinyl chloride granules, polyethylene and polypropylene which are frequently used for packaging pharmaceuticals (Neuwald & Schmitzek 1968; Quercia et al 1976; Richardson et al 1977). We have recently reported the use of reduced scale potentiometry for the analysis of several quaternary ammonium compounds employing sodium tetraphenylborate solution as titrant and a silver indicating electrode (Pinzauti & La Porta 1977). In the present paper we have extended this work to investigate the possible loss of five different cationic surfactants from 0·1–10% w/v commercially available disinfectant solutions packed in polyolefinic containers. The losses were evaluated by 6 months storage tests at 37 °C and 12 months at room temperature (15–25 °C) and compared with the same solutions in brown glass.

Direct determinations were made either automatically, using a Mettler titrator provided with the essential equilibrium titration control module DK15, or manually by means of a digital pH-meter (Metrohm, E500) and a 5 ml piston microburette calibrated to 0·001 ml (Metrohm, E457). The indicating electrode was a silver spiral 30 cm long. Before each titration the electrode was briefly brought to red heat on a bunsen lamp. It was then soaked for 3 min in a magnetically stirred 3% w/v sodium tetraphenylborate solution previously stabilized (Cooper 1957) and freshly prepared every two weeks, finally it was rinsed with distilled water. This pretreatment replaced that described in our earlier report (Pinzauti & La Porta 1977). When not in use, the electrode was stored in air. The three electrodes employed gave reproducible end point potentials over 14 months. Potentials were referred to the mercurous sulphate electrode (Metrohm, EA406). An appropriate volume of each disinfectant solution, based on the label claim and corresponding to 8·75–10 mg of surfactant, was transferred into a 50 ml beaker from a 10 ml piston burette calibrated to 0·01 ml, 2 ml of acetate buffer, pH 3·4, were added and the test solution was diluted with water to approximately 20 ml; a 0·01 M sodium tetraphenylborate solution was the titrant. Titration curves, automatically or manually recorded, showed a sharp rise in the potential at the end point (approximately 70 mV per 0·01 ml of titrant operating automatically, and 80 mV per 0·025 ml of titrant operating manually).

Six commercial brands of quaternary ammonium compounds disinfectant solutions, marketed in Italy and freshly prepared, were used (Table 1). Brands A–C were packed in linear polyethylene bottles with polypropylene screw closures, and brands D–F in polypropylene bottles with polypropylene screw closures. Containers of brands A and B were unpigmented, while those of brands C–F contained titanium dioxide. The pH values of commercial solutions ranged from 3·3 to 6·7. Some simulated disinfectant solutions were also prepared, stored in new low density polyethylene (Kartell, Milan, Italy) and glass bottles, and tested for six months at 37°C (0·1 and 15% benzalkonium chloride), or every second day for two weeks at 70°C (0·1% cetylpyridinium chloride, 0·1% benzyldodecylbis-(2-hydroxyethyl)-ammonium chloride, 0·1 and 15% benzalkonium chloride). In the latter case comparative analyses between the potentiometric and spectrophotometric procedures were carried out. The absorbance of aqueous solutions was measured at λ_{max} 269 nm, ϵ = 1408, for benzyldodecylbis-(2-hydroxyethyl)-ammonium chloride; at λ_{max} 259 nm, ϵ = 4920, for cetylpyridinium chloride; and at λ_{max} 263 nm, ϵ = 390, for

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benzalkonium chloride. Linear relations were found between extinction and concentration at λ_{max} for all solutes. The percentage of surfactant after the storage test with respect to the initial amount was calculated.

Due to the volatile ingredients in the formulations assayed, all the results were corrected for an eventual loss in weight particularly caused by permeation (Autian, 1963a). The losses in weight verified in the solutions after a six month's storage at 37 °C ranged from 0·4 to 1·2% w/w of the liquid content. Accepting the range 98·5–101·5% of the original concentration as complete quaternary ammonium salt retention, the solutions examined exhibited on the average (n = 4) no cationic surfactant loss over 6 months at 37 °C or 12 months at room temperature (15–25 °C). Furthermore, there was no significant difference between the solutions stored in the original plastic packaging and those in glass containers. On the other hand these results could mean that an equilibrium had been reached following a container-content interaction in the period between the manufacturer's preparation of the formulation and the initial assay. Also the good agreement between the declared amounts and those found (Table 1) could depend upon the manufacturer's initially supplementing the germicide. However, no apparent reduction in concentration resulted from both 0·1 and 15% w/w benzalkonium chloride aqueous simulated disinfectant solutions packaged either in low density polyethylene or glass containers, during a 6 month's at 37°C (n = 8). The negligible amount of cationic surfactant lost from the 15% solution (—0·7% ± 0·4 after 6 months in plastic bottles) was not consistent with the result of Quercia et al (1976).

Accelerated storage tests were used in preliminary experiments at 45°, 55° and 70°C, to determine the possible thermodegradation rates of simple aqueous solutions of different quaternary ammonium salts packed in low density polyethylene bottles, but negligible losses of strength were obtained, and no evident proportionality between an increase of temperature and an increase of uptake was found, while such an effect was described for the interaction of cationic agents and nylon (Autian, 1963b). To verify the reliability of the potentiometric method, the aqueous solutions were also analysed spectrophotometrically. Distilled water stored for comparison under the same conditions, did not give absorbance in the 250–300 nm region. The results were comparable with the potentiometric method. Thus we may presume a long shelf-life for the examined disinfectant solutions packed in polyolefinic containers.

Table 1. Automatic potentiometric analyses on commercial disinfectant solutions before storage tests.

Label claim (% w/v)	Found (%)† (s.d.)	Equivalence of 1 ml of 0·01 M $NaB(C_6H_5)_4$, mg	Other main ingredients††
A. Benzododecinium chloride			
0·175	112·27 (0·02)	3·40	Ethanol; nonoxynol; bergamot, lemon and thyme oils
B. Benzyldodecylbis-(2-hydroxyethyl)-ammonium chloride			
0·1	101·17 (0·58)	4·00	Ethanol; acetone; ethyl acetate
C. *Cetylpyridinium chloride*			
0·200	97·95 (0·50)	3·40	Lignocaine hydrochloride; 2-phenoxyethanol
D. Benzethonium chloride			
0·1	103·47 (0·35)	4·48	Acetone; isopropylacetate
E. Benzalkonium chloride			
0·10	103·61 (0·42)	3·60	Lemon spirit
F. Benzalkonium chloride			
10	104·42 (0·28)	3·60	

† Percent of label claim with s.d. on 8 samples of the same lot.
†† Colouring agents were present in all samples with exception of the brand F which was a simple aqueous solution.

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